Evolution of a Diving Response: Divergent Transcriptomic Adaptations in Aquatic Versus Terrestrial Mammals.

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Some mammalian lineages, such as cetaceans and pinnipeds, transitioned from land to sea and evolved unique adaptations to this new environment. One key adaptation is the diving response, a series of physiological and metabolic adjustments that maximizes oxygen use during dives. This process can lead to extremely low blood saturation, leading to tissue hypoxia followed by reoxygenation upon surfacing. Although hypoxia/reoxygenation can induce oxidative stress by generating reactive oxygen species, these marine mammals show no evidence of associated tissue damage, indicating highly efficient protective mechanisms. Here, we investigated the basis of this adaptation by analysing transcriptomes of cultured cells exposed to treatments that mimic diving. The expression profiles varied across species, ranging from a modulated response in deep divers to a nonspecific response in terrestrial species. In the treatments, only marine mammals presented differentially expressed genes with enriched GO terms related to response to oxygen levels. Meanwhile, the terrestrial species responded by modulating energy metabolism and mitochondrial function, reflecting insufficient oxygen to meet cellular demands. Finally, deep diving species showed the top upregulated genes involved in the response to oxygen levels, indicating the higher effort allocated in protective mechanisms compared to non-adapted species. Overall, we characterized the cellular strategies that enable marine mammals to respond to oxidative stress in chronic cycles of hypoxia and reoxygenation. Our experimental data revealed how their cells evolved a targeted and efficient response that prevents oxidative damage, distinguishing them from terrestrial species lacking these adaptations.

Parallel Molecular Evolution Across Replicated Anolis Lizard Adaptive Radiations

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Whether convergent phenotypes arise from similar or distinct genetic underpinnings is a central question in evolutionary biology. In this study, we sequenced the genomes of all 435 extant anole lizard (Anolis) species to dissect the molecular basis of their convergent adaptation and parallel adaptive radiations in the Greater Antilles. We find that anoles exhibit widespread positive selection on loci which regulate developmental processes. Using branch-level selection screens, we find these lizards exhibit a genome-wide excess of parallel positive selection, indicating that repeated co-option of loci has shaped these adaptive radiations. In addition, we find that selective regimes at genes underlying limb development—a hallmark of convergent evolution in anoles—co-vary with phenotypic state, with each ecomorph experiencing distinct selection pressures. Lastly, we show that a transcription factor involved in limb development has undergone remarkable parallel evolution in minute and slender twig-specialist anoles, discovering a single missense mutation at a highly conserved position arising independently in three subgenera over approximately 40 million years, mirroring the parallel evolution of twig anole craniofacial and limb morphologies. Together, these findings provide a unified view that natural selection can predictably yield convergence which scales multiple biological hierarchies, from the assembly of ecological communities, to the phenotypes of individual species, to the specific allelic variants potentially underlying such phenotypes.

Genome reorganisation and expansion shape 3D genome architecture and define a distinct regulatory landscape in coleoid cephalopods

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Our understanding of how genomic changes translate into organismal novelties is often confounded by complex and multi-layered genome architecture, and the deep evolutionary time-scales over which genomic innovations can accumulate. Coleoid cephalopods (squid, octopus and cuttlefish) offer a unique system in which to study the impact of macroevolutionary genomic processes on phenotypic complexity. A large-scale chromosomal rearrangement in the coleoid ancestor (~450 MYA) resulted in an extensively modified karyotype. Following this shared genomic shift, octopodiformes (octopuses) and decapodiformes (squid and cuttlefish) followed distinct evolutionary trajectories, shaped by lineage-specific chromosomal changes including fusions, translocations, and repetitive element expansions. These processes are hypothesised to underpin the evolution of coleoid innovations, including their large and elaborately structured nervous system, novel organs, and complex behaviours. Yet, how exactly these processes have impacted regulatory architecture remains poorly understood. To address this, we integrate Micro-C, RNA-seq, and ATAC-seq data across several coleoid species, developmental stages, and tissues, and examine syntenic genes, conserved non-coding elements, and topological interactions. We find that compartments tend to be conserved, yet exhibit divergent evolutionary paths depending on their ancestral context. Conversely, hundreds of putative regulatory chromatin loops are species-specific and often show stage- or tissue-specific activity with complex expression dynamics. Furthermore, CRISPR knock-out of an enhancer within a conserved loop highlights its function in neural development. We propose that differential levels of relaxed evolutionary constraints on the coleoid 3D genome enables species-specific patterns of chromosomal rearrangement and expansion, facilitating the emergence of novel regulatory configurations underlying complex traits in the coleoids.

Paleogenomics Reveals Arctic Range and Aquatic Specialization in the American "cheetah", Miracinonyx trumani

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The extinct “American cheetah” (Miracinonyx trumani) has long been considered a North American ecological analog of the African cheetah based on convergent cursorial morphology, yet this paradigm rests on limited data and untested assumptions about its evolutionary relationships and ecology. Here, we generate nuclear paleogenomes (22- and 38-fold coverage) from M. trumani specimens from Wyoming (ca. 23 kya) and Yukon (ca. 30 kya), plus two additional mitogenomes from Yukon, definitively placing this enigmatic felid within the evolutionary tree of cats. Phylogenomic analyses confirm M. trumani as sister to pumas (Puma concolor), not cheetahs, with divergence ~2.6 million years ago during rapid Plio-Pleistocene climate oscillations. The Yukon specimens extend the species' known range by over 20˚ latitude into Arctic environments, revealing populations that diverged 43,000 years ago yet maintained similarly low effective population sizes despite occupying vastly different habitats. Stable isotope analyses expose striking ecological differentiation, showing that the Arctic population occupied an elevated trophic position consistent with exploitation of anadromous fish, while the Wyoming population functioned as a terrestrial generalist predator. Genomic scans identified positive selection in sensory perception genes associated with auditory and visual processing and loss-of-function mutations in circadian regulators, providing mechanistic insights into behavioral flexibility. Our results suggest that, rather than specialized pursuit predators, M. trumani exhibited remarkable ecological versatility across their range, and underscore how morphological convergence can obscure the true diversity and complexity of extinct megafaunal ecosystems.

Navigating Tribal Collaboration in Environmental and Genomic Research in California

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Collecting genetic data in California carries a responsibility to the Indigenous Peoples who have stewarded these lands for millennia. Traditional Ecological Knowledge is increasingly influencing land-management strategies; for example, California's 2024 SB 310 recognizes tribal sovereignty over cultural burning and waives standard state burn-permit requirements. Yet when research occurs on lands co-managed by federal or state agencies and Tribal partners, the only legally required authorization for sample collection is often the federal or state permit. Memorandums of Understanding for genetic research are uncommon, and many Tribes in California do not yet have established processes for approving permits for genetic data collection.

At UC Berkeley, collaboration with Tribal Nations can be circuitous because different research activities, such as collecting materials, accessing or using data, setting up formal collaborations, or providing honoraria are handled by different campus offices. As a result, responsibilities are not always clearly outlined in research agreements, necessitating additional time, relationship-building, and a better understanding of what researchers can offer Tribal partners beyond requests for access.

Currently, at least ~40,000 acres in California are under documented Tribal stewardship or co-management through state agreements, with additional acreage under federal co-stewardship. This talk will outline practical, ethical, and administrative considerations for collaborating with Indigenous partners and strategies for supporting Tribal sovereignty and mutual benefit in environmental and genomic research. I will draw on experiences from the Coast Redwood Genome Project and discuss what actually motivates Tribal communities to engage with researchers, based on conversations with my Tribal collaborators.

Rooting the deep divergence of land plants

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Unravelling the deep phylogenetic structure of embryophytes is essential for understanding their evolutionary success on land. However, pronounced phylogenetic dispute remains: while recent phylogenomic studies have recurrently recovered the bryophyte monophyly in the presence of algal outgroups, absence of such outgroup representatives yields paraphyletic bryophytes. Here, we assembled a large-scale genome dataset encompassing 243 embryophyte species and 12 representative algal species to test the hypothesis of bryophyte monophyly. Across different substitution models and species tree inference methods, we recover strong support for bryophyte monophyly in the presence of algal outgroups; by varying the algal outgroup sampling, we revealed a salient outgroup effect that can significantly alter the embryophyte deep divergence relationship. We show that (1) bryophyte monophyly is consistently supported across three distinct outgroup-free rooting methods; and (2) incomplete lineage sorting, substitution saturation, heterogeneous site and branch profiles through deep time underpin prevalent phylogenomic discordance across genes and sites. Our data explain decades of difficulty in resolving the deep dichotomy of land plants. Bryophyte monophyly is not an artefact by outgroups but underpinned by genuine phylogenetic signal.

Museum specimens characterize natural repertoire of antimicrobial resistance in

wildlife and reveal human impact of antibiotic use.

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Antibiotic use has resulted in the spread of antimicrobial resistance genes (ARGs) throughout the environment. Contamination is so widespread that virtually no unaffected regions remain to serve as baselines for comparing against current ARG levels. However, fossilized host-associated oral microbiota
(dental calculus) enable characterization of environmental resistomes pre-dating anthropogenic contamination. These historical resistomes can be used to identify geographic and taxonomic reservoirs
of ARGs and better understand the response dynamics of oral microbiota to AMR selection pressures leading to ARG transfer and spread into clinically relevant microbes. In this study, we used host-associated microbiota from historical, museum-preserved specimens to characterize the ARG repertoires of 34 mammalian species spanning the 19th and 21st centuries. We found evidence of many
ARGs circulating in the environment decades before they were reported in clinically-relevant pathogens,
including ARGs conferring resistance to synthetic and last-resort antibiotics. We also determine elements of host biology and ecology that affect ARG diversity and abundance in the oral microbiome.
We found significant increases in total oral microbiome AMR load across all species after the mid-20th
century intensification of antibiotic production. This allows us to link human actions to changes in environmental resistomes, driving evolution, diversification, and spread of naturally-occurring ARGs.

tSNP: A dimensionality reduction algorithm for genetic data

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Population structure reflects non-random genetic relationships shaped by geography, culture, and history. Dimensionality reduction methods, most notably principal component analysis (PCA), are widely used to visualize genome-wide single-nucleotide polymorphism (SNP) data in two or three dimensions
while trying to preserve patterns of population structure. However, these generic methods do not explicitly exploit the ternary nature of SNP genotypes, which encode the count of reference alleles per locus (either 0, 1, or 2), and may therefore fail to capture subtle structure.
Here, we introduce tSNP, a dimensionality reduction algorithm specifically tailored to ternary genetic data. It represents SNPs as lines, and genotypes as dots, and finds a two-dimensional embedding that optimizes geometric relationships between them in a way that captures allele-sharing patterns that are
informative about population structure. We benchmark its performance against PCA, UMAP, and t-SNE on multiple simulated and empirical datasets, and examine cases where tSNP outperforms other methods in revealing large-scale patterns of population structure. These results indicate that directly exploiting the ternary representation of SNP data is a promising direction for dimensionality reduction in population genetics.

Time to rethink how to analyse ancient collagen

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Palaeoproteomics is emerging as a valuable tool for deep time sequence recovery and species identification. However, there is a fundamental mismatch between the assumptions underlying conventional proteomics workflows.

Conventional proteomic software continues to generate biologically implausible sequences of the most widely studied ancient protein, collagen. Collagen presents a perfect storm of analytical challenges that expose the limitations of software optimised for modern, intracellular proteins, from model organisms. Current proteomics tools impose limits on the number of variable modifications per peptide to manage computational complexity, while databases poorly represent both phylogenetic diversity and modification states. The expansion of search spaces to accommodate multiple modifications paradoxically worsens false discovery rate control, while standard parsimony-based protein inference strategies arbitrarily assign shared peptides, distorting quantitation in complex mixtures.

Taken together, these problems result in a well-known "dark matter" problem: large proportions of valuable spectral data are discarded as uninterpretable. Collagen just makes matters worse; its unusually high proline content suppresses fragmentation, yielding spectra with incomplete ion series. The repetitive Gly-X-Y motifs lead to ambiguous peptide identifications, in which a single sequence maps to multiple proteins. Beyond these intrinsic properties, ancient collagen accumulates extensive post-translational modifications: not only the biological hydroxylations and glycosylations critical for structural function, but also diagenetic modifications including deamidation, oxidation, and sample preparation artefacts.

This presentation will examine why current approaches systematically fail and discuss how to build the next-generation analytical strategies tailored to the unique demands of palaeoproteomics.

Extensive Reorganization of the Escherichia coli Chromosome Over 75,000 Generations of Laboratory Evolution

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Chromosomal rearrangements can shape the evolutionary trajectories of populations by opening regions of genotypic space inaccessible through point mutations alone. In the context of bacteria, rearrangements contribute to operon formation, genome streamlining, gene birth, and adaptation to new niches. Here, we use long-read sequencing of 144 genomes to characterize the occurrence and dynamics of chromosomal rearrangements that arose in 12 populations of Escherichia coli over 75,000 generations of laboratory evolution. We found that all 12 populations have multiple deletions and have evolved smaller genomes, and 9 populations have evolved one or more chromosomal inversions. In particular, several populations evolved highly rearranged chromosomes, with successive overlapping inversions causing translocations. In some instances, these rearrangements also combine with duplications to translocate new gene copies to another region of the chromosome. Analysis of the sequences flanking the rearrangements indicates that homologous recombination is the primary mechanism underlying these events, and insertion sequences play a central role by providing dispersed sites of homology. Some rearrangements were convergent between populations, suggesting they were beneficial. We also find evidence of purifying selection preserving key aspects of bacterial genome architecture: inter-replichore inversions are constrained to be symmetric around the origin–terminus axis, and intra-replichore inversions tend to be shorter, likely minimizing disruptions to gene dosage and sequence directionality. Together, our results demonstrate that extensive chromosomal rearrangements can arise and fix in bacterial populations over laboratory timescales, and highlight the selective and structural forces that shape and constrain genome evolution in bacteria.

The genomic underpinning of variation in vision across a global sample of ant workers

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The ants have evolved a stunning global diversity with more than 15,000 extant species belonging to over 330 genera. Their foraging strategies are highly diverse with some species relying entirely on chemical cues while others depend primarily on visual perception. Some species can discriminate between colors and exhibit remarkable orientation skills and visual acuity while other ants are blind. This functional diversity is correlated with substantial variation in eye morphology across the worker castes, ranging from prominent compound eyes to eyes having been reduced or entirely lost. Here, we provide new insights in the evolution of these visual systems using a comparative genomic dataset generated by the Global Ant Genomics Alliance (GAGA). Analysis of 163 ant genomes shows that the five genes encoding opsins – G-protein-coupled receptors in photoreceptor cells – are conserved across the ants, with episodic gene losses in some species potentially affecting the ability for color vision. The opsin genes also show different selection constraints and decreased expression in species with reduced eyes. We further show that reductions in eye size are related to foraging habits and diet. Finally, we identify signatures of selection on genes and pathways involved in Drosophila eye development, providing insights into the molecular mechanisms associated with the ants visual systems.

Adaptive evolution under extreme genetic erosion in invasive Spotted Lanternfly

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Loss of genetic diversity is increasingly recognised as a fundamental component of the global biodiversity crisis, yet its evolutionary consequences remain poorly understood. This uncertainty is particularly acute in biological invasions, where potential founding events, and rapid environmental change impose extreme genetic erosion, yet adaptive evolution and population expansion frequently occur in novel environments. Here, we use whole-genome sequencing to examine the interplay between urbanization, genetic erosion, demographic history, and natural selection during the invasion of the spotted lanternfly (Lycorma delicatula).

We analysed genome-wide variation from native populations in Shanghai, China, and invasive populations across the northeastern United States. Demographic reconstruction reveals three sequential bottlenecks associated with urbanisation in the native range and subsequent invasion events, resulting in pronounced reductions in genome-wide heterozygosity, elevated inbreeding, and extensive runs of homozygosity in the invasive population. Despite severe genetic erosion, we detect strong signatures of natural selection in both native and invasive ranges. In the native range, urban and rural populations show genomic divergence at loci associated with stress response, metabolism, immunity, and detoxification, indicating habitat-specific selection prior to invasion. In the invasive range, genotype–environment associations and population genomic scans identify ongoing selection linked to climatic and anthropogenic gradients. Notably, heterozygosity at loci under selection is maintained despite genome-wide diversity loss, suggesting that adaptive genetic variation can persist under extreme demographic constraint. Together, these results demonstrate that evolutionary processes remain active in populations experiencing substantial genetic erosion and highlight how environmental change may shape molecular evolution prior to and during biological invasions.

Functional verification of a genetic trigger for female sex determination in the Marsabit clawed frog (Xenopus borealis)

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A central question in biology asks why in some groups, the genetic basis of sexual differentiation evolves so quickly even though disruption of this process has severe risks such as sterility. A challenge to understanding mechanisms of this rapid evolution is a lack of functionally verified genetic triggers for sex determination. To begin to remedy this, we used fieldwork, bioinformatics, cytogenetics, and genetic engineering to isolate and functionally test a candidate sex determining gene in the Marsabit clawed frog X. borealis, which has a species-specific and newly evolved W chromosome. Whole genome re-sequencing data identified several candidate triggers for female sexual differentiation, and RNAseq data indicates that only one of these was expressed specifically in female gonads during sexual differentiation. Using genetic engineering, we knocked out this gene, which is a female-specific duplicate of wnt3.L – hereafter wnt3-W – and induced complete female-to-male sex reversal. The sex reversed individuals have male-typical external and internal morphology, mating behavior, testis histology, and mating calls, and are fertile. These results demonstrate that wnt3-W is the genetic trigger for feminization in X. borealis and bring the number of functionally verified triggers for sex determination in amphibians from one to two. WNT signaling is known to play key roles in ovarian development, but this typically involves wnt gene family members other than wnt3. The discovery of wnt3-W raises the question of whether this female-determining function involves crosstalk with the TGFβ pathway, which plays important roles in triggering and determining sex in several other species.

Population-scale genotyping from low-coverage sequencing using pangenome graphs

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Purpose: Pangenome graphs capture population-level genomic diversity, but efficient methods for genotyping structurally complex loci from short-read data remain limited. We present COSIGT, a computational pipeline for accurate genotyping at challenging loci using pangenomes, with particular advantages for low-coverage sequencing data.

Methods: COSIGT builds variation graphs from known haplotype sequences, maps sequencing reads to graph nodes to generate read coverage vectors, and compares these to reference haplotype copy number vectors using cosine similarity. The pipeline selects the diploid haplotype combination with the highest similarity score. We benchmarked COSIGT against Locityper on 48 pharmacogenes (HLA, CYP, MUC) using simulated ancient DNA at varying coverage and contamination levels as well as modern samples downsampled to 1-2x coverage, and on 326 challenging medically-relevant genes and 260 structurally variable regions.

Results: In leave-zero-out analyses (genotyping samples whose haplotypes are present in the reference panel), COSIGT outperformed Locityper across all pharmacogene datasets, with superior accuracy maintained at ultra-low coverage (61% of loci) and in ancient DNA samples (100% of loci). For challenging medically-relevant genes, COSIGT achieved performance comparable to Locityper in leave-zero-out settings and maintained robust genotyping accuracy in leave-all-out scenarios (genotyping samples with novel haplotype combinations), with 91% of calls falling in the top similarity quintile (0.8-1.0). Similar performance advantages were observed for structural variant loci, demonstrating COSIGT's versatility across variant types and coverage depths.

Conclusions: COSIGT enables population-scale genotyping of structurally complex loci from low-coverage data, making it particularly valuable for large-scale biobank studies and ancient DNA research.

The Vertebrate Genomes Project Phase I: A global reference genome resource

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The Vertebrate Genomes Project (VGP) aims to produce complete and near error-free reference genomes for all ~70,000 vertebrate species. Organized in four phases, it progressively targets all vertebrate orders, families, genera, and eventually all species. Here we present the completion of VGP Phase I, which includes a representative reference genome for over 90% of vertebrate orders, and for additional species deeper within those orders, totaling over 600 species from around the planet and 1.2 trillion base pairs of primary haplotype sequence. These genomes were assembled and annotated between 2018-2026, contributing to a period of rapid evolution in genome sequencing, assembly, and annotation methods, multiple scientific initiatives, and international partnerships. Among the highest quality available, most have become the primary references of the species in the public databases. The emerging analyses across these more complete vertebrate genomes, revealed the reconstructed common ancestor genome of all vertebrates, diverse sex chromosome evolution, genome structure complexity and 3D architecture specific to each vertebrate clade, epigenetic patterns specific to and universal to all vertebrates, and more accurate understanding of gene families evolution, such as complex immunoglobulin loci, odorant receptors, miRNAs, and cancer-associated genes. Of the species sequenced, 27% are listed as Vulnerable to Critically Endangered by the IUCN Red List of Threatened Species, enabling us to characterize species extinction risk. The VGP Phase I collection of complete to near complete genomes now allows unprecedented investigations, opening up a window into what it will be like to have a representative DNA collection of all extant life.

Fine-scale genotyping reveals assemblage-wide introgression in ants

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Introgression following hybridization is increasingly recognized as an important driver of species and genome evolution. However, its relevance for evolution depends on its frequency, which has been challenging to measure. To provide a snapshot of the amount of introgression ongoing in nature, we genotyped a whole assemblage consisting of 4126 ant colonies. 23.2% of all 82 local species showed signs of introgression, which is more than twice higher than previously thought. Both the amount of introgression (0.001% – 17.3%) and its contribution to genetic diversity (-0.16% – 29%) were variable among species. Classical prezygotic reproductive barriers (mating phenology, ecological niche, fine-scale habitat use) did not predict introgression, suggesting that the main barriers to gene flow in these ants are postzygotic.

Strong bottlenecks constrain adaptive evolution in a host–parasite metapopulation

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Two important characteristics of metapopulations are extinction–(re)colonization dynamics and gene flow between subpopulations. Colonization is often associated with population bottlenecks, which lead to low genetic diversity and may constrain the adaptive evolution of a species and its co-dispersed symbionts. We investigated the role of host population structure on host and parasite evolution in a long-term metapopulation study. We used pooled co-sequencing of hosts and parasites to characterize spatiotemporal genomic variation in more than 100 subpopulations of the planktonic crustacean Daphnia magna and its microsporidian parasite Hamiltosporidium tvaerminnensis. Compared to non-metapopulations, we found reduced (synonymous) genomic diversity, weak purifying selection, and low rates of adaptive evolution in the D. magna metapopulation. In the parasite genome, we found subpopulation-specific deleterious runs of homozygosity, which originate from loss of heterozygosity events during asexual recombination, and which are fixed in subpopulations following host-mediated parasite population bottlenecks when host and parasite co-disperse. These findings support the idea that genetic bottlenecks are a main driver of evolution in highly dynamic metapopulations. Thus, we shed light on the genomic consequences of extinction–(re)colonization dynamics to an unprecedented degree, giving a genomic perspective of the effects of colonization on genome-wide allele frequencies. Our results demonstrate that the focal metapopulation evolves differently from non-metapopulations and that ignoring the effects of metapopulation dynamics in population genomic studies can lead to strongly biased inferences.

Transposable Element Co-Option Drives Transcription Factor Neofunctionalization.

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Gene duplication and domain shuffling are major drivers of transcription factor (TF) diversification, yet the molecular innovations arising from these processes remain poorly characterized. In this study, we uncover a striking case of regulatory innovation through transposable element (TE) capture. Using comparative genomics across 100 vertebrate species, we demonstrate that the DUF3669 domain, present in a subset of KRAB zinc finger proteins (KZFPs), originated from the co-option of a fragment of the LINE-1 ORF1p protein in the common ancestor of amniotes.

By combining cryo-EM, confocal microscopy, and proximity biotinylation assays, we show that DUF3669 retains the trimerization ability of its LINE-1 ancestor and drives the formation of nuclear foci resembling ribonucleoprotein particles. Furthermore, Cut&Tag profiling reveals that acquisition of DUF3669 profoundly reshaped KZFP chromatin recruitment and genomic targeting. Finally, by probing DKZFP function during human development, we show that DUF3669 is required for cell fate decisions during gastrulation.

These findings reveal a direct path from TE capture to transcription factor neofunctionalization, demonstrating that mobile DNA contributes not only regulatory sequences but also modular protein domains that diversify transcriptional regulators. This work establishes TE co-option as a key mechanism shaping the evolution of gene regulatory networks.

Comparison of Methods for the Capture of Virus Genomes Using Formalin-Fixed Paraffin-Embedded Tissues

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Formalin-fixed paraffin-embedded (FFPE) tissues are one of the most abundant specimen types in the world. Although the fixation process damages the nucleic acids, it is possible to retrieve material for qPCR and sequencing of various etiological agents. Illumina platforms are the primary method for sequencing FFPE nucleic acids. To decrease costs and turnaround time we aim to establish and optimize methods for FFPE sequencing on Oxford Nanopore (ONT) devices. Our sample set comprises of FFPE and fresh-frozen salmon tissues infected with piscine myocardial virus. We will test a validated probe-based capture approach using Illumina and ONT sequencing alongside a multiplex PCR combined with ONT sequencing, to determine the most reliable method for sequencing FFPE-derived RNA. Successful RNA extractions show variability in RNA yield, short fragments, and minimal protein/salt/organic contamination. Preliminary data suggests reverse transcription is a limiting step, likely due to RNA cross-linking causing polymerase stalling and ejection. Varying the amount of input RNA and increasing 2nd strand synthesis incubation time will be explored. We hypothesize that the probe-based enrichment will provide more even coverage, but ONT will require deeper sequencing to overcome errors introduced by the number of amplification cycles required to generate sufficient library. Overall, reliable ONT FFPE RNA sequencing methods will make accessing genetic data stored in clinical and museum collections easier. Obtaining these old genomes will increase our understanding of how RNA viruses are evolving over longer time scales, such as what genomic changes underlie host-adaptation and host-shifts.

From Core to Periphery: Mapping Evolutionary Potential Across Species Ranges

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Peripheral populations are often thought to exhibit reduced genetic diversity and increased genetic differentiation due to smaller effective population sizes and greater isolation, yet this widely accepted idea—central to the center-periphery hypothesis—has rarely been tested using whole-genome data. Understanding how genomic diversity, inbreeding, and mutational load are distributed across species' ranges is critical for evaluating the evolutionary potential of populations under environmental change. Here, we integrate whole-genome sequencing data from 88 avian species with geographic range data to investigate how spatial position within a range affects key genomic metrics. By combining estimates of heterozygosity, inbreeding, and genomic load with spatial measures of peripherality, we aim to disentangle the effects of demography, drift, and selection across biogeographic gradients. This work provides a foundation for understanding how evolutionary processes shape genetic variation within species.

Pervasive inter-chromosomal recombination shapes human subtelomeric architecture

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Pseudoautosomal regions (PARs) on sex chromosomes are canonical examples of pseudo-homologous regions (PHRs)—segments sharing sequence similarity between non-homologous chromosomes that enable recombination and rearrangement. While additional PHRs have been characterized on acrocentric chromosomes, comprehensive population-level assessment of inter-chromosomal homologies has been precluded by incomplete assemblies and the limitations of reference-based approaches. Here, analyzing near-complete assemblies of 466 human genomes with implicit pangenome graph methods, we show that the PAR architecture is not unique to sex chromosomes but represents a general organizational principle of human chromosome ends. We identify extensive subtelomeric PHRs across essentially all chromosome arms except acrocentric short arms, with each chromosome end sharing sequences with multiple non-homologous chromosomes. Spanning hundreds of kilobases per chromosome end, these PHRs display chromosome-specific architectures with variable sequence identities that reflect different evolutionary timescales and form complex many-to-many homology networks across the population. The universality of subtelomeric PHRs establishes inter-chromosomal homology as a fundamental architectural feature of human chromosomes and provides a framework for understanding structural variation, chromosomal rearrangements, and evolutionary dynamics at chromosome ends.

Understanding the rules of regulation: Rewiring gene networks with synthetic regulators from random sequence

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Gene regulatory networks are central to organismal adaptation, yet how novel regulatory interactions arise and integrate into existing genetic networks are not fully understood. To address this gap, we developed a synthetic biology framework in Escherichia coli to study the de novo emergence and evolution of novel regulatory interactions from random or nonfunctional sequence space. Using diverse expression libraries of randomly generated DNA sequences and high-throughput selection screens, we investigated how unstructured genetic diversity can be co-opted into functional regulatory elements in vivo, isolating de novo synthetic regulators that rewire genetic networks to restore E. coli growth under non-permissive conditions such as nutrient limitation and antibiotic stress. These synthetic regulators include small proteins and noncoding RNAs that act through RNA–protein and protein–protein interactions to upregulate alternative metabolic pathways, modulate signal transduction cascades, and alter cellular interactions with the environment. Detailed characterization of these selected regulators helps define the determinants necessary for robust, context-dependent regulatory interactions and informs the design of targeted synthetic genetic regulators. By integrating these synthetic library screens with experimental evolution approaches, we can now track in vivo evolutionary trajectories from “gene birth” to better understand the fundamental constraints, sources of robustness, and pathways to innovation in genetic networks. Together, this work establishes random sequence library screens as a powerful tool for dissecting the molecular basis of gene regulatory network evolution and for guiding the rational design of novel synthetic regulators for basic research, biotechnology, and drug development.

Extensive sex chromosome rearrangements in cichlid fish

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Discoveries of sex chromosomes across the tree of life have seen a tremendous uprise with the advance of sequencing data, yet our knowledge on mechanisms of sex chromosome emergence and consequences of sex chromosome turnover is limited.
The cichlid fish radiation of East African Lake Tanganyika offers an unmatched system to study sex chromosome evolution based on a solid understanding of species relationships comprising an entire radiation and comprehensive genome sequencing data. We previously detected an unprecedented high rate of sex chromosome turnover with non-random sex chromosome recruitment. We now show that intraspecies variability also exists in sex chromosome presence. Further, within a particular lineage of the radiation, one chromosome has evolved three times as sex chromosome lending support to the limited options theory of sex chromosome emergence. By reconstructing haplotype resolved genome assemblies, we find that novel sex chromosomes are often formed through chromosomal fusion. However, we also show that fusions and other chromosomal rearrangements are not limited to sex chromosomes suggesting that large-scale genomic changes are coupled not only to sex determination but ultimately might be linked to speciation in Lake Tanganyika cichlids. Sex chromosome phased assemblies reveal that differently sized inversions are the concurrent driver for recombination arrest. Sequence content in inversions differs in transposable element content compared to surrounding genome sequence potentially impacting gene regulation. By combining sequencing data with cytogenetics we show further support for massive chromosomal rearrangements, demonstrate the formation of neo-sex chromosomes and a rare case of heteromorphic sex chromosomes in cichlids.

Interplay of gene conversion and nucleotide skews is driving the evolution of macrolide antibiotics

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Like many other antibiotics used in the clinic, macrolides are natural products secreted by members of the bacterial genus Streptomyces. They are biosynthesized by modular polyketide synthases, massive and complex enzymatic machines encoded in biosynthetic gene clusters.
Gene conversion is a key evolutionary mechanism to generate the large chemical diversity of naturally occurring macrolide antibiotics. It is a kind of non-reciprocal recombination event that "copy-pastes" stretches of DNA from one homologous region to another. Gene conversion homogenizes sequences within an individual genome but increases sequence diversity in a population. Using a set of synthetic constructs, we demonstrate that gene conversion happens at remarkably high frequencies in Streptomyces. Surprisingly, DNA regions that have undergone gene conversion have a highly biased nucleotide composition, prompting us to name these sequences GRINS - genetic repeats of intense nucleotide skews.
Using experimental evolution of genetically modified strains coupled with long-read sequencing and population dynamics modeling, we have captured the molecular processes responsible for the diversification of macrolide antibiotics. Gene conversion can help create combinatorial libraries of polyketide synthases with modified enzymatic functions, while nucleotide skews change the DNA sequence and amino acid composition of these synthases.
More generally, our work demonstrates a new mechanism for accelerating molecular innovation and sheds light on the co-evolution of antibiotic biosynthesis and resistance.

Paleogenomics and habitat modeling reveal temperate Eurasian origins of Late Quaternary woolly rhinoceroses

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The woolly rhinoceros was a prominent Ice Age megafaunal species, with limited knowledge regarding its origin of genetic diversity and responses to past glacial cycles. We sequenced 29 mitochondrial and 14 nuclear genomes from Pleistocene specimens sampled from across Eurasia, and modeled the species' spatiotemporal habitats over the past 500,000 years. Unlike woolly mammoths that originate in northern Siberia, our results suggest that the woolly rhinoceros' genetic diversity evolved in temperate Eurasia around 460-420 thousand years ago during a major glacial-interglacial transition. We find that an approximately 170-thousand-year-old East Asian individual occupies a basal position relative to all later populations in the nuclear genome phylogeny, suggesting that this individual may represent one of the major Middle Pleistocene ancestral lineages of Late Pleistocene woolly rhinoceroses. Our results also suggest that the Altai region served as a major refugium and dispersal hub amid climatic changes. These findings highlight the crucial role of mid-latitude Eurasia in shaping the evolutionary history of the woolly rhinoceros and the importance of temperate regions in the diversification of cold-adapted megafauna.

Loci under balancing selection can change the recombination landscape around them

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Loci under strong balancing selection, such as sex-determining, mating-type, and self-incompatibility loci, are frequently flanked by regions of suppressed recombination. The reasons why recombination suppression evolves around these loci, thus changing the recombination landscape, remain poorly understood. Here, we propose that one reason may be that loci under balancing selection facilitate the emergence of pseudo-overdominance, a phenomenon under which linked recessive deleterious mutations in repulsion mimic overdominance. Pseudo-overdominance arises when linkage disequilibrium gradually builds up between recessive deleterious mutations, often due to strong genetic linkage and genetic drift. Once complementary haplotypes form, homozygous and recombinant offspring are selected against because they carry homozygous recessive deleterious mutations. The observed recombination patterns in genomes then mimic recombination suppression. Using individual-based simulations, we demonstrate here that the presence of loci under balancing selection eases the establishment of pseudo-overdominance, by facilitating the maintenance of recessive deleterious mutations and linkage disequilibrium in their flanking regions. We further show that, under some conditions, such resulting pseudo-overdominant zones can ultimately lead to selection for genuine crossing-over suppression around permanently heterozygous loci, for example by selection for inversions, preventing the creation of unfit homozygous recombinant offspring. These results suggest new avenues for understanding the evolution of recombination landscapes around loci under balancing selection, in sex chromosomes and supergenes.

The origins and molecular evolution of sperm

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Sperm is a nearly universal cell type among animals, yet its evolutionary origins remain unclear. Using comparative proteomics and phylogenomics across 32 species, we reconstruct sperm evolution across more than 700 million years of animal history to define the Last Universal Common Sperm (LUCS), a conserved core of 301 gene families enriched in motility and energy metabolism. By tracing ancestral duplication events, we show that the LUCS toolkit was mostly assembled through concerted gene family expansions at least ~400 million years before the origin of Metazoa, revealing sperm as a reconfigured legacy from our unicellular past rather than an invention of multicellularity. Sperm shows a within-cell evolutionary gradient, both spatial and temporal, where ancient proteins dominate the tail, while younger innovations concentrate in the head. The oldest sperm components are disproportionately associated with human infertility, establishing an empirical bridge between evolutionary depth and clinical relevance. Together, our findings show how evolutionary history is inscribed within a single cell and can guide clinical insights.

Epigenetics in Archaea: Chromosome conformation underlies heritable resistance to oxidative stress in Sulfolobus islandicus

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Given the increasing appreciation for the complexity of prokaryotic chromatin regulation and recent work demonstrating that eukaryotes evolved from an archaeal ancestor, it is tempting to ask whether some of the epigenetic processes found in eukaryotes originated from archaea, and whether epigenetic phenomena are present in modern archaea? Here, we describe a chromatin conformation-based epigenetic mechanism conferring resistance to oxidative stress in the archaeon Sulfolobus islandicus. In the resistant strain, a heritable gene expression profile is associated with persistent local chromatin loop structures that are stably maintained for over a hundred generations in the absence of selection. Interestingly, the persistence of this elevated transcription-associated conformation correlates with enhanced occupancy an atypical Structural Maintenance of Chromosomes (SMC)-superfamily protein, coalescin. While the loops are not detected during response to acute oxidative stress in the parent strain, transient coalescin enrichment alongside elevated transcription is observed. Thus, we describe a scenario where coalescin, which is primarily associated with compacting more lowly transcribed regions of the genome, stimulates gene expression. Our results suggest that coalescin occupancy, itself, is the molecular basis underlying this phenomenon.

A fast-evolving C-terminus underlies species-specific function of an orphan gene required for sperm nuclear shaping

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Orphan genes are lineage-restricted and encode proteins without detectable homology. In Drosophila melanogaster, the orphan gene saturn is required for male fertility and encodes an adaptively evolving protein, but its cellular function and the consequences of its rapid evolution have remained mysterious. We used a CRISPR-generated null allele, tagged rescue constructs and immunofluorescence to demonstrate that saturn is required for spermatid nuclear shape changes. Null males are near-sterile, show defective spermatid nuclear shape, and fail to complete sperm individualization, while immunofluorescence in wild-type males shows that Saturn protein localizes to the condensing nuclear membranes. To understand the functional consequences of Saturn's adaptive evolution, we performed gene swap experiments in which we assayed the ability of saturn orthologs from other Drosophila species to restore fertility in D. melanogaster males lacking endogenous saturn. The degree of fertility rescue declined with evolutionary distance, culminating in the complete inability of the D. ananassae ortholog to restore fertility, despite its robust expression and proper localization to spermatid nuclei. By constructing chimeric proteins containing portions of the melanogaster and ananassae orthologs, we mapped this cross-species incompatibility to Saturn's rapidly evolving C terminus, suggesting that this region may coevolve with other spermatogenesis components. Finally, using an antibody raised to the ananassae Saturn ortholog, we found that this protein's subcellular localization is conserved in its native species, suggesting that Saturn evolved this localization pattern ancestrally. These results reveal an essential role for an orphan gene in spermiogenesis and demonstrate concrete functional consequences to its rapid, adaptive evolution.

An in-vivo approach to population 3D genomics: age and sex affect 3D genome in a healthy controlled cohort of chickens.

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Linear DNA sequence variation has been extensively studied at the population level, yet three-dimensional (3D) folding of the genome and its diversity across individuals in healthy populations remains largely unexplored. Likewise, while epigenomic features are known to be fluid and dynamic in response to developmental and environmental cues, a systematic population-level assessment of 3D genome variation is still lacking.

Here, we investigate population-level variation in 3D genome organization using a well-controlled cohort of Ross chickens (Gallus gallus). We generated Hi-C data from liver samples of 16 individuals (8 males, 8 females), with balanced sampling at two life stages (day 7, day 35). For each individual, we also obtained RNA and whole-genome DNA sequencing data. We quantified 3D genome differences across multiple levels, including interchromosomal contacts, chromatin compartments, looping, and TADs. Hi-C data showed stark clustering by age and sex explaining a large proportion of variance. Interchromosomal contacts, as well as long-range compartmentalization and decay profiles also followed sex-specific trajectories between days 7 and 35. Moreover, integrating Hi-C with RNA-seq data highlighted several sex-specific differentially expressed genes involved in liver metabolism and chromatin structure remodeling, potentially explaining the observed sex-specific 3D structural differences.
Our results highlight how often-overlooked variables such as age and sex may condition 3D genome organization in a tissue-specific manner, revealed by unexpected sex-specific plasticity even over short developmental timescales. This study provides a framework for future analyses of population-level 3D genomic variation and underscores the risks of interpreting 3D structural features without accounting for common population variation.

Ancient Epigenetic Insights into Woolly Mammoth Adaptations

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Investigating epigenetic changes in ancient species provides insights into the molecular basis of evolutionary adaptations. Here, we compared DNA methylation patterns between woolly mammoths (Mammuthus primigenius) and modern Asian elephants (Elephas maximus), examining both skin and tooth. We reconstructed methylation maps of two woolly mammoths and compared them to methylation maps of two Asian elephants. Differential methylation analysis revealed significant differences between mammoths and elephants, identifying thousands of differentially methylated regions, affecting the methylation of over 1,600 genes in skin and over 2,500 genes in tooth. They include genes associated with hair development and sebaceous gland function in skin, and with skeletal system development in tooth. Additionally, substantial differential methylation was observed in genes associated with circadian rhythm regulation in both skin and tooth. These findings suggest that regulatory changes played a role in adaptations to cold environments and polar habitats in woolly mammoths and highlight the importance of paleoepigenetics in revealing evolutionary processes.

Pedigree-based analysis reveals rapid de novo insertion and purging of retroviral integrations in the koala genome

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Retroviruses that colonize the germline become heritable genetic elements and can drive rapid genomic change. The koala (Phascolarctos cinereus) is experiencing recent germline colonization events: KoRV first invaded the koala genome ~312,191 years ago, phaCin-β ~1.6 million years ago, whereas phaCin-β-like colonizations are much older (~6.9 Mya). We analyzed integration-site segregation and diversity of endogenous KoRV, phaCin-β and phaCin-β-like elements in 111 pedigreed koalas from the San Diego Zoo Wildlife Alliance and seven European zoos. Using multigenerational pedigrees and individual health records, we document rapid evolutionary dynamics—ongoing generation of novel heritable insertions, differential persistence among loci, and recurrent loss of integrations, notably from proto-oncogenes. Of 714 detected integrations, many do not persist in the extant population, and among 55 parent–offspring triads we found 21 integrations present in offspring but absent in both parents, consistent with recent germline insertion or early somatic-to-germline transmission. We also link specific integrations to phenotypes (leukemia, fertility, longevity) to estimate genetic risk scores and develop a longevity breeding index to reduce neoplasia risk in captive populations. Together, these results highlight the recent and ongoing impact of retroviral colonization on koala genome evolution and offer actionable metrics for conservation breeding.

Ancient DNA from Shimao city records kinship practices in Neolithic China

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The discovery of Shimao city (around 2300–1800 BCE), a premier state-level Neolithic fortified settlement in Shaanxi, China, played an important role in helping us understand the emergence of socially stratified urban societies. However, key questions remain regarding how ancestry and kinship shaped the hierarchy of this class-based society characterized by human sacrifice. The origin of the founding populations of Shimao and other Loess Plateau settlements, and their interactions within the broader ancestral landscape, have yet to be determined. Here we present, by sequencing 144 ancient genomes from Shimao city and its satellites, pedigrees among tomb owners spanning up to four generations. These findings reveal a predominantly patrilineal descent structure across Shimao communities, and possibly sex-specific sacrificial rituals. We also characterize the population history, revealing that Shimao culture-related populations originated mostly from a Yangshao culture- related population present at least 1,000 years earlier, and the lasting inflow of Yumin-related populations from Inner Mongolia did not interrupt regional genetic continuity. Broader genetic influence from southern mainland ancestry over Shimao culture-related populations supports evidence of rice farming expanding further north than previously expected. Together, these results uncover fine details of the regional peopling and social structure of early state establishment.

ANCIENT PLANT DNA DOCUMENTS CEREMONIAL CONTINUITY AT PICURIS PUEBLO

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Plants play a key role in ceremonial practices of Indigenous peoples of the Americas. In the U.S. Southwest, these relationships have persisted despite four centuries of colonial disruption, yet direct evidence for the long-term continuity of ceremonial plant use is rare. Scientific approaches, when in partnership with Indigenous communities, provide one pathway to document this knowledge while respecting its living ritual significance. In this study initiated by Picuris Pueblo, a federally-recognized Native American tribe from New Mexico, we generated ancient environmental DNA data from soil taken from the floor of an underground ceremonial chamber – known in Picuris as thètáne and in English by the Hopi word kiva – used between 1611 and 2016 CE. Across sixteen stratigraphic layers, we identify a stable assemblage of domesticated plants central to Pueblo subsistence and ceremony, such as maize, beans, pumpkin, sunflower, goosefoot and amaranths. We also detect plants with primarily ceremonial roles, such as coyote tobacco and hallucinogenic sacred datura, as well as taxa associated with construction and maintenance of the kiva, such as reed and oak. Strikingly, we find no evidence of European-introduced crops, such as wheat or barley, despite their early historical adoption at Picuris, suggesting a deliberate exclusion from ceremonial contexts. Genome-scale data from maize and its edible fungal pathogen (corn smut) demonstrate 2,000 years of genetic continuity between archaeological and historical Picuris lineages. Together, these results reveal enduring Indigenous plant use and highlight the power of collaborative ancient DNA research.

Self-organizing map as a new AI algorithm for motif characterization

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A self-organizing map (SOM) is an artificial neural network algorithm that can learn from the training data, which conventionally consists of numerical vectors, and perform non-linear clustering, highlighting the relationship in a 1-D, 2-D, or 3-D grid of neurons. It has conventionally been widely used in transcriptomics to identify co-expressed genes as candidates for co-regulated genes. In such applications, SOM is just a more advanced equivalent of principal component analysis, with the advantage of non-linear, topology-preserving dimensionality reduction. However, SOM can also be used to characterize sequence motifs, although it has never been used in this way. Each neuron (node) can be represented by a position weight matrix (PWM). Input strings can be assigned to the winning neuron by PWM scores and modify the state of the winning neuron and its neighboring neurons. I will illustrate the conceptual framework of this novel application and apply SOM to the characterization of 5' and 3' splice sites of yeast introns. This facilitates the understanding of how mutation and spliceosome-imposed selection shape the variation of these sequence motifs.

A new genomic foundation model and a sequence-only gene prediction model for plant evolutionary biology

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Functional interpretation remains a fundamental challenge in plant biology and genomic foundation models are a promising technology for overcoming this. In this talk, I will present PlantCAD2, a long-context DNA foundation model pre-trained on 65 angiosperm genomes. PlantCAD2 efficiently captures evolutionary conservation and regulatory architecture with 676 million parameters, outperforming substantially larger models in zero-shot tasks and achieving state-of-the-art performance in predicting chromatin accessibility and gene expression across diverse species. Along with the model, we developed a new suite of cross-species benchmarks for evaluating genomic foundation models in plant evolutionary biology and agricultural applications. Building on PlantCAD2, we developed GeneCAD, a new gene prediction approach that predicts complete gene models directly from DNA without requiring species-matched transcriptomes or proteomes, improving transcript-level accuracy by 8–10% on average over current methods across phylogenetically diverse angiosperms, including polyploids. I will then illustrate the power of this method by introducing a phylogenetic comparative study of genome content and structure across angiosperms. Beyond these applications, I will close by discussing the ways in which genomic foundation models mirror traditional phylogenetic comparative methods. I will show how this connection can improve foundation model training efficiency and provide new insights into how population genetic processes shape interspecific divergence.

Assessing Growth–Survival Trade-offs in Fluctuating Environments

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Microbes are evolutionarily robust organisms capable of rapid adaptation to complex stress, enabling them to colonize harsh environments. In nature, microbes are regularly challenged by starvation, a particularly complex stress because resource limitation often co-occurs with changes in pH, osmolarity, and toxin accumulation created by metabolic waste. Often overlooked are the additional complications introduced by eventual resource replenishment, as successful microbes must withstand rapid environmental shifts before swiftly capitalizing on renewed resources to avoid invasion by competing species.

Using longitudinal population-genomic analysis of Escherichia coli populations evolved under extreme feast–famine conditions, we found that adaptation is characterized by narrow evolutionary trajectories with high mutational parallelism and reproducible mutational order. Genetic reconstructions reveal that early-arising mutations impose trade-offs for biofilm formation and motility but trade-ups for growth and survival, as these mutations confer positively correlated advantages during both short-term growth and long-term starvation.

To expand these investigations and directly quantify how fitness effects vary across distinct periods of the growth cycle, we developed a Bayesian multilevel framework for longitudinal randomly barcoded transposon sequencing (RB-TnSeq). By applying this framework to a 10-day feast–famine starvation regime in Escherichia coli, we can generate a one-dimensional Fisher's geometric "seascape" model. Ultimately, resulting in a compact, genome-wide description of growth–survival trade-offs, linking short-term competitive fitness effects to long-term adaptive outcomes.

The evolution of exceptionally low mutation rates in plant mitochondrial and plastid genomes

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Unlike humans and many other eukaryotes in which mitochondrial mutation rates are very high, plants maintain exceptionally low rates of nucleotide substitutions in their organelle genomes. However, the mechanisms by which they maintain these low rates have remained unclear. I will present data from Arabidopsis mutation accumulation lines, high-fidelity sequencing of low-frequency variants in vegetative tissues, ddPCR analysis of heteroplasmy dynamics, and protein biochemistry studies that collectively identity novel mechanisms associated with the plant-specific MSH1 gene as being key to the low mutation rates in these genomes. This gene is a member of the MutS family and was horizontally acquired by the ancestor of green algae and land plants -- possibly from a nucleocytovirus. These findings highlight how horizontal transfer of DNA repair machinery can lead to radical variation in mutation rates across the tree of life.

Recovery of an 18th Century Rhinovirus Genome through Ancient RNA Isolation of Human Lungs

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While ancient DNA (aDNA) studies have transformed our understanding of past pathogens, the study of viruses with RNA genomes is currently restricted to RNA recovered from extremely well-preserved tissue specimens in permafrost or those that are chemically stabilized in formalin. To advance ancient RNA (aRNA) research and our understanding of RNA viral evolution, we optimized aRNA isolation techniques on non formalin-fixed human lung tissues with documented history of respiratory disease from medical museums in the United Kingdom dating back to the Industrial Revolution (c. 1783 to 1916). We tailored well established aDNA protocols to effectively isolate both aDNA and aRNA from a single sample and followed library preparation protocols that capture small nucleic acid species. These techniques have successfully uncovered a near-complete genome of a historical Human Rhinovirus A (HRV A), a +ssRNA virus of the Picornaviridae family, from a lung specimen dating to 1783 C.E. Phylogenetic analyses indicate that this historical HRV genome is an extinct lineage related to contemporary genotypes, and missense mutations throughout the polyprotein highlight regions potentially involved in the long-term functional evolution of viral proteins. Together, this HRV A genome is the oldest known human RNA virus genome recovered to date, expanding the boundaries of our ability to characterize aRNA viruses from human remains and highlights the potential to understand the evolutionary dynamics between RNA viruses and host antiviral defenses through time.

Evidence supporting a viral origin of the mitosing nucleus

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The Viral Eukaryogenesis (VE) model posits that the eukaryotic nucleus, like the mitochondrion, is endosymbiotically derived and did not originate in an archaeon via an autogenous evolutionary process. In the VE model, the First Eukaryotic Common Ancestor (FECA) was an emergently complex virocell formed when a virus built a phage nucleus in the cytoplasm of an Asgard archaeon and enslaved the ancestor of the mitochondrion. Because the model predicts a Nucleocytoviricota viral genome was ancestral to the nuclear genome, it makes different phylogenetic predictions to models deriving the eukaryotic genome from a prokaryotic archaeal genome. Supporting the VE model, a suite of genes integral to eukaryotic nuclear function share a most recent common ancestor with Nucleocytoviricota genes rather than Asgard archaeal genes. When some of these phylogenetic relationships have been observed previously, they have been explained by proposing that viruses acquired these genes from ‘proto-eukaryotes’ that were incrementally evolving across the prokaryotic/eukaryotic divide. This explanation is currently both untestable and unfalsifiable since no hypothetical ‘proto-eukaryotes’ have ever been observed. It will remain untestable if intermediate ‘proto-eukaryotes' never existed as predicted by the VE model or have all become extinct as commonly proposed. By contrast, the parsimonious argument made here is that these essential nuclear genes show a phylogenetic affinity with modern giant viruses because eukaryotic nuclear genomes and nucleocytoviricota genomes are vertically derived from a common ancestral viral genome. The VE model has significant explanatory power but controversially challenges fundamental biological paradigms.

A theoretical perspective on the two-speed genome model

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Whether self-replicating elements are associated with adaptive processes in their host genome has long been debated. In fungal pathogen genomics, the hypothesis is known as the "two-speed genome", as several species exhibit a genome compartmentalization in which virulence-related protein-encoding genes are associated with an increased density of transposable elements (TEs). The excess of TEs around genes that are typically under strong selection is generally justified by a TE-induced elevated mutation rate, which may foster rapid adaptation. However, another argument is that TE-accumulations result from a locally reduced population size and are, therefore, a consequence rather than a driver of recurrent positive selection.
To disentangle these hypotheses, we study a two-locus model with a distance modifier and assess the impact of the selection regime on the modifier's evolution by changing the distribution of fitness effects at the two loci. In the basic model, the modifier only affects the genetic distance. We then extend the model to allow the modifier to jointly influence the mutation rate at the flanking loci and the recombination rate between them.
Our results demonstrate that a simple model in which TEs have no impact on flanking loci is sufficient to explain their differential accumulation around loci undergoing recurrent positive selection. Adding the effect of TEs on the recombination rate, however, generates complex feedback loops in their spreading probability that depend on the population size and the average recombination probability. We posit that these complex interactions with life-history traits explain the broad diversity of observed genome architectures.

Ancient DNA Reveals Millennia of Morphological Stability Despite Climate-Induced Gene Flow in European Crows

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Using ancient DNA, we reconstruct 20,000 years of phenotypic and genomic change across the hybrid zone between all-black carrion and grey-coated hooded crows. Genome-wide data from 51 ancient samples, combined with 588 modern individuals, reveal that populations were genetically isolated during the Last Glacial Maximum. Following postglacial expansion from southern refugia during the early Holocene, bidirectional gene flow gradually intensified. Reconstruction of ancient plumage phenotypes provides direct evidence for stability of the hybrid zone and for colour loci to act as persistent barriers to genome-wide homogenisation. This study illustrates the utility of aDNA in speciation genomic research.

The genomic basis and evolution of maternal genetic effects on early-life immunity in Soay sheep

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Maternal effects, where a mother's genetics and environment influence her offspring's phenotype beyond the direct effects of inherited alleles, are a key source of heritable variation and can shape evolutionary potential in natural populations. One important example is the transfer of antibodies from mothers to offspring, providing crucial early-life immune protection but at a physiological cost that may constrain immune evolution. Despite their importance, the genetic basis and evolutionary consequences of maternal effects in generating immune variation remain poorly understood. We investigate the genomic basis and evolutionary consequences of maternal genetic effects on early-life immunity in wild Soay sheep (Ovis aries), naturally infected with the gastrointestinal parasite Teladorsagia circumcincta. Anti-parasite immunoglobulin A (IgA) plays a central role in defence against this parasite and exhibits high heritability and genetic variation in adults ($h^2 = 0.57$, $I_A = 0.38$). Using >3,500 IgA measures from newborn lambs, we show that maternal genetic effects explain a significant proportion of phenotypic variation in neonatal IgA ($Mg^2 = 0.31$), while the lambs' own genetic contribution is effectively zero ($h^2 = 0.007$). Genome-wide association analyses reveal that variation in lamb IgA is partly driven by a large-effect locus on chromosome 12 in maternal genomes, identifying a specific genomic mechanism underlying maternal immune effects in the wild. However, despite a clear genetic basis to maternal antibody transfer, there was no evidence of selection acting on this region. These results provide new insight into the genetic basis and evolution of maternal immune effects in the wild.

Indels in genotype-phenotype maps cannot simply be ignored because of their low rate

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Evolutionary predictions require good models of selection, but also of variation: which phenotypes are introduced through random mutations on the genotype. This depends on the relevant genotype-phenotype map (GP map). There has been significant progress in our understanding of GP maps and their evolutionary implications. However, past research has primarily focused on short substitutions, neglecting insertions and deletions (InDels), even though InDels are found in natural sequence families. Here we investigate how the inclusion of InDels would change our models of variation, relying on computational models for several phenotypes: RNA secondary structure, a data-driven enzyme family model, and a toy model for protein quaternary structure self-assembly. First, we assess the likelihood of phenotype-conserving “neutral” mutations, finding a decrease with InDel length. Nevertheless, neutral indels remain more common than in null models, for example a null model representing multiple disjoint mutational events. Secondly, we compare neutral indels and neutral substitutions, focusing on the phenotypes accessible through subsequent mutations. Working with the RNA and self-assembly models, we find that neutral InDels of increasing length provide access to an increasing number of novel phenotypes. These results imply that InDels may facilitate new phenotypic variation under stabilizing selection. Using evolutionary simulations with Wright-Fisher dynamics, we show that InDels can indeed make an important contribution to the arrival of phenotypic variation, even when their rates are 10 times lower than the rate of single substitutions.

Predicting Fitness in Future Climates: A Proof of Concept in Arabidopsis thaliana and Vitis vinifera subsp. sylvestris

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Climate change has already started to affect wild organisms, and has led to the extinction of multiple species. Recent research therefore focused on studying the impact of climate change on organisms to mitigate its effects. These efforts focused both on understanding adaptation to climate change in wild and farmed organisms, and on identifying the species or populations most at risk of decline in current and future climates. The latter is especially important to implement conservation and breeding programmes to limit biodiversity loss and maintain agricultural production.
A common goal of these studies is to predict the fitness of organisms in future climatic conditions. Recent methods have been implemented to estimate the association between adaptive genetic loci and current climatic conditions, and to use future climatic projections to identify populations that will have a large number of maladaptive loci, and are therefore expected to face strong selective pressure and be at high risk of extinction (i.e., genomic offset or genomic vulnerability). While these methods are potentially useful tools to predict the impact of climate change, the accuracy of their predictions is seldom tested. One way to assess these methods is to predict fitness in common garden experiments under current climatic conditions and compare predictions with empirically measured fitness. Here, we applied this framework to Arabidopsis thaliana and Vitis sylvestris, finding that genomic offset predictions explained a significant but limited proportion of measured fitness variation (~7%). I will discuss the implications of these findings and future methodological improvements to enhance predictive accuracy.

Alternative splicing and sex-specific adaptation in stick insects

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Males and females are often subject to antagonistic selection pressures over shared traits. While research has focused on the role of gene expression regulation in the evolution of sexual dimorphism and the resolution of sexual conflict, other regulatory mechanisms, such as alternative splicing, remain comparatively understudied. We leverage the multiple, independent transitions from sexual to parthenogenetic reproduction that have occurred in Timema stick insects, together with PacBio long-read sequencing of somatic and reproductive tissues, to study sex differences in gene splicing and expression and to investigate how these change following the loss of sex and sexual conflicts. Alternative splicing is widespread in Timema, with the greatest transcriptional complexity occurring in male gonads. Differentially spliced genes between males and females undergo faster lineage-specific turnover and are evolving under distinct selective constraints compared to sex-biased genes. However, we identify a core set of gonadal-expressed genes with conserved patterns of sex-specific transcript usage across the phylogeny. Following the transition to asexuality, we consistently detect a decrease in sex-biased isoform abundance. Taken together, our results suggest that relaxed selection in parthenogenetic lineages reshapes the transcriptome not by increasing splicing noise, but through the decay of sex-specialized isoforms.

Leveraging standardised frameworks for genetic monitoring of populations

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Rapid environmental change, compounded by anthropogenic activity, is imposing novel selection pressures on biodiversity. The ability of species to persist under these conditions depends on both the magnitude of environmental change and the genetic diversity (neutral and adaptive) present within intraspecific populations. Despite substantial advances in genomics and spatial informatics, standardized tools for assessing population vulnerability across taxonomic groups and geographic regions remain limited. Here, we briefly outline Life on the Edge (https://cdbarratt.github.io/Life_on_the_edge.github.io/), an integrative framework that combines population genomics with spatial modelling to quantify predicted climate exposure, neutral and adaptive genetic diversity, landscape connectivity, and population vulnerability under future global change scenarios. As an empirical demonstration using novel genomic datasets, we apply multiple components of this toolbox to several economically important aquaculture species in the Netherlands (Turbot, Zander, Eel, Mussel, Flat oyster, Pacific oyster), enabling the identification of genetically diverse populations with high conservation value. Our study highlights the utility of integrative genomic–spatial frameworks for evaluating genetic diversity and population vulnerability in applied and conservation-relevant contexts.

Construction of unbiased pangenomes to better characterize standing variation and structural rearrangements between closely related butterfly morphs

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Heliconius butterflies have a rich history of ecological and genetic exploration due to their wing pattern mimicry and dramatic geographic diversity. However, the contribution of structural and standing genetic variation on the maintenance and integrity of mimicking patterns remains murky for many members of this clade. This is further complicated by the remarkable ability of Heliconius butterflies to stably hybridize with other Heliconius that do not participate in the same mimicry ring, which would otherwise be expected to carry a major evolutionary cost to produce intermediate, non-mimicking, phenotypes. These outbred populations also have higher heterozygosity than many other sequenced species, meaning that the issue of missing or hidden genetic variation in Heliconius could be a major concern if our biological inferences are based on single-individual reference genomes or previously sequenced sister species. To address this bias, we assemble reference-free pangenomes from multiple individuals with long-read sequencing to better characterize the landscape of standing variation that occurs between two recently diverged, phenotypically distinct, yet persistently hybridizing subspecies of Heliconius erato. Further, we construct a third pangenome to characterize the landscape of admixture in a neighboring Heliconius that is hypothesized to be of hybrid origin between the two H. erato subspecies, but participates in the same mimicry ring as only one of the putative ancestral subspecies. This resource will allow us to explore a variety of questions, particularly the diversity and relative contribution of structural variation to the persistence of hybridization between divergent phenotypes of Heliconius.

Consistent signatures of selection on gene expression level at different evolutionary scales

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Detecting selection on quantitative traits requires comparing observed phenotypic variation against neutral expectations. By contrasting trait divergence between species to trait variance within species, normalized by neutral molecular markers, deviations from neutrality can be identified. An excess of between-species divergence relative to within-species variance indicates selection driving trait change at phylogenetic scales. Gene expression levels constitute an ideal quantitative trait for this comparative framework, given their role as intermediate phenotypes linking genotype to organism-level traits. The availability of transcriptomic data across individuals and species now enables estimation of expression variance both within and between species, while accounting for biological covariates such as sex, developmental stage, and organ. Whether selection shapes expression evolution, and at what timescales, remains debated. Here, we leverage the Bgee database of curated mammalian transcriptomes to identify genes under selection for their expression levels, analyzing multiple organs independently. We test whether selective regimes detected at the mammalian phylogenetic scale predict selection at shorter timescales within primates or in human populations. Our results show that integrating within- and between-species expression variation identifies genes evolving under non-neutral regimes, and that selective signatures across mammals predict selection within primates. This cross-scale consistency indicates that forces shaping expression evolution are correlated over macroevolutionary time, validating comparative approaches for understanding regulatory evolution.

Where to Publish? Building a database of for-profit and non-profit journals in life sciences.

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The scientific publishing system is in crisis. High profit margins of commercial publishers, proliferation of predatory journals, excessive article processing charges, and reviewer scarcity are eroding the foundations of scholarly communication. Early-career researchers face particular pressure: the publish-or-perish culture pushes them toward prestigious journals owned by for-profit publishers, under the assumption that no viable alternatives exist. This assumption is false.

Where to Publish? is a project that emerged from our own experience navigating these decisions as early-career researchers in evolutionary biology. We created a database of life-science journals to highlight alternatives to the dominant publishing model, focusing on three criteria: non-profit publishers, open access, and affiliation with scientific societies. By systematically cataloguing journals across biological disciplines, we aim to demonstrate that researchers can make informed choices aligned with healthier publishing practices without compromising on scientific quality or visibility.

The database serves multiple purposes: helping authors identify suitable venues for their manuscripts, guiding reviewers in deciding which journals merit their volunteer labor, raising awareness about journal ownership structures, and facilitating statistical analyses of the publishing landscape in life sciences. We present the current state of the database, including coverage across fields and the distribution of journals.

Every submission or review for a journal affiliated with scientific societies, and published by a non-profit, contributes to shifting the balance of power in scholarly publishing. We invite the SMBE community to use Where to Publish?, at https://wheretopublish.github.io, as a resource and to join us in building a more sustainable publishing ecosystem.

Rethinking human AMY1 copy number evolution in light of demographic history

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Dietary change has long been considered a major selective force in human evolution, with increased salivary amylase (AMY1) copy number (CN) often interpreted as an adaptation to starch-rich agricultural diets and cited alongside other genes (e.g. LCT, FADS) as a paradigm of dietary adaptation. Here, we present droplet digital PCR estimates from 390 individuals representing 30 Sub-Saharan populations and combine them with previously published AMY1 CN estimates from 810 to 1307 individuals worldwide, to re-evaluate this model within a phylogenetically informed, ancestry-aware framework. Our analyses indicate that AMY1 CN is not consistently associated with the practice of agriculture across geographical subsets and, when all populations are considered together, the differences in AMY1 CN are significantly smaller than previously reported, complicating arguments for its biological significance. We also find that population structure and shared ancestry account for a considerable part of the observed variation in AMY1 CN worldwide. Lastly, phylogenetic tests further indicate baseline differences in AMY1 CN between Sub-Saharan and non-Sub-Saharan populations, pointing at deep evolutionary processes shaping present-day variation. These results challenge the long-standing “agriculture hypothesis” and put forward demographic history, rather than subsistence strategy, as the primary driver of AMY1 CN evolution worldwide.

Sex-specific modifications of gametogenesis in natural and lab-bred Fundulus spp. hybrids

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Successful hybridization between species can be limited by a variety of reproductive barriers; the emergence of asexual lineages is an example of a strong post zygotic barrier that is relatively rare in animals. In vertebrates, asexual reproduction typically arises through gametogenic alterations such as premeiotic genome endoreplication or meiotic failure, yet the relative frequency and conditions leading to their emergence remain poorly understood. We investigated natural, all female clonal hybrid lineages and laboratory-bred hybrids of both sexes between two North American killifishes, Fundulus diaphanus and F. heteroclitus, to determine the mechanisms underlying and maintaining the emergence of asexual reproduction and male sterility. By combining cytogenetic, molecular, and gametogenetic analyses, we learned that both natural and lab-bred F1 hybrid females can produce diploid and tetraploid oocytes. In diploid oocytes, we observed both bivalents and univalents. In contrast, tetraploid oocytes formed exclusively bivalents with normal crossover formation, consistent with premeiotic genome endoreplication restoring proper meiotic pairing and facilitating clonal reproduction. Hybrid males do not undergo premeiotic genome duplication and exhibit extensive chromosomal mispairing, leading to aberrant meiotic divisions, elevated apoptosis, and decreased fertility or sterility. Together, these findings highlight sex-specific differences in gametogenesis, paralleling patterns observed in other systems, and emphasize the relative ease with which asexual reproduction can arise in hybrid females, in contrast to the sterility commonly observed in hybrid males.

Using petabase-scale sequence alignment to describe the host and phylogenetic diversity of microsporidian parasites

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Microsporidia are large group of parasites that are suggested to infect most types of animals. Using a recently developed resource of assembled publicly available sequencing data, we have performed large scale sequence alignment, discovering over 15,000 data sets containing microsporidia sequences. Over 50% of previously reported microsporidia 18S SSU RNA sequences are found in our data and we identify 18S sequences representing over 1300 novel species of microsporidia. Our data shows the diversity of animals and environments where microsporidia are found, including several phyla of animals not previously reported to be infected by microsporidia. We also identified several novel species of microsporidia associated with humans and laboratory mice. Data sets containing microsporidia protein coding genes were identified, and at least 10% complete genomes were recovered from over 4000 datasets. These genomes are from about 400 species and all 6 major clades as well as the minor clades Caudosporida and Areosporida are represented. No novel clades are identified, but many novel groups are observed within the major clades. Arthropods serve as hosts across all clades, and we observe phylogenetic groups of microsporidia species that show enrichment for specific arthropod classes or animal phyla. For many microsporidia species we recover dozens of strains including many high-quality genomes for Enterocytozoon bieneusi, which phylogenetically clusters in a host specific manner. Together our analysis enhances our understanding of the sequence and host diversity of microsporidia and provides a foundation for studying microsporidia genome evolution.

Beyond Molecular Error: Developmental Selection Biases Germline Mutation Rates

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Mutations are the ultimate source of heritable variation in populations, and their rates shape both the tempo and direction of evolutionary adaptation. The generational mutation rate is typically understood to reflect underlying molecular processes, including DNA replication fidelity, damage, and repair, as well as organismal life-history traits such as body size and generation time. However, an important and largely overlooked dimension is the developmental context in which new mutations arise and the functional consequences they exert at the cellular level when they first occur.

Here, I present experimental results from Drosophila melanogaster demonstrating that selection operating within organisms can substantially bias observed mutation-rate variation. Specifically, mutations arising during development may be subject to cell-lineage selection before contributing to the germline, thereby confounding inferences about the underlying causes of mutation-rate variability. Using controlled experimental designs, we show that germline cell-lineage selection can lead to systematic biases in mutation-rate estimates. Both the magnitude and direction of this bias depend on species-specific features, including developmental architecture, life-history traits, and genomic context.

Our findings indicate that mutation rates cannot be interpreted solely as products of molecular mutational processes. Instead, they emerge from interactions between molecular mutation rates, organismal development, life history, and the fitness effects of mutations expressed at the cellular level. These results have important implications for the interpretation of comparative mutation-rate studies and for understanding how mutation rates evolve. More broadly, they highlight the need to integrate developmental and cellular selection processes into evolutionary models of mutation.

Tandem repeat variation is functional with signatures for directional and balancing selection in humans and chimpanzees

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Tandem repeats (TRs) are highly mutable DNA elements that comprise nearly 8% of the human genome and influence gene regulation, protein coding, and disease. Despite their functional importance, our understanding of TR evolution has remained limited, as their repetitive nature hindered accurate sequencing with short-read technology. Here, using telomere-to-telomere (T2T) reference genomes for seven ape species and population-scale long-read sequence data for humans and chimpanzees, we generated a comprehensive comparative catalog of TRs. We identified over 3 million TR loci per species and nearly 2 million homologous loci between humans and chimpanzees, with overrepresentations of TRs in 5'UTRs and promoters. We see consistent evidence for stabilizing selection on TRs, particularly those located in UTRs and CDS. For instance, TRs in UTRs and CDS have increased conservation across the examined apes, reduced genetic variation within species, and increased correlation of mean allele lengths between humans and chimpanzees. To control for locus-specific mutation rate variation, we adapted an HKA-like approach to detect TRs with signatures of directional or balancing selection by comparing their divergence between species to their diversity within species. For instance, one TR with a strong signature for positive selection is in the 5'UTR of PROX1, a transcription factor essential for embryonic nervous system development, whereas we see a TR with a strong signature for balancing selection overlapping an exon in PCGF3, a gene involved in innate immune activation. Together, these results establish a population and species-resolved framework for studying TR evolution and interpreting TR variation in functional contexts.

Functional characterization of archaic introgression reveals immune system adaptation in Near Oceania

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Understanding the evolutionary and phenotypic impacts of adaptive human variation has been a difficult to achieve goal. Near Oceanic populations—which harbor exceptional archaic introgression levels—remain especially underrepresented in genomic and functional studies. Here we comprehensively characterize archaic introgressed variants using massively parallel reporter assays (MPRAs) and deep learning based variant classification.

Using 278 high-coverage Near Oceanic genomes produced by the Tucci lab, we analyzed 33,355 high-frequency archaic variants, identifying 167 missense, 10 loss of function, and 60 predicted splice-disrupting variants. The vast majority (97%) are non-coding, with significant enrichment in immune cis-regulatory elements (OR=1.30, p=6.5e-94), including T and B cells. 51 variants overlap fine-mapped associations in the UK Biobank and Biobank Japan, including for white blood cell count and height.

We applied MPRA to assess the regulatory impacts of archaic variants in immune cell lines. We identified 1,551 significant expression modulating variants (emVars) linked to 1,422 candidate target genes. Pathway analysis identified putatively functional adaptive variants in multiple components (JAK1, OAS1, STAT2, MX2, TRIM10) of both the interferon gamma and alpha signaling pathway across multiple populations. We detect 4 functional emVars near the antiviral OAS1 gene on a Denisovan haplotype unique to Oceanic populations distinct from the COVID-19 protective Neanderthal version found in Europeans and East Asians. At T-cell differentiation TRPS1 locus, we identify expression increasing emVar predicted to increase STAT1::STAT2 affinity that resides in an active hematopoietic enhancer. Together, our functional analysis suggests parallel immune system adaptation from archaic sources.

Characterizing tumor-specific human endogenous retroviruses in clear cell Renal Cell Carcinoma patients

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Human endogenous retroviruses (HERVs) are remnants of ancient viral infections and comprise roughly 8% of the human genome. Expression of HERVs in clear cell renal cell carcinoma (ccRCC), a common and aggressive form of kidney cancer, correlates with tumor immunogenicity and response to immunotherapy. Our hypothesis is that HERV products function as immune triggers, due to their absence in normal cells, and can thus prime the anti-tumor immune response, resulting in a HERV specific T-cell populations. To investigate the potential immunomodulatory role of HERV expression in ccRCC, we deployed a comprehensive and standardized database of HERV loci (HERVdb) developed in the Blanco-Melo Lab to characterize HERV expression in 8 ccRCC patient biopsies, published datasets, and ccRCC cell-lines through bulk, long-read, and single-cell RNA-seq, as well as mass spectrometry to discover HERV peptides. Several of the same HERV loci were expressed in ccRCC tumors across datasets; interestingly, many of these elements belong to the Harlequin family of mosaic HERV elements and HERV-K (HML2). ScRNA-seq indicated expression of these HERVs is cancer-cell specific. HERV peptide candidates will be further explored using immunopeptidomics and T cell studies to elucidate the immunogenic function of HERV products. Our results establish a clear baseline of HERV expression in ccRCC, highlight tumor-specific HERVs, and explore relevant HERV-derived peptides that could serve as potential therapeutic targets. Ultimately, this project aims to demonstrate the utility of HERVdb to identify HERVs as targets for ccRCC treatments and to establish a reproducible workflow for the interrogation of HERVs in other cancers.

Streptococcus amylase-binding proteins in geladas and baboons reveal convergent oral microbial adaptation to starch-rich diets in humans and primates

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The salivary alpha-amylase gene underwent a major copy number expansion in multiple mammals, and in humans this expansion has been interpreted as the result of selection imposed by dietary starch consumption. Specific human oral Streptococcus species carry amylase-binding proteins that hold active alpha-amylases adjacent to bacterial cells, ensuring bacterial access to host-derived starch break-down products. The presence of amylase-binding protein A (abpA) genes in oral Streptococcus species of humans and Neanderthals but not chimpanzees or gorillas suggests that the acquisition of abpA reflects co-evolution between commensal microbiota and their hosts due to host dietary adaptation. If so, abpA-carrying Streptococcus might also be present in the oral cavities of other salivary amylase-producing mammals. We investigated the oral microbiota of two primates, wild geladas (n=15) and baboons (n=19), plus 6 additional wild primate species (n=36) and pigs (n=19) for the presence of abpA using de novo metagenome assembly. A hidden Markov model identified genetically heterogeneous apbA genes with high confidence in contigs assembled from baboons and geladas but not from other primates or pigs, with the majority of genes in Streptococcus genomes. Phylogenetic analysis determined that the Streptococcus species carrying abpA in geladas and baboons are genetically distant from those in humans, suggesting independent acquisition by Streptococcus. Overall, we find evidence of oral commensal microbial co-evolution related to host dietary adaptation in starch-dependent, but not non-starch-dependent primates, suggesting that carrying oral streptococci with abpA may be an acquired primate trait correlated with levels of dietary starch consumption.

Parallel adaptation and genomic vulnerability of bottlenose dolphins in a changing ocean

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The pace and magnitude of anthropogenic change are unprecedented, making biodiversity conservation one of the defining challenges of our time. Marine ecosystems are especially vulnerable, yet adaptive responses in marine organisms remain poorly understood. Using one of the largest whole-genome sequencing datasets generated for a marine mammal, we applied a seascape genomics framework to Indo-Pacific bottlenose dolphins (Tursiops aduncus) distributed across the environmentally heterogeneous Australian coastline. Genome-wide variation strongly reflected geography, consistent with a northern origin followed by two independent north-to-south colonisation pathways along the east and west coasts. In contrast, putatively adaptive SNPs grouped individuals by tropical versus temperate waters irrespective of geographic distance or coastline, providing rare evidence for parallel adaptation to tropical conditions on both coasts. This pattern was likely facilitated by selection on standing genetic variation retained from a tropical northern origin and highlights the importance of considering demographic history when interpreting signatures of selection. Together, these results suggest tropical-temperate, ecotype-like differentiation across Australian waters. Extending this framework into a predictive context, we estimated genomic offset (GO) under moderate (RCP4.5) and high (RCP8.5) emission scenarios. Southeastern Australia consistently showed the highest offsets, whereas the more climatically stable southwest may represent a potential refugium. High GO values indicated that some populations would require substantial genomic change to remain adapted, posing a particular challenge given dolphins' long generation times. By uncovering environment-associated adaptive genetic variation and identifying areas of predicted genomic vulnerability, our work highlights the importance of genomics-informed conservation strategies in a fast-changing ocean.

Introgression from an unsampled lineage in Southern African genomes

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Admixture from other hominin groups such as Neanderthals and Denisovans has played an important role in shaping the genetic diversity among human populations. Meanwhile, genomic characterization of present-day human populations carrying genetic diversity not present elsewhere, such as the Khoe-San populations of Southern Africa and Central African rainforest hunter-gatherers, is key to understanding our evolutionary history as humans. Although contributions from unknown deeply diverging lineages into the ancestors of different present-day African populations have been proposed previously, there is no coherent picture due to differences in datasets, methods and frameworks considered. This problem is particularly difficult since no genomes from archaic populations in Africa are available.
Using methods that do not require genomes from a source population, we analysed high-coverage genomes from Khoe-San and rainforest hunter-gatherers populations for traces of archaic admixture, in the context of African genomic diversity. We found that a model with introgression from an unsampled source population into the ancestors of Khoe-San populations best explains their patterns of variation. Notably, various models of early human population structure are not sufficient to explain the observed amounts and length distributions of genomic outliers in the individual genomes. We obtained introgressed genomic fragments in a panel of Khoe-San individuals across the autosomal as well as the X chromosomes, characterising the landscape of introgression in this population. We find that changes in these fragments might influence functions related to traits such as sensory perception.

FastSpeciesTree: Fast and Scalable Species tree Inference

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The generation of species trees from genomic data is an important step in understanding evolutionary relationships across the tree of life. With the increasing availability of genomic data, species tree inference methods which can easily and rapidly produce accurate species trees from large datasets are required to enable downstream analyses of these resources. Here we present FastSpeciesTree, a fully automated species tree inference method designed to leverage advances in rapid pairwise sequence alignment and scalable phylogenetic inference methods. We show that FastSpeciesTree is able to produce species trees with accuracies equivalent to trees produced through manual-curation and best-practice approaches. We further demonstrate that FastSpeciesTree can produce these high accuracy phylogenies substantially faster than any competitor method. Finally, we show that FastSpeciesTree is capable of building a species tree comprising almost the entirety of the RefSeq databases available proteomes (n = 33285) in less than 12 hours using standard computing resources.

Sex chromosome turnover has dramatically different consequences between closely related cichlid fishes

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Differentiating between drivers and consequences of sex chromosome turnover remains difficult, however studies of young, homomorphic sex chromosomes have greatly enhanced our ability to understand this dynamic. The Lake Tanganyika radiation of cichlid fishes shows a remarkably high rate of sex chromosome turnover amongst closely related species, providing a prime resource to investigate this enigma. Within one tribe of this radiation, Cyprichromini, our phylogenetic reconstruction revealed two turnovers involving the same homologous chromosome pair (LG05): a turnover from an XY to a ZW system; and a turnover involving a chromosome fusion, and an additional turnover to a different chromosome pair (LG15). Illustrating these turnovers, we generated haplotype-resolved whole genome assemblies of four species of this tribe, and combined this with cytogenetic investigations to precisely characterise the sex chromosomes, and understand what has driven their transitions. We find that, despite sharing LG05 as (at least part of) their sex chromosome, patterns of inversions, rearrangements and accumulation of deleterious mutations have followed independent evolutionary trajectories in three species of Cyprichromini. One of these species has undergone multiple chromosomal fusions, including a sex-specific neo-sex chromosome fusion, resulting in a Z_1Z_2W system. Finally, we show that a fourth species, Paracyprichromis nigripinnis (LG15 XY), has a degenerated Y chromosome, rare among cichlids, and remarkable considering the young age of this sex chromosome. The species-specific characteristics of sex chromosome evolution among these very closely related species shows how various factors can influence the evolution of sex chromosomes and why comparative studies are needed to understand this.

The evolutionary dynamics between viral mimics and host proteinss14

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Viral proteins interact with host proteins to hijack cellular pathways important for viral replication. Viral mimics are proteins whose structural similarity to host-mimicked proteins allows them to interact with mutual host targets. This mimicry poses an evolutionary challenge for the host – how to avoid mimics without compromising essential interactions with host-mimicked proteins. Despite the prevalence of mimicry, the evolutionary dynamics between host and viral mimics remain largely unknown. We address this by integrating structural modelling, host-virus interaction networks and comprehensive evolutionary analyses of host and viral proteins. We show that host proteins targeted by both mimics and host-mimicked proteins are highly conserved, and that this is related to functional constraints imposed on host proteins. Host interface residues that interact with both mimics and host-mimicked proteins evolve slowly, while residues that exclusively interact with mimics evolve significantly faster. Surprisingly, viral mimics do not evolve rapidly, instead displaying complex evolutionary patterns. Our analysis reveals host's limited capacity to escape mimicry and viral evolution to exploit this, and highlights how constraints lead to unexpectedly slow evolution of host-virus interaction networks.

Reticulation dominates protein structural evolution in bacteriophages

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Bacteriophages are among the most diverse and abundant biological entities on Earth. Resolving their phylogenetic relationships is challenging due to rapid evolution, low sequence identity, and extensive horizontal gene transfer. Traditional phylogenetic methods that rely on sequence alignment often suffer from weakened evolutionary signal due to saturation. Recent advances in protein structure prediction allow for large-scale structural evolutionary analysis.

Phylogenetic analysis was performed on a large set of phage proteins clusters from INfrastructure for a PHAge Reference database. Three-dimensional protein structures were discretised and aligned using a vector-quantised variational autoencoder in combination with a structural alignment tool. Phylogenetic trees were inferred under discrete Markov models using maximum likelihood, with parallel analysis using amino acid sequence alignments.

Structural phylogenies showed higher tree certainty across clusters than sequence-based trees, indicating that structural conservation is less affected by saturation. Sequence trees exhibited longer branch lengths and were enriched for PHROG tail functions, suggesting that tail protein function is conserved at the structural level despite rapid sequence divergence. Consensus phylogenetic networks revealed that phage evolution is non-treelike at both structural and sequence levels. Caudovirales show complex reticulate network structures, whereas relationships among Alphasellovirus yellowstone, hengillense, beppuense and Bicaudovirus polluoliense were comparatively tree-like. Despite the additional evolutionary signal from structural phylogenetics, phage evolutionary histories remain complex and discordant across biological levels.

Crossover and consequences: are individual recombination rates under selection?

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Meiotic crossovers are a fundamental feature of sexual reproduction. They ensure proper chromosome segregation and shuffle linked alleles into novel haplotypes, facilitating adaptive evolution. However, they can also introduce novel mutations and break apart favourable haplotypes. These trade-offs suggest potential impacts on individual reproductive success and offspring survival, yet empirical studies are rare. A major hurdle is that direct estimates of crossover positions in females are highly invasive, and genomic estimates in both sexes can only be obtained for individuals with genotyped offspring. These introduce sampling biases, as fitness analyses cannot include individuals with no offspring. Genomic prediction (GP) uses genomic data to estimate genetic and phenotypic values in unmeasured individuals, and is a transformative tool in predicting human disease and breeding outcomes in crops and livestock. Here, we use a GP approach in a long-term study of house sparrows (Passer domesticus) to determine sex-specific genomic estimated breeding values (GEBVs) for individual crossover rates in >2,600 phenotyped and >2,900 unphenotyped individuals. We then relate GEBVs to sex-specific reproductive success and survival measures. Our findings suggest potential stabilising selection against extreme values of ACC, especially in male sparrows. By inferring crossover rates in individuals without offspring, our approach overcomes the “missing fraction” problem and provides rare evidence of selection on recombination in a wild population.

RegEvol: detection of directional selection in regulatory sequences through phenotypic predictions and phenotype-to-fitness functions

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Regulatory DNA controls when and where genes are expressed, making it a key driver of phenotypic evolution. Yet detecting selection in non-coding regions remains difficult, as most approaches rely on sequence conservation or changes in substitution rate rather than molecular effects. RegEvol bridges this gap by linking machine learning-based predictions of transcription factor binding to explicit evolutionary models. It uses the distribution of predicted mutational effects to infer fitness functions under different evolutionary scenarios (random drift, stabilising selection, or directional selection). Through maximum-likelihood estimation, it identifies the regime that best explains observed changes along a lineage from an ancestral sequence. RegEvol corrects biases that affected previous tests based on machine learning of transcription factor binding, while remaining conservative across different levels of divergence. Applied to over 3 million Drosophila melanogaster regulatory regions, we identify 5.1% of them under directional selection, enriched near reproductive and immune genes. The framework is readily applicable to experimentally detected regulatory elements with alignable ancestral sequences and is flexible to future advances in understanding regulatory function, providing a powerful basis for investigating adaptation in non-coding regions.

Single-cell phylodynamics reveal rapid late-stage colorectal cancer expansions

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Colorectal cancer (CRC) arises through successive genetic mutations and clonal expansions, yet the temporal and spatial dynamics of these processes remain incompletely resolved. We conducted whole-genome sequencing of 350 single cells from multiregional tumor samples in seven CRC patients and applied Bayesian phylodynamic models that explicitly account for technical noise and phylogenetic uncertainty. Our analyses indicate that most malignant lineages originate decades before clinical diagnosis, remain in prolonged indolent phases, and undergo rapid expansion within approximately two years of detection. Tumors exhibited pronounced spatial structuring with limited interregional mixing, whereas substitution rates were consistently elevated in malignant cells, varied across patients, and were uncoupled from growth tempo. These results provide one of the most detailed reconstructions of CRC evolutionary history to date, revealing extended periods of stasis followed by sudden growth, with important implications for early detection, intervention, and spatially informed sampling strategies.

Self-fertilization can reverse the selection coefficient on a recombination landscape modifier during experimental evolution

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Recombination rates are well-known to correlate with self-fertilization rates in plants. Theoretical work has highlighted mechanisms predicting increased selection on recombination modifiers under higher self-fertilization rates. However, these models assume uniform recombination landscapes, whereas in nature they are highly heterogeneous. Here, we investigate the evolution of recombination landscapes under varying self-fertilization rates using experimental evolution in Caenorhabditis elegans populations segregating a rec-1 polymorphism. Mutation at the rec-1 gene homogenizes the otherwise heterogeneous C. elegans' recombination landscape. Strikingly, predominant self-fertilization not only increases the strength of selection acting on the rec-1 modifier, but also reverse its direction. Simulations mirror the experimental results and show that they can arise from the persistence of associations between the modifier and the genetic combinations it generates at distant loci. Under outcrossing, the modifier is only briefly associated with most genetic combinations it creates; only locally generated combinations are in sufficiently strong linkage to allow indirect selection of the modifier through hitchhiking. Conversely, increased linkage under predominant self-fertilization enables the modifier to form persistent associations with genetic combinations across the genome. When a mismatch exists between local and genome-wide effects of a modifier on selection efficiency—as is the case for rec-1—a reversal of selection under predominant selfing becomes possible. This mechanism should apply to trans-acting modifiers but not cis-acting ones, which lack genome-wide effects. By distinguishing between these two classes, we present a model that explains the evolution of increased recombination in self-fertilizing species and predicts differences in recombination architecture compared to outcrossing relatives

Building realistic genotype-phenotype-fitness maps that predict mutant fitness in diverse environments

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Predicting evolution remains difficult because evolution unfolds through stochastic processes, such that small differences in initial conditions lead to divergent outcomes. High-throughput evolution experiments embrace this probabilistic nature by capturing a broad spectrum of possible adaptive mutations. Yet without understanding the phenotypic mechanisms that mediate the fitness consequences of mutation, we cannot predict how their fitness effects will change across environments, limiting our ability to forecast evolution in natural settings.

Here, we combine massively-parallel experimental evolution in Saccharomyces cerevisiae, fitness profiling across environments, single-cell transcriptomics, and dimensionality-reduction approaches to 1) resolve the phenotypic mechanisms through which adaptive mutants affect fitness, and 2) investigate predictability in the genotype–phenotype–fitness map. We generated ~1,000 drug-resistant yeast lineages and quantified their fitness across multiple conditions. Despite extensive genetic variability, these adaptive mutants collapse into six clusters defined by characteristic genotype-by-environment interactions. Thus, while the genetic basis of resistance is numerous, the accessible phenotypic space is constrained, providing an organizing framework for otherwise overwhelming mutational complexity.

Mutants from different clusters exhibit distinct transcriptional states that respond differently to environmental change. Thus, clustering by how fitness changes across environments recovers mutants that alter fitness via divergent underlying molecular phenotypes. Together, these data establish a rare empirical bridge from genotype-phenotype-fitness and demonstrate how diverse genetic routes to adaptation converge on a small number of transcriptional states that determine environmental responses. This integrative framework moves beyond cataloging fitness effects toward mechanistic, predictive genotype–phenotype–fitness maps—exactly the kind of foundation needed for realistic evolutionary prediction.

Natural selection acting on complex traits hampers the predictive accuracy of polygenic scores in ancient samples

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The prediction of phenotypes from ancient humans has gained interest due to its potential to investigate the evolution of complex traits. These predictions are commonly performed using polygenic scores computed with DNA information from ancient humans along with genome-wide association study (GWAS) data from present-day humans. However, numerous evolutionary processes could impact these phenotypic predictions. In this work, we investigate how natural selection shapes the temporal dynamics of variants with an effect on the trait and how these changes impact phenotypic predictions for ancient individuals using polygenic scores. We find that stabilizing selection accelerates the loss of large-effect alleles contributing to trait variation. Conversely, directional selection accelerates the loss of small- and large-effect alleles that drive individuals farther away from the optimal phenotypic value. These phenomena result in specific shared genetic variation patterns between ancient and modern populations that hamper the accuracy of polygenic scores to predict phenotypes. Our results assume perfectly estimated effect sizes at the causal loci of complex traits segregating in a GWAS performed in the present and, therefore, provide a putatively loose upper bound on the polygenic score portability to predict traits in the past. Furthermore, we show how natural selection could impact the predictive accuracy of ancient polygenic scores for two widely studied traits: height and body mass index. Our results emphasize the importance of considering decreases in the reliability of polygenic scores to perform phenotypic predictions in ancient individuals due to allele frequency changes driving the loss of alleles via natural selection.

Modeling the Evolutionary Advantage of Plasmid Persistence Strategies

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The evolutionary success of plasmids and other extrachromosomal elements depends on their ability to persist across host generations despite imperfect inheritance. While individual plasmid persistence mechanisms—such as active partitioning or toxin–antitoxin (TA) systems—are well described, their combined evolutionary consequences remain poorly understood. Here, we use a mathematical modeling framework, grounded in empirically measured plasmid loss dynamics, to investigate how different persistence strategies shape plasmid fitness over evolutionary timescales. Our model integrates intracellular competition between plasmid genotypes with population-level inheritance dynamics, allowing us to quantify the long-term selective advantages of plasmid persistence mechanisms. We find that combining active partitioning with post-segregational killing via TA systems consistently maximizes plasmid fitness, outperforming either strategy alone. These results follow from the synergistic reduction in segregational loss and the elimination of plasmid-free cells, which together increase long-term persistence in host lineages. Experimental competition assays between engineered plasmid variants closely match model predictions, validating the inferred evolutionary trajectories. Extending these insights to natural systems, comparative genomic analyses indicate that partitioning and TA systems are core features of large plasmids in enterobacteria, as predicted by the model. We further identify and experimentally validate a previously unrecognized type I TA system in IncX3 plasmids. By integrating mechanistic segregation dynamics with evolutionary competition at the population level, our work reveals general principles shaping the architecture of extrachromosomal elements and underscores the evolutionary advantage of combined persistence strategies. This synthesis offers a quantitative framework for understanding plasmid evolution within the broader landscape of genome plasticity and mobile genetic elements.

When plasmids settle down: domestication and chromid-like evolution in Pantoea

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Plasmids play a central role in prokaryotic evolution by promoting genetic innovation and ecological adaptation. While typically perceived as mobile elements, some plasmids evolve stable inheritance within their host lineage and become integral components of their host genome. Here, we investigate the evolutionary trajectories of two large plasmids (LPP-1 and LPP-2) in the plant-associated genus Pantoea. Using comparative and phylogenomic analyses, we identify single events of plasmid acquisition followed by vertical inheritance, which may be explained due to the synchronisation of replication between plasmids and chromosome. Moreover, LPP-1 and LPP-2 encode core genes, whose chromosomal or plasmid localisation varies across species. Phylogenomic analyses reveal a deep evolutionary split between plasmid and chromosomal homologs, reflecting limited gene transfer between replicons. We infer that plasmid acquisition introduced genetic redundancy, followed by lineage-specific waves of gene loss. Together, stable vertical inheritance, synchronised replication and conserved core gene content are hallmarks of plasmid domestication in Pantoea LPP-1 and LPP-2, that may precede the emergence of chromids/secondary chromosomes. Our findings demonstrate that LPP domestication coincided with species divergence and likely contributed to ecological specialisation in Pantoea. Our study provides a model for how plasmids transition into stable, adaptive replicons during bacterial genome evolution.

Gene-culture coevolution in the European Upper Palaeolithic

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By their nature, human palaeogenomic studies have traditionally been focused on the biological relatedness and possible patterns of migration and replacement. Many of the resulting papers have repeatedly been criticised for ignoring or underplaying the parallel complexity of the archaeological record and how it articulates – or contradicts – the genetic interpretations. Studies that analysis palaeogenomic and 'palaeosocietal' (i.e. archaeological) data in true parallel are lacking. Here, we focus on the European Late Ice Age from ca. 22,000 to 11,000 years before present as a case where a steadily increasing size of palaeogenomic samples can be articulated with a rich archaeological record, all set against an environmental canvas of at times dramatic climatic changes. Drawing on high-quality, publicly available data, we present a methodology for directly linking genetic samples with extensive archaeological material, and to query these for patterns of gene-culture coevolution, migration, and changing population sizes as captured in both genetic and archaeological data. Our results suggest overall concordance between genetic and cultural phylogenies, suggesting that the evolution of these inheritance systems was linked at this time. By the same token, some differences in the coevolutionary histories of the genetic and cultural systems can be observed. We interpret these patterns in light of the most likely practices of kinship and of social transmission of knowledge, which together determined how cultural and genetic information respectively circulated in this metapopulation. Grounded in well-established gene-culture coevolutionary theory, our approach contributes to a more robust integration of archaeology and palaeogenomics.

Tetrapolar mating relaxes host boundaries through sexual recombination between wheat- and barley-adapted Puccinia striiformis rust fungi.

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Reproductive barriers maintain genetic structure in host-specialized plant pathogens, yet it remains unclear whether host specialization alone prevents sexual reproduction when mating mechanisms are conserved. We tested sexual compatibility between the phylogenetically divergent (~8 million years) wheat-adapted Puccinia striiformis f. sp. tritici (Pst) and barley-adapted P. striiformis f. sp. hordei (Psh), which share common barberry (Berberis vulgaris) as an alternate host for sexual reproduction.

Chromosome-scale assemblies showed that the homeodomain (HD) and pheromone receptor (PR) mating-type loci reside on different chromosomes (chr2 and chr6, respectively). Replicated reciprocal crosses on barberry produced viable sexual progeny, and locus-specific restriction assays at the HD locus confirmed segregation of parental alleles, providing genetic validation that tetrapolar mating remains functional despite host specialization. Host specificity assays on wheat and barley differentials, near-isogenic lines, and wild relatives confirmed strict parental host specificity, whereas progeny displayed dual-host compatibility and recombinant virulence phenotypes.

These results demonstrate that ecological divergence on primary cereal hosts can coexist with sexual compatibility on a shared alternate host, enabling recombination that reshuffles host-associated virulence and relaxes strict host boundaries. More broadly, they highlight how mating-system architecture can preserve opportunities for sexual reproduction and genetic exchange across host specialization boundaries, with implications for host range evolution and sexual diversification in fungal pathogens.

Convergent genome evolution shaped the emergence of terrestrial animals

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The challenges associated with the transition of life from water to land are profound, yet they have been met in many distinct animal lineages. These constitute a series of independent evolutionary experiments from which we can decipher the role of contingency versus convergence in the adaptation of animal genomes. Here we compare 154 genomes from 21 animal phyla and their outgroups to reconstruct the protein-coding content of the ancestral genomes linked to 11 animal terrestrialization events, and to produce a timescale of terrestrialization. We uncover distinct patterns of gene gain and loss underlying each transition to land, but similar biological functions emerged recurrently pointing to specific adaptations as key to life on land. We show that semi-terrestrial species evolved convergent functional patterns, in contrast with fully terrestrial lineages that followed different paths to land. Our timeline supports three temporal windows of land colonization by animals during the last 487 million years, each associated with specific ecological contexts. Although each lineage exhibits distinct adaptations, there is strong evidence of convergent genome evolution across the animal kingdom suggesting that, in large part, adaptation to life on land is predictable, linking genes to ecosystems.

The day after the drug: Investigating drug-induced cellular memory

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Many cancer patients who initially respond to first-line therapy show diminished response to subsequent cycles of treatment. This reduced therapeutic response often precedes acquisition of any genetic alterations, suggesting that drug-exposed cells are epigenetically distinct from drug-naïve cells. It has been established in other cellular contexts that epigenetic reprogramming creates sustained memory of prior stimuli across generations of cells. Nevertheless, it is currently unknow whether cancer cells have capacity to build memory to previous drug insults. Here, we combine lineage-tracing with longitudinal single-cell multiome sequencing and patient data to delineate the mechanisms underlying cancer cell drug-induced cellular memory. Using a model of non-genetic drug resistance, we show that despite resuming normal proliferation, a subset of cells retains features inherent to the on-drug state even following a prolonged drug-holiday period indicating memory properties. This cellular memory is primarily encoded by changes in the chromatin landscape. We further show that the capacity of cells to form the memory is lineage-specific and that while some lineages have high memory capacity others readily revert to naïve state once the drug is removed. Differential memory capacity is mediated by the transcription factors C/EBPα and C/EBPβ, known regulators of memory in innate immune cells (i.e. trained immunity). Finally, we show that C/EBPα is transiently expressed in cancer cells of patients under treatment. Taken together, our study reveals how treatment is selectively inscribed in the epigenetic landscape of cancer cells. These insights may guide novel strategies to sustain treatment efficacy by targeting cancer cell memory.

Intraspecific variation in the duration of epigenetic inheritance

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Epigenetic inheritance is generally less stable across generations than DNA sequence-based heredity. One common form of epigenetic inheritance, found in plants, fungi, and animals, is the transgenerational memory of gene silencing mediated by small RNAs. These small RNAs can be amplified through RNA-dependent RNA polymerases, thus maintaining the silenced state across multiple generations. Such molecular mechanisms raise questions regarding their natural variation and evolutionary impact. We here ask whether the presence and duration of epigenetic inheritance vary within a species. We use the ability of the nematode Caenorhabditis elegans to silence genes for multiple generations after an initial RNA interference trigger. We find that the duration of silencing memory in number of generations differ across C. elegans wild strains. Strikingly, several wild strains show no memory, while some display a longer memory than the reference strain. Natural DNA sequence polymorphisms, such as in the set-24 gene, affect the duration of small RNA inheritance. We further show that the duration of the silencing memory in wild strains increases with temperature and that memory is retained upon early starvation arrest and passage through dauer diapause. Altogether, these results demonstrate intraspecific diversity in the regulation of small RNA-based heredity, a prerequisite for selection acting on genetic variants affecting epigenetic inheritance duration.

Experimental reconstruction of the domestication, evolution, and adaptive role of horizontal gene transfer in eukaryotes.

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New genes are crucial for organismal evolution providing new functions key for cellular innovations. Recently, horizontal gene transfer (HGT), defined as the acquisition of genetic material from different species, has been shown to have an important effect on eukaryotic genome evolution. HGT has an unprecedent adaptative potential as it can introduce key functional innovations in the absence of genetic predecessors. However, important constraints impair HGT, making foreign genes unstable and likely to be lost. Overcoming these challenges requires gaining expression in the host genome, eliciting functional effects upon which selection can act, and avoiding conflicts with pre-existing cellular components. Accordingly, only a small fraction of HGTs overcome these challenges but even these few HGTs have the potential to underpin major biological transitions. Despite this, our understanding of eukaryotic HGTs is almost entirely based on observational comparative genomics and phylogenetics which are correlative and can only depict transferred genes at a single point in time, usually after domestication. Here we experimentally mimic the early stages of HGT by randomly introducing a bacterial antibiotic resistance gene, depicted of any regulatory element, into the genome of Chlamydomonas reinhardtii. By identifying hundreds of antibiotic-resistant strains with de novo bacterial gene insertions we are characterizing how bacterial genes can gain expression following integration. By using long-term experimental evolution of resistant strains we are tracking in real time the domestication of HGT. Our results reveal the importance of co-option during foreign gene establishment and highlight important cost-benefit tradeoffs which may dictate HGT retention over evolutionary time.

Coevolution of microRNAs and their gene targets leads to novel traits – insights from across the vertebrate tree of life.

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MicroRNAs (miRNAs) are short regulatory molecules found across Metazoa, which act as crucial post-transcriptional regulators of gene expression. Expansions in genomic miRNA repertoires are associated with periods of major physiological innovation and diversification. While miRNAs are known to be crucial parts of gene regulatory networks, their functional significance has often focused on human clinical studies. Here we use recently-available genomic resources to elucidate their significant role in shaping a variety of phenotypes across the whole of Vertebrata. As part of the Vertebrate Genomes Project, we have annotated genomic miRNAs in over 500 vertebrate species, and reconstructed the punctuated bursts of miRNA gains and dispersed periods of miRNA loss which permeate the vertebrate tree. Using a combination of algorithmic and machine learning target prediction methods, we show distinct coevolutionary patterns of association between miRNAs and their mRNA targets. Using a large, consolidated database of animal traits, we find associations between shifts in miRNA repertoires and associated changes in a range of life history traits. Our findings propose strong links between miRNA repertoires and placental phenotypes in eutherian mammals - a clade which underwent one of the most substantial expansions in miRNAs in evolutionary history.

Functional characterization of the male-specific mitochondrial ORFan protein in DUI bivalves reveals a role in spermatogenesis

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Bivalves represent a rare and intriguing exception in the animal kingdom, in which atypical mitochondrial genes may influence sex determination or sex differentiation. This possibility is linked to Doubly Uniparental Inheritance (DUI), a unique system of mitochondrial transmission found in over 100 bivalve species, whereby males inherit mitochondria from both parents while females inherit exclusively from the mother, like all other animal species. In DUI species, “male mitogenomes” carry morf, a taxonomically restricted ORFan gene with no homologs outside DUI lineages. Although the function of morf remains enigmatic, it has been hypothesized to participate in male-specific sex determination or sex differentiation, or alternatively in the molecular mechanisms underlying DUI itself. Understanding how taxonomically sex-restricted genes can acquire essential functions is fundamental in evolutionary biology, yet the molecular networks through which ORFan proteins like MORF operate remain largely unexplored. Western blot analyses revealed that MORF is exclusively expressed in male gonads of two distantly related DUI bivalves, Mytilus edulis and Venustaconcha ellipsiformis, during the reproductive season, suggesting a key role in spermatogenesis. Immunocytochemistry localized MORF in mitochondria and acrosomes of late spermatids and mature sperm, positioning it at critical sites for gamete maturation and fertilization. Co-immunoprecipitation and GST pull-down coupled with mass spectrometry identified MORF’s partners. Gene Ontology analyses revealed a predominance of extracellular matrix proteins, particularly laminin and collagen, alongside ribosomal and cytoskeletal proteins. These results illustrate a distinctive, conserved and sex-specific role for MORF in spermatogenesis and mitochondrial dynamics providing insights into molecular innovations underlying alternative mitochondrial inheritance systems.

The specialist – generalist trade-off for infection ability of a parasite

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In highly specific host–parasite systems, infection depends on parasite effector genes that match particular host genotypes. Although accumulating many effector variants should in principle allow parasites to infect many hosts, parasites rarely become broad generalists. We tested whether this limitation reflects a cost of generalism. Using the bacterium Pasteuria ramosa, a virulent parasite of Daphnia, we focused on parasite attachment, an essential first step of infection. Attachment is mediated by highly specific adhesion genes, which we identified by genome-wide association mapping. We predicted that parasites able to infect many host genotypes pay a cost in reduced attachment strength. Across parasite isolates, we measured adhesion strength and quantified both the number of host genotypes infected and the number of attachment sites bound. Isolates with strong adhesion were restricted to few host genotypes or few attachment sites, whereas isolates with weak adhesion infected more host genotypes and bound more sites. This pattern is consistent with a specialist–generalist trade-off. We further provide a molecular genetic model explaining how this trade-off arises. Together, our results offer a mechanistic explanation for why parasites do not evolve into unconstrained generalists.

Disentangling patterns of variation in the human genome: the roles of mutation, recombination and selection revisited

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Decades of theoretical and empirical work have struggled to reconcile competing views on how evolution
shapes patterns of genetic variation. We now understand the genome as a mosaic molded by both neutral
and selective forces, but quantifying their relative contributions remains an open challenge. A major obstacle has been the tendency to analyze each evolutionary process in isolation, which is problematic
because they leave similar signatures on sequence data. Consequently, correlation-based analyses have
talked past each other. To address this gap, we develop structural equation models describing how mutation, recombination and selection jointly shape the genomic landscape of diversity. This approach offers a more realistic representation of biological interactions and enables rigorous evaluation of hypothesized causal structures, marking both conceptual and practical improvements over previous studies. Analyses of human data reveal large variation in the explanatory power of candidate models across chromosomes. We find that previous studies likely overestimated the predictive accuracy of background selection; although it emerges as the overall main driver of diversity, mutation rate variation has a comparable impact. We also show that recombination increases diversity more strongly through its impact on background selection than through its mutagenic effect, resolving a longstanding debate. We conclude that modeling molecular processes substantially improves our ability to explain the genomic landscape of diversity. At the same time, evidence for unmodeled covariance between mutation rates and density of constrained sites revives an ongoing discussion, although further studies are needed to determine its origins.

Genomic Language Models for DNA sequence Analysis

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Understanding evolutionary variation in genomic sequences through the lens of language modeling has the potential to revolutionize biological research. Afterall, DNA is a unique biological language. However, standard Large Language Models have limited applicability to DNA sequences. To maximize the utility of language modeling in genomics, we must develop novel tokenization strategies and model architecture adapted to diverse genomic features across evolutionary timescales. We investigated key elements in genomic language modeling (gLM), including tokenization, pretraining datasets, fine-tuning approaches, pooling methods, and domain adaptation, and applied the language models to diverse genomic data. We gathered two evolutionarily distinct pretraining datasets: one consisting of 19,551 reference genomes, including over 18,000 prokaryotic genomes (115B nucleotides) and the remainder eukaryotic genomes, and another more balanced dataset with 1,354 genomes, including 1,166 prokaryotic and 188 eukaryotic reference genomes (180B nucleotides). We trained five byte-pair encoding tokenizers and pretrained 52 gLMs, systematically comparing different architectures, hyperparameters, and classification heads. We introduce seqLens, a family of models based on disentangled attention with relative positional encoding, which outperforms relatively similar-sized models in 13 of 19 benchmarking phenotypic predictions. We further explore continual pretraining, domain adaptation, and parameter-efficient fine-tuning methods to assess trade-offs between computational efficiency and accuracy. Our findings demonstrate that relevant pretraining data significantly boost performance, alternative pooling techniques can enhance classification, tokenizers with larger vocabulary sizes negatively impact generalization, and gLMs are capable of understanding evolutionary relationships. These insights provide a foundation for optimizing gLMs for identifying diverse evolutionary genomic features and improving genome annotations.

Science Wise: Career mentorship through a storytelling interview podcast

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Abundant evidence supports that science is more innovative when performed by teams with diverse lived experiences and technical expertises, highlighting the importance that all motivated early career scientists are supported and encouraged. We present Science Wise, a podcast to support early career scientists to thrive by amplifying the unspoken truths, struggles, and triumphs of relatable experienced scientists. Through storytelling, we offer practical career guidance and preserve collective wisdom across generations—so that listeners not only see what's possible, but hear from those who helped make it so. Each episode of Science Wise shares the real-life journey of a scientist who has walked a path others now follow. Listeners gain access to career-shaping insights, honest personal stories, and practical strategies to help them navigate their own scientific careers—while honoring the legacy of those who came before. With the support of SMBE IDEA funding, we released a second season of Science Wise, featuring SMBE's own Dr Anne Stone. We additionally released an episode where experienced scientists responded to listener questions. We discuss some of the key lessons we've learned through extended interviews with 15 inspiring scientists, as well as the potential of podcasts to reach broader scientific audiences and beyond.

Genomic signatures of increasing disease burden in recent prehistory

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Diseases induce some of the strongest selection pressures experienced by human populations, leaving deep imprints in immune-related genomic regions. While individual pathogens mainly induce directional selection for resistance alleles, cumulative disease burden is expected to generate balancing selection that increases genetic diversity, particularly in the major histocompatibility complex (MHC). To identify temporal patterns of diversity change, we developed a new pipeline for extracting heterozygosity from ancient genomes, ImpHet, and validated it using a novel framework that mimics aDNA-specific biases by simulating sequencing read structures of ancient genomes. Using these methods, we estimated heterozygosity for 3,847 ancient individuals across all genes and genomic windows and quantified changes over the last 12,000 years, focusing on the cultural centers of Southwestern Eurasia and Eastern Asia. Although MHC genes compose <1% of all genes tested, more than 66% of genes showing significant increases in heterozygosity were located in the MHC, and rates of MHC heterozygosity increase were 16-fold (Southwestern Eurasia) and 7-fold (Eastern Asia) higher than genome-wide rates. Thus, the MHC emerges as the primary genomic region of recent diversity increase. Rates of change for individual genes were highly correlated between cultural centers (r = 0.91), indicating convergent genic-level selection pressures. Finer temporal analyses revealed pronounced peaks in MHC diversity increase around ~7,000bp, coinciding with settlement intensification, increased connectivity, and expanding animal domestication. These results suggest that the most intense disease burden followed the transition to sedentism but preceded urbanization, and support the hypothesis that disease burden increased substantially in recent prehistory.

Intraspecific diversity shapes functional variability of bats innate immunity

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Host-virus-environment interactions are critical drivers of immune evolution, yet their role in shaping intraspecific diversity in innate immunity remains poorly understood, particularly in reservoir hosts. Here, we investigated the contemporary evolution of innate immunity in six divergent bat species sampled across contrasted environments (metropolitan France, Gabon, French Guiana). By combining population-level sampling (n>15 /species), transcriptome-wide data, evolutionary analyses, and in vitro assays, we reveal, for the first time, pervasive intraspecific variation in key components of bat innate immunity.

Notably, two rapidly evolving and broad-spectrum antiviral effectors in bats, exhibit accumulation of nonsynonymous polymorphisms and indels that alter key domains for viral dsRNA recognition and enzymatic activity. Moreover, these changes map to positively selected coding sites targeted by viral antagonism. Importantly, we uncover marked contrasts between environments. In several tropical species, but not in metropolitan species, antiviral variants show significant signatures of balancing and positive selection, consistent with the adaptive maintenance of allelic diversity under heterogeneous and intense viral pressures. These patterns point to distinct selective regimes shaping immune evolution at the population level.

To assess the functional impact of this diversity, we are experimentally testing whether naturally occurring allelic variants differ in their antiviral activity during infection with bat-associated zoonotic viruses, including poxviruses, rotaviruses and Tonate virus.

Overall, our findings show that bat innate immune evolution is an ongoing, population-level process driven by contemporary viral pressures and environmental context, stressing the importance of population-based immunogenomics for understanding host-virus co-evolution and viral circulation in wildlife reservoirs.

A holocentric pangenome links karyotype evolution to meiotic recombination

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Chromosomal fissions, fusions and whole-genome duplications propel genome evolution, yet their impact on meiotic recombination is obscured by the centromere constraint, since in monocentric species most large rearrangements are lethal. Holocentric organisms, which distribute kinetochore activity along the entire chromosome, overcome this barrier and therefore offer a unique window onto the interplay between karyotype change and crossover control. We assembled chromosome-scale genomes for 20 holocentric Rhynchospora species (including 56 haplotypes), representing all major clades of the genus, featuring satellite-based holocentromeres, and integrated single-gamete crossover maps, high-resolution meiotic synapsis immunocytochemistry and Hi-C chromatin architecture. Breakpoint analysis shows that holocentromeric Tyba satellite arrays are recurrent hotspots for both chromosome fusions and fissions, contributing to the genus's extraordinary chromosome number variation from 2n = 4 to 36. Crossover landscapes group into two apparent modes: strongly distal-biased versus irregularly distributed, which is correlated with divergent patterns of synapsis elongation. Moreover, crossover number scales with chromosome count and meiotic axis length. In contrast, crossover density per megabase is inversely related to chromosome length and to chromatin-loop size. We propose that chromosome fissions create karyotypes with smaller chromosomes folded into shorter loops, thereby increasing the axial substrate accessible for double-strand break formation and elevating recombination frequency. Together, our results provide a structural link between large-scale structural chromosome evolution and meiotic recombination through coupled changes in chromosome number, size, loop geometry, and synapsis dynamics.

Massive genetic diversity loss within Asian elephant subspecies: new insights for determining conservation priorities

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In this study, we present a comprehensive genomic analysis of population structure, genetic diversity, and genetic load across the four recognized Asian elephant (Elephas maximus) subspecies using whole-genome sequencing data from 81 wild-born individuals. We reveal striking contrasts in inbreeding among subspecies. The Bornean elephant (E. m. borneensis) shows the highest inbreeding, with approximately 65% of the genome occurring in runs of homozygosity (ROH), and the lowest genome-wide heterozygosity, averaging ~46 heterozygous sites per 100 kb. The Sumatran subspecies (E. m. sumatranus) displays intermediate inbreeding (35% ROH) and heterozygosity (~101 sites per 100 kb), whereas the mainland and Sri Lankan subspecies (E. m. indicus and E. m. maximus) exhibit similarly low inbreeding (~10–11% ROH) and high heterozygosity (~130–134 sites per 100 kb). When ROH regions are excluded, heterozygosity levels converge across all subspecies (~136–155 sites per 100 kb), indicating that observed differences in genetic diversity are primarily driven by inbreeding-associated loss of heterozygosity rather than post-divergence accumulation of unique variation. Despite pronounced inbreeding, genetic load remains relatively low in all subspecies, including E. m. borneensis, particularly within highly conserved genomic regions, consistent with effective purging of deleterious alleles. The unexpectedly high genetic diversity of the island-dwelling E. m. maximus likely reflects historical gene flow associated with intensive human-mediated elephant trade, raising questions about its current taxonomic status. Given its extreme inbreeding and low genetic diversity, E. m. borneensis emerges as the highest conservation priority. Our results suggest genetic rescue as a viable management option, with limited risk of outbreeding depression.

Inferring ancestral alleles and signatures of selection in cattle from a pangenome graph

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Natural and artificial selection during cattle domestication have resulted in hundreds of breeds with distinct genetic and phenotypic characteristics. Accurate inference of ancestral and derived states at polymorphic sites enhances the statistical power to detect signatures of selection, thereby improving our understanding of cattle adaptive evolution. This study aims to predict ancestral alleles and identify selection signatures in the Brown Swiss cattle breed from a bovine pangenome graph. HiFi sequencing-based genome assemblies of 35 Brown Swiss individuals resulting in 31 primary and eight haplotype-resolved assemblies and six publicly available assemblies from other cattle breeds were integrated into a bovine pangenome. The resulting graph (~2.75 Gb) contained 24.1 million SNPs, 5.3 million Indels and 89 k structural variants. Clustering and phylogenetic analyses recovered the expected population structure, distinctly separating taurine from indicine lineages. To infer ancestral and derived allelic states of the pangenome variants, we aligned short read sequencing data from seven species to the graph, identifying 158.5 million biallelic sites for polarization. Subsequently, to reveal the genomic regions under selection in Brown Swiss cattle, long and short read data of 94 and 111 individuals in this cohort, respectively, were mapped against the pangenome. Ancestral allele sites, well-established statistical measurements (e.g., Tajima’s D, nSL, Fay and Wu's H and SweepFinder2) were used for signatures identification. This study provides a framework to integrate graph-based genotyping and ancestral state inference to enhance our understanding of how selection has influenced the cattle genome.

Genealogy-based analyses shows modern humans were formed through multiple deep admixtures

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Over the past decade, genomic data have revealed numerous admixture events among human populations. However, detecting admixture involving ancient groups remains extremely challenging, particularly in regions such as Africa, where ancient DNA is sparse. Here, we introduce GhostBuster, a method that leverages inferred genome-wide genealogies to detect and characterize hidden admixture events. GhostBuster robustly identifies admixture spanning the recent to deep past between ancestral modern human populations and archaic groups, while simultaneously enabling accurate local ancestry inference.

Applying GhostBuster to understand deep human history, we uncover three major events. First, we identify a series of Holocene-era back-to-Africa migrations involving at least three source groups, which introduced Eurasian and Neanderthal ancestry into all present-day African populations. Second, we detect ancient admixture between two deeply divergent African populations, one closely related to the lineage that later gave rise to all present-day non-Africans. These two ancient groups help explain genetic diversity and polygenic score portability differences within Africa, suggesting a younger out-of-Africa expansion consistent with fossil evidence. Finally, we infer that two populations present ~300 kya – 1 Mya, and possessing different recombination landscapes, admixed to form modern humans, with one group more closely related to both Neanderthals and Denisovans, and the other admixing into Neanderthals. Local ancestry segments allow us to corroborate each finding by revealing differences in mutational processes, recombination landscapes, and population diversity. Our results imply a series of ancient migrations both into and out of Africa and highlight the power of genome-wide genealogies to identify and characterize such events.

The multi-species ancestral recombination graph reveals admixture dynamics in a hybrid baboon population

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When populations diverge, they accumulate new, population-specific variation. In hybrids, these variants encounter each other for the first time and can act as reproductive isolating barriers. Current methods for inferring local ancestry cannot distinguish introgressed variants that arose post-split from those that were segregating in a common ancestor, limiting our understanding of reproductive isolation and selection against admixture. Here, we report a new hidden Markov model, iTRAILS, that infers gene trees using the coalescent with recombination, in the presence of both incomplete lineage sorting and gene flow. The resulting gene trees contain information about topology and coalescent times that can be used to time the origin of mutations (pre-split or post-split). We apply iTRAILS to hundreds of admixed genomes from an extensively studied hybrid baboon population in Kenya, aided by four new near–T2T baboon reference assemblies. We show that local ancestry estimates derived from iTRAILS gene trees generate a stronger signature of selection against admixture than other local ancestry inference methods. Further, incorporating coalescent time information from iTRAILS significantly improves predictions about which introgressed fragments will be retained over time. Introgressed genomic fragments tolerated in the hybrid population are enriched for deep coalescences—i.e., variation observed in the ancestral population—and depleted for gene trees with shallow coalescences in the minor parent (i.e., variation that arose in the minor parent post-split). Together, our results show that coalescent approaches can both improve estimates of selection against admixture and help identify regions of the genome that contribute to reproductive isolation.

Causes and consequences of sex-chromosome turnovers in Diptera

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Sex-chromosome systems are highly variable across animals, but how they transition from one to another is not well understood. Diptera have undergone multiple sex-chromosome turnovers and expansions while maintaining their general chromosomal content, which makes them an ideal clade to study such transitions. We analyzed more than 100 dipteran whole-genome assemblies and identified 4 new lineages that underwent sex-chromosome turnover (in addition to the 5 previously reported). We find that the majority of turnovers happened in the group Schizophora, which tend to have fewer genes on Muller element F. (the chromosome homologous to the ancestral insect X chromosome) than lower dipterans, a factor previously hypothesized to facilitate turnover. Most derived X chromosomes have higher GC content than autosomes, consistent with a high prevalence of male achiasmy in Diptera. In addition, an excess of gene movement out of the X is detected for most of these new X chromosomes, and many of these moved genes have high testis expression in Drosophila, suggesting that out-of-X gene movement contributes to the long-term demasculinization of X chromosomes.

Spatial proteomics reveals lipid droplet reorganization in symbiotic Paramecium bursaria cells

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Endosymbiosis is one of the major forces driving the evolution of eukaryotes. Complementation between the endosymbiont and the host enables the interacting partners to explore new niches or resources that are inaccessible to them when living alone. Despite its important role in evolutionary history, the cellular mechanisms that initiate and stabilize new symbioses remain poorly understood, as most modern partnerships are ancient and obligate, which makes the reconstruction of initial mechanisms extremely challenging. The flexible relationship between the ciliate Paramecium bursaria and green algae serves as a model system for studying the evolution of early endosymbiosis. Both ciliates and the endosymbiotic green algae can be cultured independently in the laboratory, suggesting that they are still at an early stage of endosymbiosis. Moreover, free-living green algae can be reintroduced into the hosts to establish endosymbiosis. Here, we use LC-MS/MS-based proteomics to generate a subcellular localization map of P. bursaria with and without endosymbionts. This atlas defines the protein composition of the endosymbiont-containing compartment (the perialgal vacuole) and reveals pronounced remodeling of host lipid droplets upon symbiosis. Imaging analyses confirm that lipid droplets change in size, morphology, and positioning, accumulating near intracellular algae. Perturbing symbiotic cells with chemical inhibitors of lipid metabolism reduces endosymbiotic algal numbers, revealing a role for lipid droplets in the host-endosymbiont interaction. Our data provide a comprehensive resource for protein localization in P. bursaria cells and elucidate how those cells remodel an existing organelle to maintain endosymbiosis.

Transposable Elements in Ant Macroevolution

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Transposable elements (TEs) are key contributors to genome evolution, yet their macroevolutionary role in the adaptive radiation of the ants remains poorly understood. We analyzed 163 ant genomes spanning 12 of 16 extant subfamilies to characterize TE impacts over the past 100 million years. We identify convergent TE bursts in ancestors of the most speciose ant clades, preceding rapid diversification following the Cretaceous–Paleogene extinction event approximately 66 million years ago. We demonstrate that TEs associate with expansions of olfactory receptors and other key gene families, and reveal striking compartmentalization of ant genomes into faster-evolving TE-rich and more conserved TE-poor regions. Our findings demonstrate the broad-scale impact of TEs on the structural evolution of ant genomes in the wake of ecological disruptions.

Investigating Parallel Adaptation to Altitude and Response to Climate Change in Neotropical Butterflies

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Neotropical butterflies offer an exceptional system to study repeatability of evolution across lineages facing similar selective pressures. Here, we investigate parallel adaptation to altitude across 12 species of the Heliconiini and Ithomiini clades to assess the extent to which adaptation is repeatable in this system. Historical constraints often limit repeatability, with the tension extending to the genetic level. Although some loci repeatedly underlie phenotypic evolution, forming “genetic hotspots” or showing gene reuse, the predictability of evolution at the genetic level varies across taxa. This predictability tends to decline with increased divergence, e.g., adaptation at the global level. However, local adaptation to replicated climatic gradients provides a clear mean of testing repeatability. Many species within our focus clades occur across a shared, extreme altitudinal gradient and are particularly well-suited for repeatability studies at the local level.

Members of these clades demonstrate strong turnover in species composition and abundance across the Andean slope. This reflects climatic clines. Together, these communities form natural “replay experiments,” enabling tests of whether similar genomic hotspots are repeatedly observed in adaptation to altitude and, hence, temperature gradients. Adaptive divergence has been previously demonstrated in Heliconius erato and melpomene across low- to highland populations. Utilising methods in evolutionary genomics, we extend this to study adaptive potential in response to environmental challenges in other members of these clades. The results will prove crucial in understanding Lepidopteran response to global warming, and more broadly, climate change.

VIEWING IMMUNITY IN THE CONTEXT OF AGEING AND EVOLUTION

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Evolutionary theory predicts that the strength of natural selection wanes in late life and becomes negligible beyond the reproductive window. During this period, harmful mutations can accumulate, accelerating ageing, characterised by an overactive immune system that causes immunopathology, along with higher morbidity and death rates. The question is: why doesn't natural selection eliminate these harmful age-specific maladaptive traits of immunity? To answer this question, we used experimentally evolving populations of Drosophila melanogaster with divergent reproductive schedules and ageing rates, exploring whether the rate of immune ageing coevolves with the rate of reproductive senescence. Does immune senescence appear earlier in early-reproducing and early ageing populations? Our findings support this prediction, showing that populations achieved their highest post-infection health near their respective reproductive peak, followed by a steady decline. In a following transcriptomics study, we found both qualitative and quantitative declines in immune function beyond reproductive ages. Maintaining optimal immune regulation is crucial for health after infection, but responses often become less specific with ageing, as shown by increased expression of Toll-pathway-induced antimicrobial peptides (AMPs) and melanisation cascade targeting Gram-negative bacteria such as Providencia rettgeri. Simultaneously, there is a decline in effectors like IMD-regulated AMPs, which previously provided specific protection against the pathogen at younger ages. This decline in immune efficiency may lead to higher mortality after infection in older flies. Our findings thus offer a rare evolutionary framework for understanding why immunity and post-infection health decline with age, paving the way for detailed molecular studies of the regulatory networks involved.

Polygenic traits adaptation leads to selection of beneficial alleles in local regulatory hubs

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Polygenic traits are involved in many key processes such as adaptation to local environments in many eukaryotic species. Deciphering their genetic architecture is key for understanding how they are inherited and how they may evolve. Polygenic traits expression is tightly controlled, and mediated through a complex, interconnected gene regulatory network, explaining the high levels of both pleiotropy and epistasis observed in polygenic traits genetic architecture. The pervasive pleiotropy raises questions on the extent to which a specific polygenic trait can evolve without causing catastrophic consequences on others. This theoretical limitation runs contrary to the many examples available in various mammals, insect and plant species (immunity, metabolism, flowering). In this study, we hypothesized that the fact that biological regulatory networks are highly structured may help confine the effect of mutations in terms of function, localization and timing.
We inferred 29 tissue-specific regulatory networks based on expression Quantitative Trait Loci derived from the GTEX datasets, and systematically analyzed the distribution of the heritability for eleven traits across those networks. We demonstrated that heritability is clustered in a small number of tissue-specific, functionally relevant modules, and preferentially carried by local regulatory "hubs". These hubs are also the preferential targets of past polygenic selection events. The structuration and tissue-specificity of regulatory networks allows for the amplification of the beneficial effects of a mutation at a local regulatory hub on a specific pathway in a given tissue, and the buffering of its deleterious effects elsewhere, explaining why they are often selected during polygenic traits adaptation.

Bacterial dynamics of evolution tracked by barcodes over 20,000 generations validate a century of theoretical models of adaptation

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In asexual bacterial populations, long-term adaptation relies on the accumulation of multiple beneficial mutations. Understanding the dynamics of this process has been a central question in population genetics for over a century. Researchers have developed a range of models, each proposing different adaptive regimes. These regimes vary according to the rate at which beneficial mutations arise and their selective effects.
Using genetic barcodes, we analysed the adaptive dynamics in a long-term evolution experiment spanning more than 20,000 generations of laboratory adaptation. Our findings show that the observed dynamics align with the regimes predicted by a century of theoretical models. Furthermore, by combining microfluidics with deep mutational scans of key adaptive genes, we identify potential mechanisms driving transitions between these regimes.

Unwanted evolutionary rescue: bidirectional adaptive introgression of pesticide resistance genes between native and invasive Helicoverpa crop pests

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Human activity alters selection pressures and redistributes biodiversity, creating opportunities for hybridization through secondary contact. It is now well-established that ancient hybridization plays an important role in adaptive radiation, but its role in recent anthropogenic adaptation remains unclear. We investigated this in a study of hybridizing native and invasive Helicoverpa moths in Brazil: native H. zea, which has recently evolved Bt resistance and is better adapted to maize as a host plant, and H. armigera, which is resistant to pyrethroid pesticides and is better adapted to soybean as a host plant. Using a decade-long time series of 975 genomes from both species, we demonstrate rapid, bidirectional adaptive introgression of structural variants that cause resistance to two distinct pesticides. In one direction, a pyrethroid resistance gene from H. armigera (CYP337B3) is now almost fixed in native H. zea. This gene arose in H. armigera by a small deletion combining the exons of adjacent genes to form a de novo detoxification enzyme. In the other direction, ~30% of invasive H. armigera carry a H. zea-derived trypsin repeat cluster. Using controlled crosses, we show that this trypsin repeat cluster confers resistance to Bt (Cry1Ac) soy in the H. armigera genomic background. Thus, hybridization has combined H. armigera adaptation to soy with H. zea Cry1Ac resistance to facilitate exploitation of a vast anthropogenic landscape: Brazilian Bt soy monoculture, which exceeds the area of Germany in size. We therefore show that evolutionary rescue can drive rapid anthropogenic adaptation via combinatorial evolution.

Detecting local adaptation to biotic and abiotic environmental conditions in the cosmopolitan ectomycorrhizal fungus Cenococcum geophilum

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Local adaptation of ectomycorrhizal fungal populations has been rarely investigated despite their critical role in providing nutrients and water uptake to forest trees. Understanding how these symbiotic organisms adapt to environmental variation is crucial given accelerating climate change and their role in the species-rich soil microbiome. Cenococcum geophilum represents an ideal study system as the most widespread generalist ectomycorrhizal fungus in temperate and boreal forests, persisting across steep environmental gradients. Using population genomics and genome-environment association (GEA) analyses of 83 whole-genome resequenced strains, we investigated genetic structure of naturally occurring C. geophilum populations and patterns of local adaptation to biotic and abiotic conditions. Population genetic analyses revealed geographic structuring, genetic recombination, and balanced mating-type idiomorph distribution within sampled sites. We also found fast linkage disequilibrium decay across chromosomes, reinforcing the support for frequent sexual reproduction. Based on structure-corrected univariate and multivariate models, we identified adaptation to biotic (vegetation-derived predictors) and abiotic (climate and soil) factors with different selection strengths. Candidate adaptive regions encompassed both single nucleotide polymorphisms (SNPs) and structural variations (SVs), with functional annotations revealing genes involved in osmotic stress response, melanin biosynthesis, and secondary metabolite production. Our findings demonstrate that selection signatures emerged in populations with heterogeneous soil conditions and repeat-rich genomes (78% transposable elements), challenging assumptions that genetic drift dominates in such systems. This work underscores the importance of understanding adaptation in symbiotic species navigating the complex soil environment under intensifying climate-driven selective pressures.

ratePlacer: A Phylogenetic Framework for Molecular Dating of Ancient Environmental DNA

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Ancient environmental DNA (aeDNA) from permafrost, lake and marine sediments provides a rich source of genetic data that captures broad perspectives of past biodiversity. Accurate dating is crucial for discovering ecologically relevant patterns from aeDNA, and increasingly samples are too old for C-14 dating. While molecular dating allows for sample ages to be estimated from the recovered genetic material itself, the fragmented and damaged nature of short-read ancient DNA from multiple taxonomic sources poses significant challenges. We have developed ratePlacer, a phylogeny-based method for analyzing aeDNA that can combine information from many short reads in a sample while accounting for DNA damage to provide maximum likelihood estimates of sample ages. Simulations demonstrate that ratePlacer accurately dates samples even under the fragmented, damaged conditions characteristic of aeDNA and outperforms tip dating methods like BEAST for taxonomically mixed samples commonly found in aeDNA. However, applying ratePlacer to exceptionally old sediment samples revealed previously uncharacterized substitution patterns that substantially complicate molecular dating. These patterns deviate from typical ancient deamination damage, suggesting that aeDNA should be carefully evaluated in future genomic and evolutionary analyses.

Learning protein interaction origination and evolution with sequence-based machine learning

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Proteins functions through dynamic and evolutionarily constrained interaction networks, yet the molecular basis of many protein–protein interactions (PPIs) remain poorly characterized. Sequence-based structural models such as ESMFold and AlphaFold2-Multimer leverage evolutionary signals in protein sequences to infer structural and functional interactions from mechanistic to network scales. Here, we apply AlphaFold2 Multimer to systematically predict 30,000 PPIs in Drosophila by integrating physical interaction datasets with functional association networks that reflect shared evolutionary and biological constraints. We find that incorporating functional associations substantially improves the confidence, coverage, and interpretability of predicted protein complexes. Structural analyses further reveal that rapidly evolving and weakly conserved intrinsically disordered regions play a pervasive role in mediating high-confidence interactions across the network, highlighting how functional constraints can preserve interaction capacity despite sequence divergence.

Beyond large-scale network inference, we show that these models can illuminate the evolutionary origins of specific molecular interactions. Using ancestral sequence reconstruction together with AlphaFold2 and molecular dynamics simulations, we demonstrate that a recently evolved ligand–receptor interaction, the Drosophila sex peptide–sex peptide receptor pair, can be structurally supported by ancestral receptor states predating the ligand's emergence. These analyses reveal that only a small number of amino acid changes are sufficient to enable novel interactions and that new ligand specificity can arise through the co-option of preexisting interaction interfaces. Together, our results demonstrate how deep learning models can bridge interaction networks to individual binding interfaces, providing mechanistic insight into how evolutionary forces shape protein interactions and cellular function.

Reconstructing the genomic history of Ice Age grey wolves

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Among large carnivores, the evolution of grey wolves from the Late Pleistocene to the present-day represents one of the most striking examples of adaptability. Grey wolves have survived the widespread large mammal extinctions of the late Pleistocene while maintaining a vast range across different climates in Eurasia and North America, and gave rise to the first species to fully adapt to an anthropogenic niche through domestication. Strong and widespread gene flow throughout Holarctic wolves is thought to have contributed to the resilience of this species, yet this striking connectedness is poorly understood. Here we generate new genomes for 45 ancient grey wolves, for a combined dataset of 135 ancient Holarctic wolves. Using a mitochondrial phylogeny, we estimate the ages of undated samples and extend the temporal range of wolf palaeogenomes into the Middle Pleistocene. In accordance with a previous study, we find evidence for several rapid genomic ancestry transformations across Holarctic wolves in the past hundred thousand years, including through the expansion of wolves from Siberia. By time-stratifying our dataset, we investigate the extent and directionality of gene flow between regions, as well as the geographic and temporal origins of dog ancestry. We also use a deep time series of wolves in the Altai Mountains to compare the continuity and genomic diversity of grey wolves between northern and southern Siberia. Overall, grey wolf evolution during the Late Pleistocene is characterised by strong gene flow and ancestry turnovers, which likely contributed to the adaptation of grey wolves to changing environments.

ARIA's Accelerating Adaptation programme: Engineering Resilience in a Changing World

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Environmental pressures now exceed the ability of species and ecosystems to adapt, such that over 25% of species now risk extinction within a century. This potential loss creates existential threats to the natural capital and ecosystem services that underpin our societies. Humanity must urgently reduce environmental pressures and expand well-established nature protection strategies. However, those efforts may prove insufficient given the pace and scale of change.

As a complementary approach, ARIA's £54m "Accelerated Adaptation" research programme aims to enable wild species to rapidly overcome the threats they face. This should help both focal species and their ecological communities to survive. Interdisciplinary teams will initially focus on single species-stressor pairings, employing a spectrum of approaches that range from physiological priming and multi-generational selection, to inducing transient phenotypic traits via molecular tools, through to strategic gene editing.

The programme's second phase scales successful approaches into platform technologies. By leveraging automation, robotics and AI phenotyping we aim to reduce costs and increase throughput 10-fold, enabling support for entire functional groups rather than individual species.

All programme work occurs in strictly confined conditions. We prioritise responsible research practices throughout, with dedicated attention to and research on ethics, social licence, governance frameworks, and societal implications. Parallel workstreams will develop predictive models to estimate risks and ecosystem-scale impacts. By creating generalisable capabilities to accelerate adaptation in wild species, this programme aims to establish evolutionary biology as a foundation for ecosystem resilience engineering—a new toolkit to enhance conservation and ultimately enable both nature and humanity to thrive.

The Gene Regulatory Evolution of the Human Skeleton

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Skeletal modifications were central to deep human evolution, facilitating upright locomotion and large brains, and influencing childbirth and our distinctive limbs. Despite their importance, the regulatory networks underlying human skeletal divergence remain poorly characterized. Here, we systematically map human-specific skeletal gene regulation. Using massively parallel reporter assays (MPRAs) in chondrocytes, we synthesized and assayed 561,410 fixed human-derived single-nucleotide variants in promoters and enhancers, identifying 15,077 loci with human-specific regulatory activity. We then generated human-ape hybrid cells and differentiated them into osteochondral progenitors. The combination of these complementary approaches enabled a multi-level investigation of the mechanisms underlying cis-regulation, from the single regulatory element through genes and pathways to phenotypes. Integrating the hybrid system with MPRA measurements yielded a genome-wide atlas of human-specific cis-regulatory expression changes, and the sequence changes that drove them. This atlas reveals extensive divergence affecting molecular networks such as Hedgehog signaling and extracellular matrix biosynthetic pathways, with pronounced downregulation of polysaccharide (glycosaminoglycan) biosynthesis likely shaped by lineage-specific selection. We further validate this reduction in polysaccharide content in human compared with chimpanzee cartilage, and propose that this shift might underlie the particularly elevated susceptibility of humans to degenerative joint diseases. Together, our results reveal coordinated regulatory remodeling of the skeletal extracellular matrix during deep human evolution and provide a comprehensive resource for studying how human skeletal biology was shaped by evolution.

Have arctic wolves adapted to the arctic environment?

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Grey wolves occupy a range of habitats, one of the most extreme of which is inhabited by the wolves in Greenland and the Canadian Arctic Islands. We hypothesise that the arctic environment has exerted strong selection pressure on arctic wolves, creating the potential for local adaptation. However, arctic wolf populations are known to be strongly bottlenecked, thus complicating detection of positive selection. Previous analysis of SNP array data found evidence of adaptation to the environment in arctic wolves, but this has not yet been explored with whole genomes.

Here, we integrated newly sequenced and previously-published whole genomes of wolves from Greenland, the Canadian Arctic Archipelago and North America to address this question. We used joint genotype imputation to increase the power and resolution of selection scans. Despite arctic wolves being underrepresented in and divergent from the majority of wolves in the reference panel, our benchmarking analysis indicated good imputation performance.

We next explored the demographic history of arctic wolves, to determine the strength of the bottleneck and population structure. We find low differentiation between Greenland and Ellesmere Island wolves using FST, and so we consider them as one population for the selection analyses. To detect signatures of selection, we used a range of techniques, including classical approaches based on population comparisons (PBS and XP-EHH), alongside ancestral recombination graph construction and assessment of local topologies. Preliminary PBSn1 analysis identified outlier genes related to muscle, collagen and the visual and olfactory pathways, as candidates of selection, in Greenland and Ellesmere wolves.

Transcription, Replication, and Recombination Shape Local Mutation and Sequence Variation at Human TSSs

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Transcription start sites (TSSs) of human genes are characterized by elevated GC-content, a pattern observed for decades, but the mechanisms shaping this local nucleotide landscape remain poorly understood. Why do TSSs accumulate GC, and how is this affected by local mutation rate biases? To address this, we analyzed population-scale polymorphism data and de novo mutations from parent-offspring trios, mapping mutations at single-nucleotide resolution around TSSs. We discovered that mutation rates peak sharply at TSSs, particularly at highly transcribed genes in the germline [Qiu et al., 2025]. Similar patterns are seen for long noncoding RNAs and RNA polymerase II pause sites. Comparing observed nucleotide composition with expectations from mutation alone, we highlight the contribution of GC-biased gene conversion (gBGC), a recombination-linked process that affects which mutations persist in shaping local GC-content. Forward simulations indicate that the combination of local mutation biases and gBGC, rather than selection, explains the nucleotide patterns at gene starts. At the level of individual genes, an XGBoost-based analysis identifies three classes with distinct GC-content, mutation rates, and genomic features. Genes with high GC-content often carry origins of replication and CpG islands, and experience elevated mutation rates, likely due to conflicts between transcription and replication machinery. Genes lacking these features show lower mutation rates and GC-content. Together, these findings suggest that the familiar GC peak at TSSs emerges from the interplay and conflicts of transcription, replication, and recombination. We provide a mechanistic explanation for a long-observed genomic feature and show how local mutation landscapes shape human gene evolution.

Ancient DNA and functional genomics retrace the path to modern chicken productivity

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Chicken is the world's most consumed source of animal protein, yet intensive production emerged only within the last ~100 years, accelerating after World War II as specialised broiler and layer lines were established. Modern commercial lines were largely developed in the 1960s by breeders in North America and Europe using genetic material from European flocks effectively transforming them into modern commercial stock. Chickens, however, were domesticated in tropical Southeast Asia over 3,500 years ago and spread to Europe by ~2500 years ago. Their expansion into temperate Europe likely required substantial phenotypic change, the genetic basis of which remains poorly understood. In fact, despite major advances in breeding over the last century, the extent to which the distinctive genetic makeup of European chicken populations, shaped by over 2,000 years of selection, outside of their ancestral range, and 19th-century admixture with East Asian populations, provided the standing variation required to establish modern high-productivity lines remains unclear. To quantify the impact of ancient and recent selection on the genomic and phenotypic evolution of European chickens, our consortium assembled a dataset comprising >5,000 genomes, including 134 ancient nuclear genomes spanning over 2,000 years, as well as >7,000 bulk, and 127,000 single-cell RNA-seq profiles. These data allow us to resolve the timing and number of introductions into Europe, identify genetic bases of adaptation to temperate environments, and quantify shifts in selection intensity leading to modern high-productivity lines.

What sets the upper bound on animal cell size?

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Molecular interactions play out within the physical arena of the cell. Animals with extremely large cells are rare – why? What constrains cell size? I address this question using salamanders; they have evolved cells <50x larger than other vertebrates, alongside gigantic genomes and nuclei. When cells and nuclei are large, intracellular distances are long. We modelled RNA diffusion out of the salamander nucleus to quantify delays in gene expression. We show that the extra time it takes RNA to diffuse to the nuclear envelope introduces delays that slow oscillatory gene expression kinetics, providing an explanation for the slow rate of salamander embryogenesis. Using phylogenetic comparative methods, we show that cells are constrained to smaller sizes when life history includes the time-sensitive, vulnerable developmental transformations of metamorphosis. Using electron microscopy, we show that salamander organelles scale proportionately with cell size, with no substantial changes in shape or network structure required to maintain functionality. This proportional scaling is consistent with organellar building blocks being incorporated from a constant cytoplasmic pool (limited precursor model). Although simple, this model requires protein concentration homeostasis in salamanders' large cytoplasmic volumes. Notably, experimentally induced large cells show proteome dilution from insufficient biosynthesis. We show that half-lives of RNAs and proteins are longer in large cells to accommodate longer transit times; we posit that this slow turnover also 1) maintains protein concentration homeostasis, and 2) lowers metabolic cost. Thus, slow molecular turnover overcomes some challenges, but slow gene expression kinetics and effects on development nevertheless constrain cell expansion.

Spontaneous mutation rate and spectrum are modulated by organismal fitness

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Understanding the principles governing mutagenesis is important because mutations are a fundamental driver of evolution and a cause of disease. Although mutation rates and spectra depend on genotype and environment, how these factors interact is unclear. We address this question using mutation accumulation experiments in 11 budding yeast strains across three environments that produce strong genotype-by-environment interactions in fitness. Analysis of over 9,000 accumulated mutations reveals that per-generation rates of all mutation types—single-nucleotide variations, small insertions and deletions, segmental duplications and deletions, and chromosome gains and losses—decline with increasing organismal fitness. Notably, relative mutation rates between strains tend to invert when environmental shifts reverse their relative fitness. The mutation spectrum is also partially fitness-dependent: higher-fitness strains show a lower transition-to-transversion ratio and a stronger AT mutational bias. Thus, organismal fitness shapes not only natural selection but also the quantity and composition of mutations available to selection, with broad implications for the molecular clock, adaptive evolution, and genetic load.

A deep-learning-based score to evaluate multiple sequence alignments

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Multiple sequence alignment (MSA) inference is a central task in molecular evolution and comparative genomics, and the reliability of downstream analyses, including phylogenetic inference, depends critically on alignment quality. Despite this importance, most widely used MSA methods optimize the sum-of-pairs (SP) score, and relatively little attention has been paid to whether this objective function accurately reflects alignment accuracy. Here, we evaluate the performance of the SP score using simulated and empirical benchmark alignments. For each dataset, we compare alternative MSAs derived from the same unaligned sequences and quantify the relationship between their SP scores and their distances from a reference alignment. We show that the alignment with the optimal SP score often does not correspond to the most accurate alignment. To address this limitation, we develop deep-learning–based scoring functions that integrate a collection of MSA features. We first introduce Model 1, a regression model that predicts the distance of a given MSA from the reference alignment. Across simulated and empirical datasets, this learned score correlates more strongly with true alignment accuracy than the SP score. However, Model 1 is less effective at identifying the best alignment among alternatives. We therefore develop Model 2, which takes as input a set of alternative MSAs generated from the same sequences and predicts their relative ranking. Model 2 more accurately identifies the top-ranking MSA than the SP score, Model 1, and several widely used alignment programs. Using simulations, we show that selecting MSAs based on our approach leads to more accurate phylogenetic reconstructions.

Following the process of sunflower domestication through space and time with ancient DNA

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Where and how many times crop plants were domesticated, how quickly genetic diversity is lost during domestication, and how domestication syndromes are assembled through polygenic evolutionary change are questions of active research and frequent debate. We are addressing these questions with archaeological DNA approaches in the common sunflower, Helianthus annuus. Native American farmers living ~5000 years ago began transforming sunflower from a highly branched wild plant with small disks and seeds into a staple oilseed crop with a large head and large seeds on an unbranched stalk. We have assembled a time series of archaeological samples spanning from ~3800 to ~400 years before present and obtained endogenous DNA sequences from these samples through genome resequencing and sequence capture approaches, revealing how human cultivation altered sunflower genetic diversity through time. We find evidence of shifting agricultural practices, as revealed by multiple genetic bottlenecks and changes in crop-wild gene flow. Our analyses also resolve a longstanding controversy about where and how many times sunflower was domesticated. Through targeted resequencing of ~425 candidate genes, our archaeological time series reveals the timing and order of selective sweeps, providing insight into how the sunflower domestication syndrome was assembled through time. Finally, ~1300 years before present, we observe concurrent shifts in morphology, gene flow from wild into cultivated sunflower, and selective sweep frequency. We interpret these temporally coinciding shifts as signatures of a period of more relaxed selection, likely reflective of reduced cultural connectivity and/or the regional expansion of maize agriculture at this time.

Evolutionary and Functional Consequences of W–Autosome Fusions in Heliconius Butterflies

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Fusions between sex chromosomes and autosomes can resolve sexual conflict, drive local adaptation, and promote reproductive isolation, thus warranting particular attention in evolutionary genomics. Heliconius butterflies typically exhibit a stable karyotype of 21 chromosomes with strong synteny across species; however, three species in the sapho subclade show deviations, with chromosome counts reaching up to 64. We generated 11 chromosome-level reference genomes and gene annotations for six of the seven species and subspecies in this subclade. Our findings confirm three W–autosome fusions we had previously suspected based on whole-genome resequencing and reveal an additional fusion in two subspecies of H. eleuchia. Analysis of the chromosome-level genomes shows that, in three species, the autosomes have undergone extensive fissions, increasing chromosome number. The Z chromosome remains conserved across species. In contrast, W–autosome fusions involve complex structural rearrangements, including translocations, inversions, and further fissions of the neo-W chromosome. Despite these rearrangements, chromatin compartment organization remains largely unchanged. Genes located on the neo-W show signs of gradual degeneration, with 50% genes disrupted or lost on the oldest fusion and 24% on the youngest. We find no evidence that lost genes on the neo-W are compensated through dosage compensation mechanisms. Interestingly, despite the overall degeneration of the W chromosome, some genes—such as the W-specific rhodopsin—remain present even on the older W-autosome fusion. Together, these results reveal the evolutionary, structural, and functional consequences of W–autosome fusions in Lepidoptera over time.

Evolutionarily dynamic enhancer transcription links chromatin regulation to drought response in rice (Oryza sativa)

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Understanding how gene regulation evolves is central to explaining phenotypic diversity and environmental adaptation. While enhancer RNAs (eRNAs) are widely used as markers of active regulatory elements in animals, their prevalence and regulatory roles in plants remain poorly characterized. Here, we integrate condition matched functional genomics datasets generated under drought and well-watered conditions to characterize enhancer transcription and its contribution to drought responsive gene regulation in Oryza sativa.

We generated high-resolution maps of nascent transcription using PRO-seq in well-watered and drought-stressed rice seedlings and applied the dREG machine-learning framework to systematically identify bidirectionally transcribed regulatory loci. This analysis revealed over 42,000 transcriptional regulatory elements, including more than 12,000 loci uniquely active under drought. The majority of drought-responsive loci were intergenic and exhibited canonical enhancer features, including open chromatin and enrichment of active histone modifications, as supported by ATAC-seq and ChIP-seq datasets. After filtering, we defined a curated catalogue of ~9,700 putative intergenic eRNAs. Motif analyses revealed enrichment for transcription factors implicated in abiotic stress responses, while Pore-C identified eRNA producing loci forming physical contacts with drought responsive gene promoters. Genes engaged in these enhancer-promoter interactions showed significantly stronger transcriptional induction under drought compared to expression matched controls. Notably, drought induced eRNAs were modestly but significantly enriched near young transposable elements, with indications that TE exaptation may contribute to the emergence of stress responsive enhancers in plant genomes.

Together, this integrative dataset provides a genome wide basis for studying enhancer transcription, genome architecture, and regulatory evolution in a major crop.

Frequency-dependent immune selection in tumors inferred from neoantigen depletion patterns

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Despite abundant evidence that immune surveillance shapes cancer development and growth, the timing and triggers of immune recognition during tumor evolution remain largely unknown. Mutations in cancer cells can generate novel peptides (neoantigens) that the immune system recognizes as foreign, leading to killing of cells expressing recognized neoantigens. To test potential recognition mechanisms, we compare forward simulations of tumor growth with tumor sequencing data from immunosuppressed and immunocompetent patients. In our simulations, a fraction of mutations create neoantigens, the immune system stochastically recognizes individual neoantigens, and cells carrying recognized neoantigens experience immune killing. We simulate three recognition scenarios: (1) no immune recognition (neutral baseline); (2) immediate recognition upon neoantigen appearance (constant selection); and (3) recognition triggered once a neoantigen-bearing lineage exceeds an abundance threshold (frequency-dependent selection). To compare simulations with data, we compute the ratio of neoantigenic to neutral passenger mutations across allele frequency bins within tumors. The neutral and constant-selection models predict approximately flat ratios across frequencies, whereas the threshold model generates relative depletion of neoantigens at high frequencies. This predicted depletion pattern is qualitatively consistent with observed data, while the alternative models are not. We are now quantitatively fitting the threshold model to estimate how recognition thresholds and killing strength vary with neoantigen quality and patient immune status. This work demonstrates that evolutionary modeling can distinguish among competing hypotheses for immune recognition dynamics using standard single-time-point tumor sequencing data.

Bacterial Disease and Viral Emergence in Holocene Hunter-Gatherers from Patagonia

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Patagonia was the last mainland territory of the Americas to be populated by humans ~ 14,000 yBP. The recovery of ancient pathogen genomes from this region offers a valuable perspective to explore the local impact of infectious diseases and their evolutionary processes. This study recovered ancient DNA (aDNA) from 32 individuals from Central Patagonia dating around 6000-100 yBP. We generated paleogenomic data, performed metagenomic characterization, and recovered one Hepatitis B virus (HBV) genome (6.8 X, 1,500 yBP) and four genomes of a leprosy-causing pathogen, Mycobacterium lepromatosis (1.1-16.2X, 4,000–100 yBP). Phylogenetics and recombination analyses of the extinct South American HBV lineages identified ancient American genomes that may have contributed to the diversification of modern H and F genotypes. Our recovered ancient HBV genome allows for a new calibration point for estimating the recombination rate and lineage split times. In parallel, we analysed ancient M. lepromatosis genomes, representing the oldest and southernmost lineages recovered to date. Their phylogenetic placement indicates an affinity with human-associated strains, suggesting a millennia-long pathogenic relationship between humans and M. lepromatosis, and adding additional calibration points to date the divergence from M. leprae, the other causative agent of leprosy. We evaluated the presence/absence of virulence genes in ancient and modern clades, as well as missense and stop-lost mutations with functional impact. Furthermore, we propose a hypothesis for the spread of M. lepromatosis to Europe and its establishment in red squirrels reservoirs. Together, these results provide an evolutionary perspective on the dynamics in ancient pathogens in the Americas.

Mutation bias is a key predictor of adaptation rate

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A growing body of work shows that mutation bias — whereby some types of mutations occur more often than others — can influence the genetic basis of adaptation. Recent studies further suggests that shifts in mutation bias can alter the distribution of fitness effects of new mutations. For instance, reversing an ancestral mutation bias (e.g., in Escherichia coli, shifting from a transition-biased to a transversion-biased mutation spectrum via loss of different DNA repair genes) enhances access to under-sampled variants, increasing the beneficial mutation supply. But are these effects strong enough to alter adaptive outcomes? We show that mutation bias reversal indeed facilitates early adaptation of E. coli, with reversed-bias strains outperforming reinforced-bias strains ~4x more often. Together, mutation bias, mutation rate, and initial fitness correctly predict adaptation rate rank for almost any pair of strains in different growth media. The adaptive benefit of bias reversal also leaves clear genomic signatures, with at least twice as many beneficial mutations, greater mutational parallelism, and distinct types of substitutions. Overall, mutation bias strongly influences the genetic basis of adaptation, and alters the type of accumulated genomic mutations that could shape subsequent evolution. Our results show that mutation bias is critical to predict the evolution of mutators, and highlight multiple ways in which mutational processes can shape the genetic and phenotypic outcomes of adaptation.

Genome-Wide Association Analysis reveals insights into Escherichia coli adaptation to specific clinical niches

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Escherichia coli is a genetically and ecologically diverse species whose evolutionary success is driven by extensive genome plasticity and frequent horizontal gene transfer. This diversity enables rapid adaptation to contrasting niches, ranging from gut commensalism to invasive extraintestinal disease. This shift in pathogenic potential is largely driven by the accessory genome, which encodes virulence and resistance factors that promote survival in diverse environments.

Here, we applied a phylogenetically stratified genome-wide association study (GWAS) based on gene presence-absence across a large and ecologically heterogeneous collection of E. coli genomes isolated from adult and neonatal bloodstream, urinary tract infections, hospital settings, and non-clinical environments. By explicitly controlling for population structure, we identified lineage-independent genetic associations, allowing us to infer signatures of niche-specific selection acting on the accessory genome.

Bloodstream and urinary isolates were significantly enriched in genes involved in metal acquisition, adhesion, biofilm formation, and stress responses, highlighting shared adaptations for survival in hostile host environments. Neonatal bloodstream isolates showed a strong association with the yersiniabactin iron-scavenging system. In addition, antibiotic resistance genes and mobile genetic elements were significantly overrepresented in hospital and urine derived isolates, underscoring the role of clinical settings as reservoirs for antimicrobial resistance.

These findings show that E. coli adapts to distinct ecological and clinical niches through the acquisition and maintenance of functionally relevant genes independent of phylogenetic background. Source-specific genetic traits identified here provide valuable insights into E. coli pathogenesis, and offer potential biomarkers for diagnostics, surveillance, and targeted intervention strategies.

Haplotype specific structural variation within a single human genome

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T2T complete chromosomal assemblies offer new avenues to study genome rearrangement and copy number variation in human populations. With new highly contiguous haplotype-resolved genomes, we can now identify variation in gene content and gene organization within a single individual across maternal and paternal haplotypes. Using genes as anchors to identify common genomic coordinates, we identify breaks in synteny that correspond to inversions, deletions, and gene family expansion. Our new method, STUNG, is available as a user friendly software with interactive GUI. This computational approach serves as a useful template for analysis of emerging T2T haplotype resolved genomes in the future. We identify inversions, deletions, duplications that drive differences in gene content even across the two haplotypes for a single individual. Among these include very large gene families (with over 50 gene members) previously intractable for copy number analysis with precision. We are able to fully resolve copy number for these large gene families across each haplotype, revealing variation that otherwise would be impossible to nail down. We further identify rapidly evolving gene families known to be unique primates with known copy number variation in humans now even with variation within a single individual. These results point to very rapid changes in duplicate gene content within human populations including genes with known clinical relevance. With this increased resolution and haplotype precision we can gain greater understanding of how copy number changes and rearrangements evolve within populations and how they contribute to genotype diversity for individuals.

A simulation framework for the study of population-level processes in phylogenetics

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Phylogenetic approaches offer a way to infer the direction and efficacy of selection based on sequence divergence between sequences of divergent species, which are each represented by a single sequence. Here, the representation of species by a single sequence means that genetic variation within species that lie at the heart of population genetics theory are ignored within classical phylogenetic methodology. In formal terms, the ignorance of intra-species genetic variation implies that any influence of population-level processes on sequence evolution is compressed within the probability of fixation. This simplifying assumption permits efficient computational implementation of phylogenetic methodology, but the impact of population-level processes on phylogenetic inference remains to be established. To progress in this direction, we have first formulated a mathematical framework of stochastic reproduction-selection models that jointly describe polymorphism within species and divergence between species. This enabled us to show analytically that estimates of selection with traditional phylogenetic methodology can be significantly biased by population-level processes even under equilibrium conditions. Then, to complement the analytical work and progress towards methodological developments, we have implemented a simulation framework of population-genetic forward simulations in a phylogenetic context that enables us to study the impact population-level processes in phylogenetic inference also under more complex non-equilibrium conditions. The simulation framework has been implemented as a software suite accessible to the community, where the generation of simulated data permits evaluation of robustness and sensitivity of phylogenetic methodology as we as development of methodology that accounts for population-level processes in the inference of selection.

Mechanisms for how cis-regulatory elements arise from transposable elements illustrated by repeated domestication in snake venom genes

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Transposable elements (TEs) can be co-opted into functional cis-regulatory elements (CREs) that regulate gene expression, yet the generalizable mechanisms underlying this process remain poorly understood. Here, we describe how the regulatory potential of TEs is dynamically shaped by predictable, repeatedly evolving, and broadly generalizable sequence features. We leverage the genomics of rattlesnake venom systems, a rapidly evolving phenotype with multiple independent opportunities to observe regulatory evolution, to investigate this process. We integrate a diverse set of functional genomic datasets across two species and nearly 1,000 sequences to examine a family of TEs that have uniquely acquired cis-regulatory capabilities for dozens of medically important rattlesnake venom genes, snake venom serine proteases (SVSPs). We identify and statistically contextualize three distinct evolutionary modes (pre-wiring, re-wiring, and un-wiring) that describe patterns of transcription factor binding site retention, gain, and loss across TE copies. We demonstrate that these modes predictably influence the evolution of trans-regulatory architecture by modifying the regulatory network underlying SVSP expression. These effects include network expansion through incorporation of tissue-specific transcription factors, and network collapse via loss of key regulatory integration points. Each evolutionary trajectory produces measurable and robust phenotypic consequences for how individual TE copies regulate SVSP expression. We further formalize un-wiring as a distinct mechanism in TE domestication, showing that the selective loss of regulatory hub binding sites functionally ablates CRE potential. Together, these findings provide the first characterization of TE cis-regulatory domestication as a predictable process, offering a testable framework for how domestication operates in general.

Population and Gene Flow Decline Following Landscape Fragmentation and it's Consequences for Genetic Load in Soil Arthropods

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The intensification of land use, particularly following the onset of agriculture, has led to fragmentation and loss of natural habitats. This can reduce population sizes and restrict gene flow between populations, processes which cause random loss of genetic diversity. Empirical data on the population genetic effects of habitat fragmentation are sparse, which is especially true for species commonly presumed to be abundant, and therefore less vulnerable, such as many arthropod species. An increasing number of reports indicate declines in species and populations of arthropods. For arthropods of small size and with limited dispersal ability, habitat fragmentation could be especially debilitating. Combining historical development in agricultural land use and whole-genome sequencing data of six species of common collembola sampled in 54 natural grasslands across Denmark, we assess the implicated consequences of habitat fragmentation on genetic composition and demography. Demographic modelling and estimates of gene flow indicates that severe declines in both effective population sizes (Ne) and gene flow coincides with intensification of agricultural land use. As Ne declines, so does the efficacy of selection, making it possible for low frequency recessive deleterious variants, masked in heterozygotes, to increase in frequency and become expressed in homozygotes, altering the composition of the genetic load, potentially reducing the viability of a species. However, genomic erosion following population decline may take many generations to become apparent; a process known as 'drift debt'. As the intensification of agriculture is relatively recent it is unlikely that the genomic impacts have been fully realized yet.

The origin and evolution of alkaloid sequestration in poison frogs

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The majority of frogs use a proteinaceous skin secretion to fend off predators. However, in Dendrobatidae and several other frog families, these gene-encoded toxins have been evolutionarily replaced by lipophilic alkaloids sequestered from a specialized diet. As these replacements imply the evolution of mechanisms that protect the frogs from the alkaloids' neurotoxic effects and promote the accumulation of the alkaloids in the frogs' skin glands, they represent a remarkable case of evolutionary innovation. To elucidate the origin of toxin sequestration, we investigated patterns of adaptative evolution in (1) Saxiphilin and Alkaloid-Binding Globulin (ABG), two secretory proteins previously proposed to be involved in detoxication, transport and storage of alkaloids and (2) voltage-gated sodium channels (Nav) known as the most common target of neurotoxic alkaloids. Genomic screening and phylogenetic analyses show that the Saxiphilin and ABG genes of alkaloid-sequestering frogs have orthologues in a wide range of non-sequestering frogs, suggesting repurposing of preexisting genes at the origin of toxin sequestration. Gene duplication events and signatures of positive selection within Dendrobatidae indicate that protein diversification and adaptive evolution may have further optimized alkaloid sequestration in this clade. Predicted structures for the secretory proteins and sodium channels demonstrate aminoacid substitutions in positions that confirm strong selective pressure for toxin processing and resistance. This is the first comprehensive phylogenetic study that targets evolutionary trends in alkaloid sequestration and brings new insights on how this special mechanism evolved in poison frogs.

From post-glacial to the Anthropocene: the adaptation landscape dynamics of arthropod species in Denmark

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Arthropods were among the first taxa to recolonise northern Europe after the Pleistocene glaciations, yet many populations are now declining in association with Anthropogenic landuse. How species have responded to historical environmental changes is reflected in the distribution of adaptive genomic signals among populations – the adaptation landscape. Past and recent selection thus inform their adaptive potential in a changing world. Here we characterize the adaptation landscape of six Collembola species, small terrestrial hexapods with limited mobility, sampled across 54 locations in Denmark. We identify a south-to-north post-glacial recolonisation history that strongly structures the spatial distribution of adaptive signals. A substantial proportion of selective sweeps shared among populations is attributed to shared ancestry rather than independent convergent evolution. Older, widely shared sweeps are significantly longer than younger, population-specific sweeps. These patterns are consistent with different selective regimes acting during early colonisation compared to the more recent post-colonization phase. In line with this, ancestral and more recent sweeps show distinct Gene Ontology enrichments, suggesting shifts in the biological processes under selection through time. Across species, effective population size (Ne) predicts the number of selective sweeps per population. Moreover, we observe fewer sweeps per unit of evolutionary time in recent times across species, which suggests a slowdown of adaptive evolution. This temporal shift of the adaptation landscape raises the possibility that the Anthropogenic land usage constrains the adaptive evolution in low-dispersive soil arthropods.

Functional impact prediction for single nucleotide variants in Drosophila melanogaster with FlyCADD

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A wealth of genomic, evolutionary, and functional information, including high-quality reference genomes, dense population genomic data, and detailed functional annotations is the result of extensive study over decades of model organisms, such as Drosophila melanogaster. Despite this rich knowledge base, understanding how individual genetic variants, particularly single nucleotide polymorphisms (SNPs), contribute to phenotypic differences remains a major challenge. While SNPs play critical roles in complex, polygenic traits, their functional effects are often difficult to infer from traditional gene-level analyses alone.

Here, we present FlyCADD, a machine-learning-based functional impact prediction framework for single nucleotide variants in Drosophila melanogaster. Based on the established Combined Annotation-Dependent Depletion (CADD) approach, FlyCADD integrates over 650 genomic and evolutionary features at nucleotide resolution. This information, encompassing conservation scores, regulatory elements, GC content, and DNA secondary structure, is combined into a single metric that reflects the predicted impact of a variant on evolutionary fitness. FlyCADD provides genome-wide impact scores for all possible single nucleotide variants in D. melanogaster.

We demonstrate how FlyCADD can be used to prioritize phenotype-associated variants, evaluate naturally occurring polymorphisms in population genomic data, and guide experimental design for CRISPR–Cas9 genome editing. The development of a CADD framework for Drosophila melanogaster is particularly impactful because it unites impact prediction with a well-established functional genetics toolbox. The combination of FlyCADD with extensive resources and precise genome editing in Drosophila provides a powerful platform for functional genetics and evolutionary genomics, advancing our ability to link genomic variation at single nucleotide resolution to phenotypic outcomes.

Population genetic analysis of G-quadruplexes across the human pangenome

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G-quadruplexes (G4s), non-canonical DNA structures that occupy approximately 1% of the human genome, are crucial for telomere maintenance and for regulating transcription and replication. Yet they also contribute to genomic instability by increasing mutations and structural variation. However, the prevalence of G4 motifs across multiple human genomes and their variation and selection patterns across functional genomic regions have not been studied in detail. Here, using the second release of the human pangenome reference dataset comprising diploid high-quality genomes from 232 individuals worldwide, we conducted a comprehensive analysis of G4 variation and quantified selection acting on G4s across population groups. We built a G4 presence-absence matrix across the haplotypes. Using these data, we could successfully reconstruct the human phylogenetic tree, clustering superpopulations into distinct clades and revealing signatures of admixture, particularly between American and European ancestral groups. Analysis of variation within and outside the G4s genome-wide supported the existing hypothesis that G4s are associated with elevated mutation rates, and consistently found higher negative selection acting on G4s in regulatory elements independent of population. Analyzing different functional regions separately, we found evidence of lower genetic variation for G4s located at promoters and 5’ UTRs compared to other genic regions. Additionally, we demonstrated that a substantial number of G4s prevalent in human populations are absent from the reference, CHM13, highlighting the value of using a pangenome reference. Our findings provide important novel insights into genetic variation and selection of G4s in human populations and their potential relevance in clinical contexts.

The New Zealand Butterfish - A model teleost to understand holobiome interactions

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Endemic to New Zealand, the butterfish (mararī; Odax pullus) is a temperate marine wrasse with an exclusive herbivorous adult phase. Given that herbivory is exhibited by only ~5% of fish species, the butterfish is a compelling candidate for more sustainable aquaculture diversification. Crucially, hindgut fermentation – a specialized microbial-mediated process involved in the breakdown of dietary algal material into readily assimilable short-chain fatty acids (SCFAs), has been demonstrated to play an integral role in the species' nutritional strategy. However, the respective contributions of the host and its commensal microbial community remain unresolved due to limited genomic resources. We assembled a high-quality butterfish genome using PacBio HiFi reads supported by complementary short-read data and multi-tissue RNA-seq for structural gene annotation. The draft assembly achieved high continuity and completeness (641 Mb; N50: 22.8 Mb; Compleasm 99.49%; BUSCO 98.3%), with 21,661 annotated protein-coding genes, of which 85.7% showed transcriptional support. We demonstrate that laminarinase, a key enzyme involved in the breakdown of structural polysaccharides in the species' predominantly algal diet, is likely of microbial origin, reinforcing the importance of the host–microbe relationship. Additionally, we identified lineage-specific gene family expansions in immune regulatory and epithelial transport functions alongside a reduced emphasis on long-chain fatty acid handling. These patterns are consistent with host genomic adaptation to a fermentation-based nutritional strategy, reflecting long-standing symbiotic interactions with the gut microbiome and enhanced reliance on microbially derived SCFAs. Collectively, O. pullus represents a compelling model for investigating host genomic evolution within a holobiome framework.

Alu-associated structural variation contributes to species-specific differences in genome organization across primate evolution

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Structural variants (SVs) account for a large fraction of genomic differences between humans and other primates, yet their contributions to species-specific genome organization and function remain incompletely understood. Many SVs arise from transposable elements, which can both insert themselves and facilitate recombination-mediated rearrangements. Among these, Alu retrotransposons are particularly abundant and have been implicated in shaping 3D genome architecture, including chromatin compartmentalization and enhancer–promoter interactions. Because Alus have evolved dynamically across the primate lineage, we hypothesized that Alu-associated SVs contribute to species-specific differences in genome folding and potentially drive divergence in regulatory programs between humans and other primates.

To test this hypothesis, we analyzed over one million SVs identified from long-read primate genome assemblies using a machine learning framework. We retrained Akita, a deep learning model that predicts 3D genome folding from DNA sequence, on the T2T primate assemblies, leveraging natural sequence variation to improve species-specific predictions. We then modeled both lineage-specific and shared SVs in silico and predicted their effects on genome organization across homologous regions of the primate genomes. We find that SVs proximal to Alu elements are, on average, more disruptive to genome folding than SVs lacking nearby Alus, and we identify cases in which Alu-associated rearrangements are predicted to create or remove species-specific structural features. Together, these results implicate Alus as a driver of 3D genome evolution in primates and provide a computational framework for linking SVs to the evolution of regulatory architectures and phenotypic divergence.

Reconstructing the origin of the genetic code

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Some gene duplication and diversification events occurred prior to the Last Universal Common Ancestor (LUCA). For example, aminoacyl-tRNA synthetases diversified to attach different amino acids to their corresponding tRNAs. We reconciled Pfam domain trees with a species tree, to classify Pfam domains, and clans of distantly related Pfam domains, as diversified-pre-LUCA, single-copy-LUCA, or ancient but post-LUCA. We inferred which amino acids were added first to the genetic code from their enrichment in ancestrally reconstructed LUCA clans, relative to ancient post-LUCA clans. Smaller amino acids came first, with different curves for amino acids handled by Class I vs. Class II synthetases. We hypothesize a series of at least 13 genetic codes, beginning with only 3 amino acids, that is compatible both with our inferred order of amino acid recruitment, and with the “2-1-3 rule” of using information first in the middle position of the codon, then the first, and finally the third. This reconstruction suggests ancient ambiguity among hydrophobic amino acids, and between alanine and threonine. The same ambiguities enable trees describing how synthetase catalytic domains diversified to match the amino acid recruitment order, with isoleucine vs. valine ambiguity not resolved until after LUCA. Ancient bacteria but not archaea used tryptophan, whose synthetase emerged post-LUCA in the archaeal stem branch, then transferred to replace bacteria’s now-lost tryptophan mechanism. While resolving tryptophan’s origin, we detected an ancient recombination event between versions of tyrosine’s synthetase on the stem bacterial vs. stem archaeal branches.

Evolution of dominance modifiers over 16 million years

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The evolution of dominance has been a hot topic in evolutionary genetics for nearly a century. A key question of this debate has been whether natural selection could ever be strong enough for genetic elements regulating dominance-recessivity interactions between alleles to evolve in a diploid genotype. Such “dominance modifiers” have long remained elusive, but were recently documented in hermaphroditic plants of the Brassicaceae family, at the self-incompatibility locus (S-locus), conferring the ability to recognize and reject self-pollen. These modifiers take the form of a simple regulatory circuit based on small RNA transcriptional regulators produced by dominant S-alleles and their target sites on recessive S-alleles. These regulators and their target sites segregate together with but are distinct from the genes encoding self-recognition specificities themselves. In this study, we take advantage of the largely shared repertoire of S-alleles between Capsella grandiflora and Arabidopsis halleri to evaluate the functional constraint on their network of dominance relationships across the approximately 8 million years since they diverged. We determine the extent to which the underlying regulatory circuit has been rewired, specifically testing whether the same sRNAs and target sites are being used, or whether new dominance modifiers have emerged. We also examine whether the regulatory interactions have been modified by the accumulation of mutations at the sRNAs or/or their targets, and whether they represent compensatory changes.These results indicate a remarkable stability of the mechanisms regulating dominance/recessivity interactions over long evolutionary times.

Investigating Effects of Inversions and Recombination Modifiers to Ecotypic Differentiation in Wild Sunflowers

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Large population genomic data, together with advances in analytical methods, now enable the identification of genomic regions with signatures of chromosomal inversions and other recombination modifiers. These haplotype blocks are widespread across plant and animal taxa and play important roles in adaptation and speciation. In wild sunflowers, multiple large haploblocks were previously identified in Helianthus annuus, H. argophyllus, and H. petiolaris and shown to underlie ecotypic differentiation within species (Todesco et al. 2020). However, the apparent absence of trans-specific inversion polymorphisms led to the hypothesis that these haploblocks originated via introgression from unsampled lineages, leaving their evolutionary origins unresolved.

Here, we extend this work to two closely related species: H. praecox and H. debilis. We generated haplotype-resolved reference genomes for both species and identified over 30 large chromosomal structural differences between them. We further characterized polymorphic inversions within each species and evaluated their contributions to ecotypic differentiation and species/subspecies divergence. Finally, we tested the overlap between inversions detected in H. praecox and H. debilis and the haploblocks previously reported by Todesco et al. (2020), providing a direct assessment of trans-specific polymorphism and new insight into the evolutionary origins of recombination modifiers in wild sunflowers.

Reference:
Todesco M., Owens G.L., Bercovich N. et al. 2020. Massive haplotypes underlie ecotypic differentiation in sunflowers. Nature 584, 602–607. https://doi.org/10.1038/s41586-020-2467-6

CMAPLE 2: High-Performance Phylogenetic Inference for Millions of Pathogen Genomes

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Phylogenetic analysis is essential to genomic epidemiology, for example, in tracing the origin and evolution of SARS-CoV-2 variants during the COVID-19 pandemic. We previously introduced CMAPLE, an efficient phylogenetic inference method integrated into the IQ-TREE software, capable of reconstructing phylogenetic trees from up to one million SARS-CoV-2 genomes. However, CMAPLE is a sequential algorithm and hence cannot cope with the rapidly growing volume of pathogen data. Here, we present CMAPLE 2, which parallelises tree search through a parallel sample placement algorithm and a parallel subtree pruning and regrafting (SPR) algorithm. CMAPLE 2 also improves memory efficiency by compressing data structures using multiple references along the tree instead of a single reference genome. In addition, CMAPLE 2 implements SPR-based Tree Assessment (SPRTA), an efficient and interpretable approach for assessing confidence in phylogenetic trees. When inferring a one-million-genome SARS-CoV-2 phylogeny using 48 CPU cores, CMAPLE 2 reduces runtime from 11 days (with sequential CMAPLE) to 17 hours (a 16-fold speedup) while decreasing memory usage from 15.4 GB to 11 GB of RAM. CMAPLE 2 can now analyse four million SARS-CoV-2 genomes within 12 days using 41 GB of RAM, a task that the sequential CMAPLE cannot complete.

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Powerful inference of bacterial evolution from genome-wide genealogies

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To make sense of the enormous diversity found in prokaryotes, it is first necessary to describe the processes that generated it. A particular challenge has been to account for the combined effects of clonal descent and homologous recombination. Recently, the technology of inferring genetic relationships from sequence data has advanced rapidly but the resulting algorithms have been designed with human genetic data in mind. We developed a software named BacRelate which can infer genome-wide genealogies and the clonal frame from bacterial genome data. BacRelate is adapted from the software Relate (Speidel, et al., 2019) and it differs from Relate in three aspects: 1. It infers clonal frame. 2. It infer local trees in an iterative way which means that it infers local trees twice with taking the clonal frame as a prior when it infers local trees at the second time. 3. We introduced an ancestral allele imputation algorithm based on mapping local mutations to local trees. The resulting genealogical trees can be used, for example to infer the recombination landscape along the genome, natural selection on specific loci, patterns of gene flow between bacterial clades and intrgressions. The wide utility of the method is demonstrated on data from Campylobacter jejuni, Escherichia coli, Streptococcus pneumoniae, Klebsiella pneumoniae and Vibrio parahaemolyticus. By allowing diverse features to be investigated within a single framework, BacRelate provides unprecedented insight into evolutionary processes in bacteria.

Deciphering and forecasting viral evolution via AI-augmented molecular evolution

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Throughout human history, our evolution has been closely shaped by interactions with pathogenic microorganisms. Evolutionary biology provides essential frameworks to understand pathogen emergence, transmission, and adaptation. Leveraging genomic data and evolutionary analyses, we have investigated the molecular evolutionary dynamics underlying pathogen evolution, including the SARS-CoV-2 pandemic. By integrating molecular evolution methods with artificial intelligence (AI), we have developed predictive models capable of forecasting pathogen evolutionary trends. In this talk, I will illustrate how AI-augmented evolutionary approaches enable early identification of key adaptive changes in pathogens, improve the accuracy of outbreak predictions, and help guide public health responses to emerging infectious threats.

How DNA methylation changes shaped recent human evolution

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Modern humans differ from Neanderthals and Denisovans at thousands of DNA methylation sites across the genome. However, how these differences shaped gene expression and phenotypes remains unknown. Here, we developed methylation massively parallel reporter assay (methMPRA), and applied it to bone and cartilage cells to systematically interrogate the regulatory activity of 105,402 sequences whose methylation levels changed during human evolution. We found that methylation affected expression in 66% of differentially methylated regions, and while methylation often led to down-regulation (81%), a considerable fraction (19%) resulted in up-regulation. CpG density strongly dictated methylation effects: high-CpG sequences strongly down-regulated expression, whereas low-CpG sequences showed balanced up- and down-regulation. Integrating methylation and sequence changes, we identified dozens of epistatic interactions between the two. We also uncovered instances of convergent evolution in which both modern and archaic humans silenced an enhancer, but through independent mechanisms. To directly assess functional consequences, we employed CRISPR-based epigenome editing to demethylate three cis-regulatory elements. This editing recreated regulatory states of extinct human lineages in modern human cells, allowing assessment of their effects on expression and phenotypes. We found that Neanderthalizing the methylation levels of the enhancers of ACAN, LRP6, and CGAT1 substantially altered their gene expression, which in turn altered bone mineralization and chondrogenic matrix production in vitro. Together, these results provide unique insights into how regulatory changes shaped recent human evolution. Our novel methMPRA provides a scalable framework for dissecting the regulatory and phenotypic impact of DNA methylation changes in evolution, development, and disease.

Reconstructing the pre-Anthropocene evolutionary history of right whales

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Despite being classified as endangered, the three extant species of the genus Eubalaena remain poorly understood in terms of their evolutionary history. Over the past centuries, intensive human activities, particularly commercial whaling, have caused drastic changes in their population sizes and geographic distributions. Consequently, information derived solely from modern populations cannot fully capture their original ecological characteristics and evolutionary history. Interestingly, extant Eubalaena species exhibit a clear hemispheric separation, with their distributions confined to the high-latitude waters of the Northern and Southern hemispheres and separated by tropical waters. This bizarre distributional pattern indicates that Eubalaena should have inhabited tropical regions prior to the Anthropocene. Thus, reconstructing their past distributions based on fossil specimens with detailed molecular identification will offer crucial and decisive data for understanding their evolutionary history and informing conservation strategies. Notably, one of the few known fossil specimens of Eubalaena globally was discovered in the tropical area of Taiwan. However, ancient DNA analysis, the most commonly used molecular approach for fossil identification, is often impractical in warm and humid environments such as Taiwan due to poor DNA preservation. In this study, we applied a palaeoproteomic analysis to identify the species of an Eubalaena fossil specimen from Taiwan, with the aim of providing new insights into the historical distribution of this genus and contributing to its future conservation.

Genomic Plasticity and Evolutionary Innovation in Avian Metabolic Adaptation

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Genomic plasticity—the capacity of genomes to accommodate functional change under shifting physiological demands—provides a fundamental substrate for evolutionary innovation. Birds exhibit exceptionally high metabolic rates among vertebrates, yet substantial variation in metabolic capacity persists across avian lineages. How genomic plasticity contributes to this metabolic diversity remains poorly understood. Here, through an integrated comparative analysis of 363 bird species, we show that avian metabolic diversification is underpinned by distinct genomic innovations operating at both coding and regulatory levels. In Passeriformes, we identify a passerine-specific amino acid substitution in ABCC8, which encodes the SUR1 regulatory subunit of the ATP-sensitive potassium channel. Functional assays demonstrate that this substitution reduces channel sensitivity to ATP, effectively shifting the energetic threshold for channel inhibition and providing a mechanistic basis for adaptive modulation of glucose regulation. Beyond protein-coding evolution, we uncover accelerated evolution within a highly conserved non-coding regulatory element that is specific to high-metabolic-rate lineages. This regulatory innovation enhances expression of FUBP1, a key regulator of antioxidant pathways, thereby strengthening resistance to oxidative stress associated with elevated metabolic demand. Together, these findings illustrate how genomic plasticity enables evolutionary innovation through complementary molecular mechanisms, integrating changes in energy sensing and oxidative buffering. Our results highlight the joint contributions of coding and regulatory evolution to physiological diversification and provide new insights into the genomic basis of metabolic adaptation in birds.

Disentangling background selection from associative overdominance in structured populations using gene trees

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Most species are geographically structured into meta-populations, leaving strong signatures in neutral regions of the genome. Yet these signatures can be distorted when neutral regions are linked to deleterious mutations. In such regions, the removal of deleterious mutations can both decrease genetic diversity (Background Selection - BGS) and increase it (Associated Overdominance - AOD). While the consequences of AOD and BGS are well documented in panmictic populations, their effects remain largely uncharacterized in structured populations. Here we investigated a non-equilibrium two-island model and performed forward-simulations varying migration, selection, dominance and recombination parameters. By tracking the tree sequences for a sample of one diploid per deme, we analyzed coalescent times and topology frequencies, as well as commonly used summary statistics (π, Dxy, FST, SFS, DAFi) directly derived from the trees. When recombination was low and for weakly deleterious co-dominant mutations, we identified a BGS regime characterized by a strong compression of coalescent times and, under isolation only, by a shift towards within-deme coalescence topologies. For weakly deleterious recessive mutations, we identified an AOD regime marked by the inflation of coalescence times and an excess of cross-deme coalescence topologies; directly followed by a subsequent BGS regime, as the deleterious effect increased. These genealogical distortions translated into predictable signatures of AOD and BGS in summary statistics. Our findings provide clear evidence for signatures of AOD, BGS and their transition in structured populations. All in all, this emphasizes the potential of ARG-based approaches with minimal sampling for inferring BGS and AOD in structured populations.

Multidimensional variation and population stratification across 8000 complete human centromeres

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Human centromeres are essential for chromosome segregation but remain poorly characterized due to their repetitive complexity. Here, we generated 6,312 complete human centromere sequences from 320 phased genome assemblies in Asian Pan-Genome project phase 1. By integrating HPRC and HGSVC assemblies, we constructed a multidimensional variation map encompassing over 8,000 gapless centromeres. Centromeric satellite arrays account for 4.19% to 6.01% of the whole genome across chromosomes. Using a refined alpha satellite clustering approach that captures global diversity, we identified 195 higher-order repeat (HOR) arrays, 56.4% of which are absent from the T2T-CHM13 reference genome. Extensive structural variations across multiple dimensions exhibit population stratification, including centromeric haplotypes (CenHaps), ultra-large pericentric inversions spanning up to 36.6 Mbp, and interchromosomal HOR sharing. Integrating CENP-A CUT&Tag experiments and long-read-based DNA methylation profiles, we demonstrate that 16.8% of centromeres harbor multiple potential kinetochore assembly sites, and CenHap-specific local HOR homogenization is highly associated with kinetochore positioning. Despite global suppression of recombination at centromeres, we observed asymmetric linkage disequilibrium flanking centromeres and an ancient recombination event of CEN19. Furthermore, contrary to the prevailing assumption of high mutation rates in centromeres, our estimates based on stringent orthology reveal that centromeric single-base substitution rates are comparable to those of flanking regions with substantial variations among chromosomes, despite extraordinary structural plasticity. Collectively, this work provides a global view of human centromere diversity, redefines centromere evolution through a dual-track model balancing structural innovation with sequence constraint, and establishes a vital resource for centromere biology and disease diagnostics.

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The mutational processes in primate spermatogenesis inferred from HiFi long read sequencing

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Eighty per cent of de novo mutations passed on from parents to offspring occur in the male germline. We used PacBio HiFi long-read sequencing to identify mutations in testis and sperm samples from nine primate species: human, chimpanzee, bonobo, gorilla, orangutan, gibbon, baboon, macaque, and marmoset. Based on quality scores and auxiliary information, we confidently identify mutations, short indels, and recombination on single reads. We apply a likelihood-based approach to classify sequencing reads to cell type using CpG methylation patterns, enabling testis reads to be classified as germline or somatic. Human sperm samples show the mutation rate, spectrum and paternal age effect expected from trio studies. In other primate sperm samples, we find changes to both the spectrum and the rate, providing insights into the evolution of germline mutations. Approximately 1% of mutations are detected in more than one read, indicating that they occur during early germline development. Testes have more non-synonymous variants than sperm, suggesting natural selection against mutations in the testes. We identify simple crossovers and gene conversions, with gene conversion tract lengths being short (40-100 bp) across species. However, we also observe complex gene conversions across all species. We interpret these as resulting from homologous repair before meiosis, and they typically move several SNVs between haplotypes over 10 kb. By identifying mutations in recombined reads, we observe a mutagenic effect of recombination, with complex gene conversions exhibiting the largest mutagenic effect.

Telomere-Specific Transposable Elements and Host Fitness in Drosophila

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Unlike most eukaryotes, Drosophila lacks telomerase and canonical telomeric repeats. Nevertheless, they avoid chromosome shortening caused by the end-replication problem by relying on three transposable elements, HeT-A, TART, and TAHRE, which are located at chromosome ends where they exclusively transpose and form head-to-tail arrays (HTT arrays). These elements are believed to contribute to telomere maintenance, but the extent of their functional similarity to conventional telomeres remains unresolved.

While the regulation of these arrays and their recruitment of capping proteins suggest host domestication, the frequent evolutionary turnover of telomere-specific TEs across lineages suggests a more complex, potentially selfish dynamic. Consequently, the evolutionary forces shaping these HTT elements remain unclear.

Here, we investigate whether HTT elements are co-opted for host benefit or persist as selfish genetic elements by linking host fitness to telomere length across the life-course. Using nine lines from the Drosophila Genetic Reference Panel (DGRP), we leverage intra-line genetic uniformity to overcome the challenges of destructive sampling. We estimate telomere length via quantitative PCR (qPCR) at multiple time points and correlate these measurements with fitness traits across lines. By determining if telomere length positively impacts fitness or remains selectively neutral, this study clarifies the co-evolutionary interaction between HTT elements and the host genome, providing deeper insight into the evolution of non-canonical telomeres.

Keywords: Drosophila, Telomere, Transposable elements, Host-parasite coevolution

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Mapping bacterial capsule diversity using protein structural homology

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Many bacteria have an extracellular structure positioned outside of the peptidoglycan cell envelope, commonly referred to as a capsule. Bacterial capsules can have a varying composition, ranging from polysaccharides, polypeptides, combinations of polysaccharides and polypeptides, poly-γ-D-glutamic acid, hyaluronic acid and others. Capsules are synthesized in both Gram-positive and Gram-negative bacteria, and have a different composition based on the synthesis pathway used by the species and can differ significantly based on the serotype. Due to the importance of the capsule as a virulence factor, it has gained a lot of attention in the field of vaccination, however, little is known about the capsule diversity across the whole of the bacterial kingdoms, particularly in non-pathogenic species.

In this work, we have undertaken a large-scale analysis of proteins participating in the different capsule-synthesis pathways, and more specifically their three-dimensional structure, which often confers more about the function than the sequence. We were able to quantify the structural diversity of the same protein across serotypes of the same species. Using model organisms participating in different synthesis pathways, starting with Streptococcus pneumoniae, which represents the Wzx-Wzy pathway in Gram-positive bacteria, we used machine learning and physics-based methods to search for structural homologs across the whole of the known species space. Applying our own structural homolog pipeline, we were able to identify a large number of capsule-producing species and order them by their structural similarity to the capsule-essential wzx flippase and wzy polymerase in Streptococcus pneumoniae.

Ancient microRNAs Reveal Regulatory Continuity in a 41,000-Year-Old Insect

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Ancient DNA has become a powerful and increasingly routine tool for reconstructing genomes and evolutionary histories of extinct organisms. However, DNA alone captures only genomic potential rather than biological activity. Ancient RNA offers a complementary window into gene regulation and function, yet its recovery has so far been limited largely to megafaunal tissues preserved in permafrost, with a current age record of ~39,000 years.

Here, we demonstrate the persistence and robust recovery of endogenous small RNAs from a single leg of an exceptionally preserved moth, Agrotis fatidica, recovered from a >41,000-year-old Siberian permafrost deposit. Using historical and modern representatives for comparison, we reconstruct its microRNA repertoire and identify both deeply conserved and bona fide species-specific microRNAs, indicating long-term regulatory continuity alongside lineage-specific innovations. Comparative analyses across three temporal points reveal subtle changes in microRNA presence, abundance, and sequence variation, consistent with ancient population-specific mutations and long-term evolutionary trends.

Our results represent successful small RNA recovery from one of the oldest known invertebrate specimens to date, extending the temporal and taxonomic limits of ancient RNA preservation. These findings highlight the potential of paleotranscriptomics to complement paleogenomics by directly illuminating functional and regulatory dimensions of ancient organisms.

Exploring architectural diversity in fungal 3D genomes to uncover new perspectives on eukaryotic chromatin organization

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Fungi represent some of the most phylogenetically and ecologically diverse eukaryotes, yet remain underexplored models for studying chromatin architecture and its evolutionary dynamics. While recent advances in genome conformation technologies have uncovered fundamental principles of three-dimensional genome organization across life, the mechanisms governing chromatin domain formation in fungi remain largely elusive. In contrast to bilaterians, where chromatin domains are shaped by architectural proteins, or plants, where they emerge primarily from chromatin state and compartmentalization, it remains unknown whether fungi follow either of these models or represent a distinct mode of genome organization altogether. To address this gap, we performed a comparative meta-analysis of high-resolution Hi-C datasets from a diversity of fungal species. We aim to identify conserved and lineage-specific patterns of chromatin interaction domains, with a focus on boundary features such as transcriptional activity, repetitive elements, and candidate binding motifs. By integrating chromatin interaction data with comparative genomics and motif discovery approaches, we explore whether domain boundaries in fungi reflect passive structural compartmentalization or active maintenance by architectural factors. This work aims to provide a foundation to identify novel chromatin domains-associated elements, informs on how genome architecture evolves across eukaryotes, and opens new avenues to understand the functional consequences of three-dimensional genome organization in non-model systems.

Paleolithic prevalence of human color vision diversity

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Humans are unique in color vision among catarrhine primates (African/Asian monkeys, apes and humans) showing diversity with “deficiency” phenotypes. The phenotypic variation is mainly due to variation of the L and M (collectively called “L/M”) opsin genes by gene conversion among them, replacing a portion of one gene with that of another. Amino acid difference at the residue 180th encoded in exon 3 accounts for ~5 nm and those at 277th and 285th in exon 5 collectively for ~25 nm of the ~30 nm spectral difference between L and M opsin visual pigments. We quantified the nucleotide differences in each exon and intron among L/M opsin genes for each individual as “L/M diversity”. We analyzed genomic data of 2,533 individuals globally from the 1000 Genomes Project and our own targeted capture (TC) project. We also analyzed public data from 17 neolithic and paleolithic ancient humans and two archaic hominins (Neanderthal and Denisovan), as well as our TC data from non-human catarrhines (14 species). While non-human catarrhines and archaic hominins showed as high L/M diversity of exon 3 as of exon 5, current and ancient (both neolithic and paleolithic) humans showed lowered L/M diversity of exon 3. These results suggest that natural selection against gene conversion among L/M opsin genes has been relaxed in exon 3 with smaller spectral effects and thus human color vision diversity has already been prevalent since the paleolithic era. This challenges a notion of “deficiency” for this ancient common variation.

An epigenetically induced hypermutator state reshapes genome architecture through elevated structural variation

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Hypermutator states can alter evolutionary dynamics by increasing heritable variation, yet the mechanisms that cause elevated mutation rates beyond canonical defects in DNA repair remain poorly characterized. Cytosine DNA methylation (5mC) is a conserved mechanism of transposable element (TE) repression and therefore represents an epigenetic control point for mutation rates. In principle, disruption of 5mC-mediated TE silencing would increase the frequency of TE-associated genetic variation, but direct experimental evidence linking methylation loss to elevated rates of structural genome change is limited. Natural polymorphism in 5mC in the fungal pathogen Zymoseptoria tritici, provides a tractable system to explore this question. Loss-of-function of the DNA methyltransferase DIM2 has led to near-complete loss of 5mC, raising the question of how variation in epigenetic TE control influences genome stability and evolutionary trajectories. Here, we combine experimental evolution with long-read and epigenomic sequencing to profile parental and experimentally evolved lines that differ in DIM2 activity. Building on our recent finding that TE-enriched spatial domains drive long-range interactions in the Z. tritici 3D genome, we also assess whether TE-mediated structural variation affects higher-order genome architecture[1]. This work demonstrates that loss of 5mC is associated with a hypermutator state characterized by elevated rates of structural genome variation and enables a multi-scale inference of de novo genetic and epigenetic changes in a fungal pathogen.

[1] Glavincheska, I. & Lorrain, C. Three-dimensional genome architecture connects chromatin structure and function in a major wheat pathogen. BMC Biology 23, 353 (2025).

Signals of hybridization between commercial and wild bumblebees revealed by temporal genomics

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Hybridization and the transfer of genetic material between domesticated and wild species are of major conservation concern. The buff-tailed bumblebee (Bombus terrestris) has been bred for crop pollination since 1987, and commercial colonies are traded globally. Hybridization between commercial and wild lineages was found in Spain and Poland, but not in Great Britain or Sweden. However, despite the high dispersal capacity of bumblebees, these studies assigned unadmixed individuals by using limited spatial distances.

To further investigate hybridization between commercial and wild bumblebees in Great Britain and Sweden, we used historical DNA to generate genomes for dry-pinned museum specimens (~50) collected before the first distribution of commercial hives. The historical samples serve as a baseline to detect signals of hybridization across modern samples (~170).

Contrary to previous results limited to modern data, we find signals of hybridization between commercial and wild bumblebees in both Sweden and Great Britain in population structure and D-statistics. We find evidence for a major inversion on chromosome 10 present in commercial and some modern wild bees, but not in historical samples. This could indicate the transfer of potentially adaptive genes. Our findings highlight the importance of museum genomics to complement modern genomic data with a temporal perspective.

Sex chromosome evolution mediated by a large inversion and a possible switch of the sex determination gene

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Sex chromosomes often evolve faster than autosomes and commonly degenerate after recombination arrest. However, the underlying evolutionary processes are under persistent debate. In particular, it is unclear whether or not recombination arrest generally evolves in a stepwise manner and how switches in sex determination genes contribute to sex chromosome evolution. Here, we investigate sex chromosome evolution in the dioecious plant genus Salix.

We identified Z and W regions (~8 Mb) on chromosome 15 of the dwarf willow Salix herbacea using a new haplotype-resolved assembly. The W region harboured a large (5 Mb) embedded inversion. Analyses of synteny with other Salix species, sequence divergence between sex chromosomes and sequence degeneration suggest that this inversion recently incorporated pseudoautosomal sequence into the W region, extending its length nearly three-fold. The W region exclusively contained seven pairs of inverted partial repeats of the male essential floral identity gene PISTILLATA, suggesting a possible PISTILLATA suppression mechanism by interfering RNA in females. Such PISTILLATA pseudogenes were also found in other Salix species with ZW sex determination, but not in those with XY sex determination.

Our study provides rare and compelling support for the long-standing theory of inversions underlying stepwise recombination reduction and raises the hypothesis that the turnover of sex chromosomes in the Salicaceae family might be associated with a switch of the sex determination gene.

Genomic constraints shape the evolution of alternative routes to drug resistance in prokaryotes

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Antimicrobial resistance (AMR) can be viewed as an accumulative process where pathogens collect resistance genes until achieving multidrug resistance (MDR). This model assumes all resistance mechanisms are compatible and predicts inexorable progression toward pan-resistance. We challenge this model through integrated pangenomic and machine learning analysis of 9,584 Escherichia coli and 7,057 Pseudomonas aeruginosa genomes.

We have discovered that bacterial genomes operate under strict grammatical rules that prohibit certain gene combinations. In E. coli, we identify eight mutually exclusive evolutionary routes to MDR. These are gene combinations that confer the same resistance phenotype but cannot coexist within a single genome. Remarkably, 33 gene pairs exhibit the opposite interaction patterns between species: combinations that cooperate in E. coli interfere with each other in P. aeruginosa, demonstrating that genomic context, not gene content alone, determines resistance phenotypes. This context-dependency explains a fundamental paradox: why 106 antimicrobial resistance genes present in >95% of strains (including 43 targeting multiple drug classes) fail to confer universal resistance. Using 55 decision tree models, we show these grammatical constraints accurately predict resistance phenotypes where simple gene presence-absence fails.

These findings reveal that bacteria cannot escape these evolutionary constraints even under intense antibiotic selection, suggesting therapeutic strategies to force pathogens toward evolutionary dead ends. The species-specific nature of these constraints necessitates precision approaches to resistance prediction and treatment, moving beyond universal markers to genome-grammar-aware diagnostics. Our work establishes that resistance evolution, rather than being an open-ended accumulation process, follows constrained trajectories that can be predicted and potentially exploited therapeutically.

Root-symbiotic entomopathogenic fungi use distinct Pth11 G-protein coupled receptors for plant and insect recognition

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Entomopathogenicity, the ability to infect insects, has evolved multiple times in fungi. While these fungi have been exploited as biocontrol agents in agriculture, some also associate with plants. This is mutually beneficial, with nutrients being traded between fungus and plant. However, how these fungi sense and recognize insect/plant hosts is not well known. We aimed to identify Pth11 G-protein coupled receptors (GPCRs) responsible for the fungus-plant interaction, using two species that represent ecological extremes from the genus Metarhizium: M. brunneum, a generalist insect pathogen and known plant associate and M. acridum, a locust-specialist with no known plant associates. We identified >80 Pth11 GPCRs and used comparative transcriptomics to assess expression when the two entomopathogens were grown in insect- and plant-derived media. This identified three Pth11 GPCRs unique to Metarhizium generalists and that were only up-regulated in the plant-derived medium. One of these was further shown to be phylogenetically related to GPCRs known for their role in plant recognition in phytopathogenic fungi. Collectively, these results show that several Pth11 GPCRs may be responsible for the capacity of generalist Metarhizium species to recognize plant hosts. Future research will include gene knockout studies and comparative genomics analyses to confirm function and determine whether these are newly evolved genes in generalist species or genes that have been lost in the specialists. Taken together, this work will shed light on the evolutionary ecology of entomopathogenic fungi, highlighting how host-sensing GPCRs may facilitate their remarkable ability to transition between plant and insect hosts.

Beyond the textbook centromere: genome evolution across monocentric–holocentric transitions in Drosera

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Textbook models of eukaryotic chromosomes are built around the monocentric chromosome, where centromere function is confined to a single region. However, holocentric chromosomes—where centromeric activity is distributed chromsome-wide, have evolved repeatedly and independently across eukaryotes, including insects and plants. Despite this striking convergence, the mechanisms enabling transitions between centromeric architectures, and their consequences for genome organization, remain poorly understood.

The carnivorous plant genus Drosera provides a powerful system to address these questions. Within a single genus, Drosera includes both monocentric and holocentric species, with evidence for multiple independent transitions, allowing centromere evolution to be studied at an unusually fine scale.To investigate the genomic basis and evolutionary consequences of these transitions, we generated chromosome-level assemblies representing both architectures.

Using a whole-genome comparative framework, we associate centromeric transitions with their potential causes and effects across multiple scales, including fine-scale patterns of gene gain/loss, enrichment and depletion of functional categories, and genus-wide comparisons of chromosomal fission, fusion, and rearrangement. We further characterize differences in genome organization, with emphasis on conserved genes involved in meiosis and kinetochore assembly.

We find early evidence for loss of the centromere deposition chaperone KNL2 alongside extensive chromosomal rearrangements consistent with holocentric organization at the base of Drosera. In addition, we identify multiple independent hexaploidy events within the genus, accompanied by recurrent reuse of chromosomal rearrangement sites.

Together, these results establish Drosera as a tractable evolutionary model for dissecting the rules, constraints, and consequences of centromere architecture transitions, with implications for chromosome biology and genome evolution.

Epistasis informed protein fitness landscapes improve evolutionary modelling in bacterial genomes

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Reconstructing bacterial evolutionary histories is challenging because purifying selection acts unevenly across genomes. Moreover, sites within proteins can exhibit highly variable and often epistatically linked distributions of fitness effects (DFEs). These constraints arise from structural and functional roles of amino acids, as well as physical interactions among sites. To capture this complexity, we use Direct Coupling Analysis (DCA) to build protein specific genotype–phenotype–fitness maps. DCA quantifies single site and pairwise epistatic effects by estimating sequence stability, which we use as a latent variable mapping genotypes to fitness and assessing mutational deleteriousness across protein positions. Embedding these epistasis informed fitness landscapes into forward Wright–Fisher simulations enables us to model more realistic evolutionary dynamics and examine how structural constraints shape patterns of sequence evolution. We apply this framework to genes from an E. coli phylogroup and show how inferred evolutionary trajectories and timing differ across phylogroups. This integrative approach improves realistic fitness landscape construction and evolutionary inference in microbial systems.

Using population structure and admixture analyses to inform management decisions of native caribou in Greenland

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Caribou have long held fundamental ecological and cultural importance in Greenland as a key local sustenance resource. Over past centuries, caribou numbers in Greenland have fluctuated markedly, and the species has entirely disappeared from the eastern and northern coasts. In the 1950s, domesticated reindeer from Norway were introduced into West Greenland to increase caribou numbers and were later translocated to several other west-coast locations. Despite the local importance of this species, no broad analysis of genetic diversity and population structure has been performed. Here, we investigate the contemporary evolutionary history of Greenlandic caribou by analysing more than 100 whole genomes from present-day samples collected across their current range to assess population structure and the extent of admixture with domesticated reindeer.
We find clear population structure within Greenland (FST above ~0.05), with the strongest differentiation between the northernmost distribution in West Greenland, Inglefield Land, and all other regions (FST > 0.3). We also find substantial recent admixture with domesticated reindeer in several regions.
These findings have major implications for management, particularly regarding the threatened genetic integrity of native caribou, the delimitation of management units, and decisions about reindeer relocations within or import to Greenland. Management advice based on our results will aim to improve long-term sustainable harvest and we hope our analyses can thereby help secure the future survival of native Greenlandic caribou.

Diversity of the protist world and the origin of animal multicellularity

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The transition from unicellular ancestors to the first animals changed the face of the Earth. It created new ecosystems, more complex body plans and organismal capacity to new and diverse physiologic processes. How did this complexity evolve? A couple of decades ago, researchers started looking into the unicellular roots of animals. Genomic comparative studies revealed that extant unicellular relatives of animals possess many molecular tools that are involved in tissue complexity and embryo development in animals. This suggests that the unicellular ancestor already had a high level of complexity. The latest studies in the field of the origin of animal multicellularity focus on elucidating how co-option of the genes and pathways from the unicellular ancestor contributed to the origin of animals, and in particular, the origin of cell differentiation and embryo development. To answer this, we use a diverse array of unicellular species that are non-model organisms. To this end, standard experimental methods and technological approaches need to be adjusted and modified. In my talk I will tell about the advances in the field and the caveats of this endeavour.

An archaeogenomic study of Black Death victims from Southern Europe

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Infectious diseases have been a major driver of human mortality throughout history, imposing strong selective pressures on human populations. The Black Death, caused by Yersinia pestis, was among the most catastrophic pandemics in European history, claiming an estimated 30–60% of the population between 1347 and 1352. Although ancient DNA studies have identified candidate genetic variants potentially associated with resistance during the second plague pandemic, these findings remain unreplicated, largely due to limited genome coverage and small sample sizes.

Here, we present 130 newly generated ancient genomes (mean coverage 3×) from individuals excavated from a Black Death–associated mass burial (1348–1350) and a post–Black Death church cemetery (1353–1545) in Toulouse, southwestern France. These imputed genomes were analyzed together with a comparative dataset comprising 730 ancient genomes (>0.5×; 3rd–18th centuries) and 4,790 modern genomes from France and the broader western Eurasian region. Presumed plague victims and descendants of survivors showed no differences in age or sex distributions but exhibited marked differences in genetic relatedness, consistent with distinct burial practices. We find no evidence for genetic discontinuity in southwestern France since the Middle Ages, enabling direct temporal comparisons across the Black Death.

Interestingly, allele frequency differences between presumed plague victims and survivors were further amplified when comparing medieval and contemporary populations, consistent with directional selection of plague resistance. While preliminary, these results suggest a long-term genetic legacy of historical epidemics, with potential implications for understanding human evolutionary responses to infectious disease.

Representing massive-scale phylogenetic uncertainty with phylogenetic networks

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Phylogenetics has a central role in evolutionary biology and genomic epidemiology. Assessing phylogenetic uncertainty is therefore crucial and the methods that do this, such as those derived from Felsenstein's bootstrap, are among the most widely used in modern science. However, these methods require enormous computational capacity, and are unsuitable for large datasets. Furthermore, most of these methods emerge from a focus on the membership of clades (groupings of taxa), which makes their results difficult to interpret in many contexts, including genomic epidemiology. Here we propose subtree pruning and regrafting-based tree assessment (SPRTA), an efficient and interpretable approach to assess confidence in phylogenetic trees. SPRTA shifts the paradigm of phylogenetic support measurement from evaluating the confidence in clades to evolution histories and phylogenetic placement—for example, assessing whether a lineage evolved from another considered lineage. In addition to being more easily interpretable, SPRTA is also highly scalable, and can be used to represent large numbers of alternative evolutionary histories as embedded within a concise phylogenetic network. We use SPRTA to investigate the uncertainty in SARS-CoV-2 evoution as inferred from more than two million genomes.

Evolutionary dynamics of extinct and extant moose hybridization in North America

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The ancestor of stag-moose (Cervalces scotti and C. latifrons) entered North America via the Bering Land Bridge around 800 thousand years ago (ka) and moved southwards during interglacial periods, eventually inhabiting all of boreal North America. Just before the submersion of the Bering Land Bridge (14-10.5 ka), the modern moose (Alces alces) also entered North America from Eurasia and spread southwards as the ice sheets retreated after the Last Glacial Maximum. Cervalces sp. became extinct in North America around 10 ka, likely due to the large-scale environmental change at the end of the Pleistocene (11.7 ka). Hybridization commonly follows secondary contact of closely-related species after range expansions. Thus, it is possible that the two species hybridized upon contact. To test this, we have generated ancient genomic data from multiple Cervalces sp. samples from Yukon, Canada and have compared these to 40 modern A. alces genomes. The results provide novel insights into the movements and evolution of moose in North America in relation to past climatic changes.

A large selfish mitochondrial deletion hints at an unexpected diversity of drive strategies

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Mitochondrial DNA (mtDNA) molecules are found in multiple copies, replicate and divide independently from nuclear DNA and are transmitted (both between cells and individuals) through seemingly random bottlenecks. Such specificities allow competition to occur between mtDNA molecules within and between cells. This creates opportunities for intra-individual selection to favour mtDNA molecules with a replicative advantage, even at the expense of the individual, rendering certain mitochondrial variants selfish. In Caenorhabditis elegans, several deletions have been found to selfishly impair individual fitness while gaining a replicative or transmission advantage. Most of the effort in unravelling the dynamics of the proliferation of selfish mtDNA in C. elegans has focused on the uadf5 mitochondrial deletion. Here we focus our efforts on a 499 bp deletion in the ctb-1 gene (Δctb-1). The Δctb-1 mitotype was found to impose extensive fitness costs and persist within large populations of deletion-bearing individuals. Comparisons of the transcriptome of Δctb-1 bearing worms at two life stages and in relation to wild-type worms show differences in OXPHOS gene expression and mitochondrial housekeeping pathways as a consequence of the deletion. Additionally, we explore the effects of an RNAi treatment suppressing UPRmt expression across 15 generations at two different population sizes (N=1 and N>1000), allowing us to differentiate the roles of intra- and inter-individual selection on the progression of the variant as well as the interaction between natural selection and RNAi knockdown. Cumulatively, those results show how selfish mtDNA deletions can both vary in their consequences and in the source of their proliferation.

Habitat Specialisation Impacts Clownfish Demographic Resilience to Pleistocene Sea-Level Fluctuations

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Pleistocene sea--level fluctuations are known to have drastically impacted marine biodiversity through habitat fragmentation. Studying the effect of these past climatic events on genomic diversity can help understand how marine populations respond to this key threat to biodiversity. Clownfishes, which rely on sea anemones for shelter and reproduction, provide an interesting model to explore how ecological specialisation mediates species responses to habitat perturbations. To assess the impact of Pleistocene sea--level fluctuations on clownfish populations, we reconstructed demographic histories and inferred spatial genetic structure of 10 species presenting a gradient of host specialisation. Leveraging whole--genome data from 382 individuals, we found that generalist species, associated with multiple hosts, maintained stable effective population sizes (Ne) and population connectivity during habitat fragmentation, reflecting resilience to environmental instability. In contrast, specialists experienced severe Ne declines and genetic structuring, driven by their dependence on specific hosts, without signs of population recovery following habitat reconnection. Spatial genomic analyses identified the Indonesian Through--Flow as a key dispersal corridor and the Coral Triangle as a critical hub of genetic diversity, while continental shelves and extensive open ocean regions appeared as barriers to gene flow. Our findings reveal how host specialisation shapes clownfish population dynamics, emphasising the importance of incorporating ecological dependencies into conservation assessments and deepening our understanding of species responses to ecological constraints and environmental changes over evolutionary timescales.

Evaluating the efficiency of captive genetic rescue versus genome editing of ancestral variation

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Severe population bottlenecks lead to genomic erosion that can drive populations to extinction. The pink pigeon (Nesoenas mayeri) declined to circa 10 individuals in the wild by 1990, and it has since recovered to >500 birds. However, genomic erosion continues to threaten its long-term viability. Before the bottleneck, 12 individuals were taken from the last free-living population to establish a captive breeding population. Through repeated reintroductions, this captive population has been instrumental to the recovery of the free-living population.

Here, we ask the question whether continued reintroductions of individuals from the captive population can further improve the species' long-term viability. We compare this strategy to genetic rescue using gene editing with museum DNA. We use forward-time population genetic simulations in SLiM, parameterizing the model to reflect the pink pigeon's demographic history.

Our results show that continued releases of captive individuals provides no further benefit to fitness and nucleotide diversity of the free-living pink pigeon population. In contrast, targeted insertion of ancestral DNA segments can restore genetic variation lost during the bottleneck, reduce realised genetic load, potentially resulting in sustained improvements in fitness and population viability.

These findings highlight the limits of traditional genetic rescue, specifically the diminishing returns of repeated releases. Our data furthermore imply that gene-editing approaches informed by historical genomics could complement conservation strategies for critically inbred species. More broadly, our work demonstrates how evolutionary simulations can be used to assess the feasibility of novel genomic interventions prior to real-world application.

Neglected microbial lineages and the birth of eukaryotic protein domains: A structural phylogenetics perspective

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Major protein databases (UniProt, AlphaFold DB) are biased toward model species, including many multicellular organisms of agronomic or medical interest. To address this gap, we curated a new, more representative set of proteomes spanning the diversity of the three domains of life. Previous sampling of extreme environments enabled the identification of novel microorganisms, which we incorporated into this dataset, thereby enriching it with understudied unicellular groups, especially in protists and archaea.

Leveraging these sequences, we utilized recent methodological advancements in protein structure prediction and analysis (AlphaFold2, ESMFold, Foldseek/Foldmason, The Encyclopedia of Domains) to uncover the prokaryotic origins of domains present in ancient eukaryotic proteins. This approach allowed us to generate over 10 million new protein structure models. Combined with publicly available models, we reconstructed a dataset of proteins likely present in the Last Eukaryotic Common Ancestor (LECA), based on structural similarity.

The domains of these proteins were then defined using the latest consensus on domain boundary delineation, providing us with unprecedented resolution in the study of protein evolution across the domains of life. By identifying protein domains similar to those present in the LECA within prokaryotic groups—and employing innovative phylogenetic tree reconstruction approaches based on structural alignments—we traced the evolutionary history of these domains. Our results demonstrate the transmission between unicellular organism groups and explore the existence of hybrid proteins in eukaryotes, with domains derived from distinct lineages.

Comparative Population Genomics of Two Pipefish Species in the Baltic Sea

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Understanding how species exist across variable environmental conditions is crucial for predicting how environmental change will impact their future viability. Marine species in the Baltic Sea present a system for exploring evolution to novel environmental conditions, since the Baltic Sea has existed only within the last few thousand years and has different salinity and temperature from the neighboring North Sea. Here, we examine the population genomics of two pipefish species in the order Syngnathiformes (Syngnathus typhle and Nerophis ophidion) which occur across the Northeast Atlantic Ocean and Baltic Sea, sampling individuals across an environmental gradient of 7 sites where the species co-occur. We assess the population structure, admixture, and rates of genetic variation between the sites, relating these metrics to the environmental conditions of the sites and the evolutionary history of these species. By comparing the population genetics of the two species, we aim to explore the parallels and dissimilarities in how the species evolved in response to novel environmental conditions and their present-day population dynamics, helping to understand the current biogeography of these species and their potential to adapt to future environmental change.

Beyond conserved markers: enhancing deep node resolution via rigorous orthology filtering of 900 protein domains

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The Last Universal Common Ancestor (LUCA) marks the divergence of Archaea and Bacteria, a critical event in the history of life. However, accurately resolving deep phylogenetic relationships remains a challenge. Most large-scale trees of life have relied on a limited set of approximately 30 conserved markers, predominantly ribosomal proteins. While robust, these markers represent a specific functional subset that may not fully capture the complexity of species-level divergence.

To address this, we present a revised tree of life reconstructed from a significantly broader sampling of approximately 900 protein domains. This expanded dataset used a novel pipeline that rigorously identifies orthologous domains using a combination of graphical and sequence-similarity based tools. The resulting phylogeny exhibits substantially improved resolution across the tree of life, particularly regarding the earliest divergence events encompassing LUCA, the Last Archaeal Common Ancestor (LACA), and the Last Bacterial Common Ancestor (LBCA).

Supported by strong genome-wide molecular evidence, this dataset facilitates more precise divergence time estimates. We leverage these findings through MCMCTree analyses to reconstruct the temporal dynamics of cellular evolution, offering new insights into the evolutionary trajectory from LUCA to the establishment of the two prokaryotic domains.

Patterns of molecular evolution across prokaryotes

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More than thirty years of sequencing efforts have produced a huge wealth of information about prokaryotic genomes. Leveraging this, we explore long-term trends in the evolution of Bacteria and Archaea, with a particular focus on Asgardarchaeota, the closest prokaryotic relatives of eukaryotes.

Our results confirm many patterns that have been previously recognised on smaller datasets, but also show that model violations lead to large biases in traditional measures of selection. While Bacteria and Archaea differ in factors such as genome size, nucleotide composition, codon usage, and tRNA content, our corrected selection metrics highlight that both groups are subject to similar selection forces.

The origin of eukaryotes is often perceived as a singularity, but it is unclear whether it was enabled by evolutionary trends already happening within Asgardarchaeota, or whether the evolutionary conditions for eukaryogenesis only appeared in the branch leading to the first eukaryotic common ancestor. Our analyses allow us to compare Asgardarchaeota and their ancestors with “typical prokaryotes”, thus shedding new light on the process of eukaryogenesis.

Evolutionary conservation and rewiring of enhancer-promoter connectivity across mammals

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Enhancers are crucial to gene regulation, often controlling genes located far away through 3D chromatin interactions. Gene expression patterns are generally conserved across evolution, yet the enhancers that control them turn over rapidly. What determines whether gene expression remains robust to enhancer turnover or undergoes regulatory divergence? Comparing orthologous genes across species offers a natural perturbation experiment, but without knowing which enhancers physically contact which genes, it remains difficult to test mechanisms for robustness or identify drivers of divergence.

To address this, we generated promoter capture Hi-C (PCHi-C) from brain, liver, and testis across five mammals spanning 94 million years of divergence (macaque, marmoset, mouse, rat, and dog). Unlike Hi-C, PCHi-C provides the high resolution needed to identify enhancer-gene contacts. Integrating with published H3K27ac ChIP-seq and RNA-seq (Roller et al., 2021), we mapped the evolution of expression, activity, and contacts for 3,444 one-to-one orthologous genes and over 86,000 enhancer-gene pairs across species.

Gene expression, enhancer activity, and chromatin interactions exhibit distinct evolutionary dynamics. Expression clusters primarily by tissue, while enhancer activity and interactions show stronger lineage-specific divergence, consistent with different selective constraints acting on each modality. Individual loci reveal examples of deep conservation of long-range promoter-promoter interactions, regulatory robustness despite proximal enhancer turnover, and lineage-specific changes in distal enhancers and interaction rewiring correlated with expression divergence. These findings demonstrate how regulatory architectures at some genes achieve robustness through maintained chromatin contacts even as enhancers turn over, while others undergo coordinated regulatory rewiring, driving gene expression divergence.

An independent phylogenomic dataset sheds new light on the eukaryotic Tree of Life

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Understanding the phylogenetic relationships between all known forms of life remains a major challenge. Molecular phylogenetic analyses using large sets of highly conserved protein-coding genes for the reconstruction of the Tree of Life have become the norm. In the case of eukaryotes, this increasing use of phylogenomics (multi-gene phylogenetic analyses) has grouped most eukaryotic diversity into a small number of monophyletic so-called supergroups (e.g., Amorphea, SAR). Nevertheless, the deepest relationships among these supergroups remain uncertain, and some new phylum-level 'orphan' eukaryotic lineages continue to be discovered, such as Hemimastigophora or Provora. Most phylogenomic studies relied on very similar datasets of core markers to infer the eukaryotic Tree of Life, raising the question of whether our current view of this tree is marker-dependent. To address this question, we tested an independent marker collection to infer such deep relationships among major eukaryotic lineages using both Maximum Likelihood and Bayesian Inference with an improved and balanced taxon sampling. We gathered a collection of 651 proteomes spanning the known eukaryotic diversity and reconstructed their phylogeny using 277 manually curated proteins derived from the BUSCO dataset, which are well conserved and vertically inherited. We applied several strategies to alleviate potential artefacts due to long branch attraction and/or compositionally biased taxa and assessed the robustness of inter-lineage relationships using state-of-the-art phylogenetic analyses. I will discuss how our results compare to previous studies, supporting some well-established clades but also revealing deep relationships not previously observed, and how they impact our understanding of the early diversification of eukaryotes.

Collapse, recovery and future uncertainty: temporal genomics and simulations of genomic erosion in the Mauritius kestrel

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Loss of genetic diversity is a critical component of the biodiversity crisis, with lasting consequences for evolutionary potential and population persistence. Using temporal genomics and advanced evolutionary modelling, we studied genomic erosion in the Mauritius kestrel (Falco punctatus), a species that experienced one of the most extreme population bottlenecks ever recorded, recovering from only four documented individuals in the 1970s.

We analysed whole-genome data from 16 historical individuals from 18-19th century, and 59 modern individuals (1986-2021), together with six other kestrel species. Genome-wide heterozygosity has remained extremely low for >250 years, retaining only ~3% of the genetic diversity observed in continental kestrels. As the Mauritius kestrel maintained a small Ne over a long evolutionary history, fluctuations in genetic load through the recent bottleneck were limited, but consistent with theoretical expectations of an initial increase in load followed by purifying selection. However, modern genomes show increasingly extensive ROHs covering over 40% of the genome, indicating ongoing inbreeding despite demographic recovery.

By combining genomic data with ecological observations of reproduction, we show that inbreeding depression and genetic load remain a threat to the species' long-term viability. We further developed realistic forward-in-time SLiM simulations parameterised with empirical demographic data and validated using the temporal genomic data. This "digital twin" accurately captures the observed genomic erosion and demonstrates that intensive conservation management was crucial in preventing both past and future extinction of the species. Our results highlight the power of integrating temporal genomics with evolutionary simulations to quantify genomic erosion and guide conservation strategies.

EvoSur: Building an interconnected network for evolutionay biology in South America

Dr. Ana Maria Agapito Vera, Santiago Herrera-Alvarez, Paco Majic, Cauã Antunes Westmann

Evolutionary and molecular biology are rapidly advancing disciplines, yet South America remains underrepresented in global research networks due to persistent structural inequities. The ongoing brain drain of talented young scientists, a form of professional extractivism, undermines the development of a consolidated regional research community, weakening scientific infrastructure and limiting local training at both national and continental scales. Linguistic barriers between Portuguese- and Spanish-speaking communities further fragment collaboration, a problem exacerbated by limited funding for research, conference participation, and international training opportunities. Addressing these challenges requires building strong, sustainable connections among early-career researchers working within the region.

To meet this need, we created EvoSur, a regional initiative designed to promote equitable access to training, mentorship and collaboration networks among evolutionary biologists in South America. The first edition of EvoSur took place in Uruguay in November 2025, bringing together 25 students from all ten South American countries for an intensive week-long workshop. With nearly 200 applications for just 25 positions, the inaugural edition demonstrated substantial regional demand for accessible, high-quality training and networking opportunities.

In this talk, we will share outcomes and lessons from EvoSur's inaugural edition drawing on participant and faculty feedback, and highlighting the process of community building, networking and training. We discuss how regionally rooted, multilingual training programs can strengthen scientific capacity, foster durable research networks, and counteract brain drain. EvoSur provides a transferable model for advancing inclusion, diversity, equity, and access within global evolutionary and molecular biology.

Evolutionary diversification of horizontally acquired pathogen-defence genes in bdelloid rotifers

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Most animals rely on sexual reproduction to generate genetic variability that helps them keep pace in arms races with virulent pathogens. Bdelloid rotifers are microscopic animals that lack observed males and would be theorised to be vulnerable to coevolving pathogens due to the absence (or extreme rarity) of sex. We recently discovered that bdelloids have acquired large numbers of biosynthetic genes by horizontal gene transfer from microbes, which they deploy to resist their specialist fungal pathogens (https://doi.org/10.1038/s41467-024-49919-1). Highly unusual for animals, these non-ribosomal peptide and polyketide synthetase genes are predicted to produce antifungal compounds that substantially augment the normal repertoire of animal immune defences. However, one-off acquisition of such genes does not necessarily bring continued success against pathogens, since those pathogens may evolve resistance to bdelloids' novel antimicrobials. This talk illustrates how bdelloids generate variability in their unusual immune defences, using comparative genomics of closely related bdelloid species and time-series data from a wild bdelloid population sampled over ten years.

A multi-omics approach to unravel the evolution of gene regulation in vertebrates

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Understanding how gene regulation evolves is essential for explaining phenotypic diversity and reproductive strategies across species. Spermatogenesis, a highly dynamic developmental program, provides an ideal framework for studying regulatory evolution because it relies on the precise establishment on gene activation in accordance with DNA methylation patterns in the germ line. Using a comparative, genome wide analysis approach that integrates chromosome conformation capture data (HiC), transcriptomics and DNA methylome profiling across four vertebrate's species representatives of eutherians (mouse), marsupials (tammar wallaby), reptiles (the bearded dragon), and fish (zebrafish) we mapped gene regulation dynamics across the stages of spermatogenesis. We find that DNA methylation levels are minimal at the onset of the process and progressively increase, reaching a peak during meiosis. During this stage, the silencing of transposable elements and the establishment of parent specific genomic imprints contribute to elevated methylation levels. Cross species comparisons reveal distinct methylation trajectories, indicating linage-specific remodeling of gene regulatory mechanisms, potentially linked to reproductive strategies and genome evolution. Overall, this study shows how functional genomics and comparative epigenomics can uncover general principles of regulatory evolution and highlights future opportunities to integrate single cell and spatial methods, together with chromosome conformation datasets, to resolve causal links between regulatory changes, gene expression, and complex traits in the germ line.

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The role of structural variants during adaptation to whole genome duplication

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Whole genome duplication (WGD) is a dramatic mutation, hugely disrupting cellular processes. To survive and thrive, polyploids undergo rapid evolution at genes regulating fundamental processes such as meiosis. Recent studies suggest an important role for structural variants (SVs) in the adaptability of young polyploids. Do SVs play a role in adaptation to WGD? We investigate this in Arabidopsis arenosa, which has undergone WGD ~30k generations ago. Here, we combine long-read pangenomics and population-level re-sequencing to look for evidence of SVs involved in adaptation to WGD. We compare this to SNP-based genome scans. We find novel candidates for genes involved in adaptation to WGD from both the SV and the SNP based analyses, with a small number of candidates indicated by overlapping SNPs and SVs. This suggests that by ignoring structural variation we are missing an important component of the genetic basis of adaptation.

Genomic consequences of population collapse and recovery in European wolves

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European wolves offer an excellent opportunity to investigate the evolutionary consequences of population collapse followed by recovery. We conducted a large-scale genomic study of European wolves analyzing 1005 genomes (746 new) sampled across 33 countries. All genomes were phased and imputed using a reference panel of 1,715 canids, generating a high-density whole-genome variation dataset (52 million variants). With this, we explore how population structure, connectivity, and hybridization shape genomic erosion under these demographic trends.

We show that European wolves are not homogeneous but have distinct evolutionary histories and dispersal patterns. Northern populations exhibit substantial ancestry influx from Asia, whereas southern European wolves show strong allele sharing with early Holocene wolves.

We refine previous geography-based European wolf groupings by identifying a more finely-scaled clustering that will enable evidence-based monitoring, which rarely incorporates genomic insights. The population collapse has had long-lasting consequences in present-day populations. Although effective population size (Ne) has increased by ~5% per generation since 1970, most clusters remain below Ne=500, a threshold considered critical to maintain evolutionary potential. Scandinavian, Italian and Northwestern Iberian wolves harbor ~20-40% of their genomes in runs of homozygosity (ROH) and have 3 times more fixed deleterious mutations than average. In contrast, the expansion into the central European lowlands shows limited inbreeding and load due to connectivity. Dog hybridization also threatens several clusters, especially the eastern European lowlands and Italian wolves.

Together, our results emphasize the need for targeted strategies specific to each region accounting for differences in demography, connectivity, hybridization, and genomic erosion.

Somatic mutation genomics to elucidate longevity in the extremely long-lived desert plant Welwitschia mirabilis

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A key molecular hallmark of biological aging is the accumulation of somatic mutations in the genome. While such mutations are typically counteracted by DNA repair pathways, their efficiency declines with age. Recent work in long-lived tree species has revealed unexpectedly low rates of somatic mutation accumulation, suggesting alternative genomic strategies for achieving extreme longevity. Among the longest-lived sexually reproducing organisms is Welwitschia mirabilis, an iconic plant endemic to the Namib Desert, with radiocarbon-based estimates suggesting lifespans of up to ~2,000 years. However, such age estimates are highly uncertain due to the plants' unusual morphology and growth patterns. Unlike previously studied long-lived plants, which are typically tall and highly branched, Welwitschia lacks branching and grows primarily through continuous radial expansion. The dynamics of somatic mutation accumulation in this species also remain unknown. Here, we present a genome-wide, somatic mutation–based framework to investigate molecular aging and to estimate the age of individual Welwitschia plants. Using whole-genome sequencing data from multiple individuals of varying size sampled from natural populations in Namibia, we quantify patterns of somatic mutation accumulation across the genome. By calibrating mutation accumulation using a young individual of known age, we extrapolate from the genomic data to infer minimum ages for larger plants. Our preliminary results yield a lower-bound age estimate for one of the largest known living individuals and demonstrate the potential of somatic mutation accumulation as a broadly applicable genomic approach for studying longevity and age in long-lived, unconventional organisms.

Deep-Time History of Balkan Brown Bears

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The brown bear (Ursus arctos) is an iconic megafaunal species that survived the Late Pleistocene extinctions. Once widespread across Europe, its range has been drastically reduced by intensive hunting and large-scale habitat loss. Today, European brown bears persist in ten fragmented populations, three of which occur in the Balkans, with Serbia likely forming a historical contact zone among them. Our ongoing project investigates the evolutionary history of Balkan brown bears over the past 50,000 years by integrating genomic analyses of ancient and modern DNA with stable isotope analysis.

Preliminary analyses of Holocene specimens from Serbia reveal unexpectedly high mitochondrial DNA diversity, indicating that past genetic variation greatly exceeded that of present-day populations. To investigate this further, we are generating new whole-genome sequence data from ancient and modern individuals and extending our temporal range to include Late Pleistocene and Holocene material. These genomic data are being integrated with information from contemporary populations to reconstruct long-term genetic change.

This interdisciplinary framework allows us to reconstruct temporal and spatial patterns of demographic change, ancestry, admixture, and migration. Stable isotope analyses of bone collagen provide insight into diet and environmental conditions, while direct radiocarbon dating establishes a robust chronological framework. Together, these approaches will clarify how brown bears persisted in the region over millennia, deepen our understanding of long-term population dynamics, and inform future conservation strategies.

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Miniaturization – a major player in Metazoan Evolution

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Microscopic body size has evolved repeatedly across the Animal Tree of Life with about one-third of the 30 animal phyla being primarily meiofaunal (typically <1mm long) and with multiple examples of miniaturization occurring within macrofaunal lineages. These genomically unexplored, microscopic lineages offer a unique window into how reduction in scale may act as a generative force in shaping animal diversity and evolutionary innovations.

With new protocols optimized for ultra-low input DNA/RNA we can generate high-quality genomes from single meiofaunal organisms. Phylogenomic analyses suggest a microscopic ancestor of major clades both within Ecdysozoa and Spiralia (e.g., Scalidophora and Gnathifera), and potentially at the base of these entire groups which encompass >90% of all animal species. However, looking for genomic signatures of miniaturization, our comparisons of architecture, gene losses/gains, and Hox cluster compositions across Gnathifera show severe losses/contractions at deeper nodes. This indicates that Gnathifera, and potentially most meiofaunal lineages, have undergone miniaturization secondarily, rather than the ur-spiralian ancestor being meiofaunal. Besides from genomic changes, our comparative transcriptomic studies reveal that miniaturization may be initiated by heterochronic shifts in gene expression during development, causing an early sexual maturation and arrest of somatic growth, resulting in a microscopic adult.

Our advancements in meiofauna genomics provide entirely new insights into the interplay between size, development, and genomic properties in metazoan evolution. We herewith address the fundamental biological questions: Is there a microscopic ancestry of major animal groups? How have meiofauna evolved across the animal kingdom? What are the genomic mechanisms and outcomes of miniaturization?

The genomics of miniature animals: the first genomes of the microscopic phyla Gnathostomulida and Micrognathozoa

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Spiralia is one of three major clades in the animal kingdom, containing most of the soft-bodied invertebrate lineages. The spiralian group Chaetognathifera comprises four phyla: Chaetognatha, Gnathostomulida, Micrognathozoa, and Rotifera. As the putative sistergroup to the remaining spiralians, chaetognathiferans are key to understanding the evolution of a major part of the Animal Tree of Life. Additionally, three of these phyla are microscopic, and include some of the smallest and rarest animals in the world. The relationship between the microscopic phyla and the large-bodied, active, predatory Chaetognatha raises interesting questions regarding the evolution of body size and body plan complexity. We present the first genome assemblies of the enigmatic and understudied Gnathostomulida and Micrognathozoa. Through comparative genomic analysis, we find dynamic genome evolution and lineage specific gains and losses that underscore the body plan diversity of Chaetognathifera and miniaturization of the microscopic lineages. We identify losses of key developmental and epigenetic pathways that have plausibly played a role in their extreme miniaturization. Despite the highly derived nature of Gnathostomulida and Micrognathozoa, we still find the conservation of certain genomic features such as linkage groups, extensive TE content, and active transposons. This suggests extreme body simplification and size reduction are not necessarily correlated with the complete loss of genomic integrity.

A deeply divergent Yersinia pestis lineage identified in Early Iron Age Romania

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Ancient pathogen genomics has advanced our understanding of the evolutionary history of Yersinia pestis, the causative agent of plague, revealing its presence in prehistoric populations as early as ~5,500 years ago and uncovering previously unknown genetic diversity with distinct transmission modes and disease potentials. Among these, two lineages exhibit distinct gene contents, suggesting that flea-adapted and non-flea-adapted strains coexisted from the Bronze Age into the Iron Age. However, the epidemiological behavior and demographic impact of these strains remain largely unexplored. Here, we investigate an early Iron Age context in present-day Romania dated to the 11th - 9th century BCE, representing communities associated with Babadag culture. Metagenomic screening of 16 individuals revealed the presence of Y. pestis and whole-genome capture enabled the reconstruction of Y. pestis genomes from three individuals. Genomic analyses identify a deeply divergent lineage that branches basal to all currently known Y. pestis diversity. Its genomic features include the absence of key adaptations associated with flea-borne transmission and the presence of large deletions (>100 kb in total), affecting virulence-associated genes. Some of these deletions are also found in Y. pseudotuberculosis, possibly reflecting the ancestral state of the Y. pestis genome, while others appear to be unique to this lineage. Ongoing molecular dating and pangenome analyses aim to further clarify the divergence timing and gene content of this lineage. The analysis of time-stamped pathogen genomes from the archaeological context of a transitory period in Iron Age Romania demonstrates how ancient pathogen genomics can shed light on prehistoric epidemiological processes.

Integrating protein structure and population genomic data to detect diversifying selection related to immunity

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As pathogens adapt to host immune systems, this can leave traces of diversifying selection in their genomes. Diversifying selection can be detected by calculating the ratio of nonsynonymous to synonymous substitutions, dN/dS. Classical methods for estimating dN/dS rely on phylogenetic trees, which limits scalability and can give misleading results for bacterial species as trees generally cannot be corrected to exclude recombination. We have developed a new tool called TOMBOMBADIL (Tree-free Omega Mapping By Observing Mutations of Bases and Amino acids Distributed Inside Loci), which computes dN/dS directly from codon counts from alignments by comparing to expected frequencies from the coalescent. We implemented TOMBOMBADIL as an end-to-end differentiable model in both Stan and JAX, allowing us to estimate dN/dS values across genes for alignments with potentially millions of samples. TOMBOMBADIL includes different models of evolution (NY98, GTR) and different assumptions of how codons evolve. We validated our method by comparing it to established, tree-based dN/dS methods and on well-known examples of bacterial genes under positive selection, including the outer membrane protein PorB of Neisseria meningitidis. We have added regression terms between protein features and selection, which will help map sites of positive selection to predictions of protein structures, leveraging the relationship of functional evolution and structure. We have analysed a large-scale dataset comprising bacterial outer membrane proteins, allowing us to study diversifying selection related to host-pathogen interactions. In summary, TOMBOMBADIL allows fast detection of positive selection in bacterial datasets using a tree-free dN/dS approach and machine learning methods.

Combining environmental DNA with nuclear loci capture for genetic monitoring of endangered butterfly populations

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Biodiversity around the world is undergoing a severe crisis, with species vanishing locally or globally. Monitoring programs increasingly track population trends, yet acquiring robust genetic data – which is essential to assess sustainability and adaptive capacity – remains complex. To address this, we combine airborne environmental DNA (air-eDNA) sampling, which captures DNA without disturbing animals, with HyRAD, a hybridisation capture technique enabling recovery of nuclear loci from trace DNA. Unlike COI metabarcoding, HyRAD delivers population-level genomic data suitable for evolutionary and conservation analyses. We demonstrate feasibility through controlled experiments showing nuclear locus recovery from air-eDNA, followed by field trials on Phengaris nausithous, an endangered Swiss butterfly dependent on Sanguisorba officinalis and Myrmica rubra. We establish a repeatable, non-invasive, scalable protocol for genetic monitoring, which fills a gap in conservation genomics. Beyond validation, this work enables inference of genetic diversity loss and population structure over time, informing adaptive management and evolutionary resilience in the face of biodiversity collapse.

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SELECTED TO SHINE:

ENZYMES REPURPOSED FOR BIOLUMINESCENCE IN BRITTLE STARS

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Light produced by living organisms, known as bioluminescence, has fascinated curious minds for centuries, but its molecular origins remain puzzling. This capacity relies on an oxidation-based biochemical reaction catalysed by taxon-specific luciferase enzymes, illustrating multiple convergent molecular solutions for acquiring bioluminescence ability. Yet, distantly related luminous lineages can occasionally use homologous luciferases, such as the Renilla-type luciferase "RLuc", found in both certain sea pens (Octocorallia, Cnidaria) and the European brittle star Amphiura filiformis (Ophiuroidea, Echinodermata). These luciferases likely evolved from ancestral proteins with distinct, non-bioluminescent functions that were widely distributed among both luminous and non-luminous taxa. This raises questions about the genetic mechanisms underlying the transition from non-luminous enzymes to light-emitting ones.

Our study focused on the evolutionary history of RLuc-like genes in brittle stars. Our computational analyses show (1) the presence of at least one gene in all investigated brittle star species, irrespective of their luminous capability; (2) a tendency towards gene duplication in some species, particularly in A. filiformis; (3) evidence of diversification processes and significant positive selection acting on several A. filiformis sequences, including the functionally validated luciferase responsible for intense bioluminescence activity; and (4) the identification of positively selected sites and specific promoter motifs that may underlie functional and regulatory adaptations associated with neofunctionalisation towards bioluminescence. These molecular changes are further supported by cellular- and organ-level adaptations that optimise the efficiency of this newly acquired light-emission capability.

Overall, the glow of these brittle stars reflects the repurposing of pre-existing molecular tools shaped by positive selection.

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Transposable element exaptation as a source of novel genes in polyploid wheat evolution

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Transposable elements (TEs) are mobile sequences that, beyond reshaping genome architecture, can create novel genes through exaptation. Exapted TEs (ETEs) lose their mobility and assume the characteristics of conventional genes, with possible beneficial phenotypic effects. Yet, despite their potential as evolutionary innovation drivers, we still know little about how exaptation occurs or how ETEs evolve.

This study provides the first genome-wide analysis of TE-derived genes in bread wheat and its relatives, linking exaptation to evolution and domestication in a major polyploid crop. With our pipeline we identified 8,873 high-confidence ETEs in the Triticum aestivum genome, representing ~8% of annotated protein-coding genes. Functional enrichment revealed one significant KEGG pathway, plant hormone signal transduction, and GO terms related to quinone/ubiquinone, ketone metabolism, and pollen development, suggesting that exaptation played a role in shaping specific functional modules associated with signalling, metabolism, and reproduction.

Of 8,873 ETEs, 1,314 occur on only one of the three homoeologous chromosomes, suggesting they either originated in a single diploid progenitor or arose de novo during bread wheat evolution and domestication. To place these loci in context, we identified ETEs in bread wheat close relatives, finding ~10% of annotated genes in Triticum turgidum, ~10% in Aegilops speltoides, ~6% in Ae. tauschii and ~9% in T. urartu. The majority of wheat ETEs can be traced back to progenitor genomes. Several species-specific ETEs encode genes involved in important traits, including vernalisation, signalling, and circadian regulation, indicating that exaptation contributed non-randomly to wheat evolution, underpinning adaptive traits during domestication and polyploidization.

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Leveraging variation of matri- and patrilinear genomes reveals contrasting patterns of sex-bias dispersal in northern sea lions

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Dispersal is a fundamental driver of species evolution as it mediates gene flow between populations with consequences for population structure. In particular, sex-biased dispersal creates predictable genomic patterns characterised as stronger population structure in markers inherited through the philopatric sex, and lower structuring in those inherited through the dispersing sex. It is therefore possible to leverage the variation in independent genomic compartments to quantify dispersal asymmetry. The northern sea lions provide a classic example of a polygynous mating system with limited observational evidence for male-biased dispersal. Here, we investigated sex-biased dispersal in Galápagos (Zalophus wollebaeki; GSL) and Steller sea lions (Eumetopias jubatus; SSL) using whole-genome resequencing data across four genomic compartments quantifying female-only (mtDNA), mixed (X chromosome, autosome), and male-only (Y chromosome) inherited genetic variation. We found clear pattern of male-biased dispersal in SSL, as well as strong isolation by distance driven by female philopatry. In contrast, for GSL, our results suggest that females disperse more than previously thought, and that isolation by environment is a main factor explaining population structure for both sexes. Our results emphasise the importance of integrating multiple genomic compartments when interpreting dispersal and connectivity in marine mammals.

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Recovering Lost Kveik Diversity in Farmhouse Brewing with Ancient Metagenomics

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Brewing yeast diversity declined sharply after 1883, when Carlsberg's pure-culture breakthrough innovation replaced diverse fermentations with single strains worldwide. As craft and microbrewers now revisit mixed and non-conventional yeasts, we asked whether historic Norwegian kveik lineages persist and can be recovered with ancient DNA. We shotgun-sequenced residues from 25 historical yeast rings and fermentation barrels from six locations in Norway. Metagenomic profiling revealed diverse fermentation microbiomes dominated by Saccharomyces cerevisiae. Mitochondrial and nuclear phylogenies separated environmental/wild strains from a kveik-specific clade and demonstrated genetic continuity between historical artefacts and modern kveik. Historical material also carried kveik-associated variants linked to thermotolerance and flocculation, consistent with long-term domestication under farmhouse practices. We further detected secondary yeasts (e.g., Debaryomyces hansenii, Pichia kudriavzevii) and lactic acid bacteria (e.g., Lactobacillus spp.), indicating mixed fermentations that may contribute to flavour. Our results demonstrate that historical artefacts can preserve domesticated yeast lineages that were largely lost to industrial monoculture, and that ancient DNA and metagenomic analyses can monitor and potentially restore microbial diversity under decline, aligning with the session theme of molecular evolution in an era of diversity loss.

The Evolution of HLA Diversity in a Native American Population from Ancient to Modern Times

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The interaction between host and pathogens is a dynamic evolutionary process that has led to extensive genetic variation in immune-related genes, particularly within the human Major Histocompatibility Complex (HLA). While pathogen-mediated balancing selection is thought to be a major driver of this diversity, the relative contributions of other evolutionary forces—such as admixture and genetic drift—remain unclear. Moreover, the specific mechanisms of balancing selection and the pathogen-specific versus broad protective effects of HLA alleles are still under debate. To address these questions, we investigate HLA Class I and II diversity in pre- and post-European contact Native American populations from Xaltocan, Mexico—providing a temporal perspective on the impact of pathogens during European invasion of the Americas. Using ancient DNA-specific HLA genotyping, we characterized allele frequency changes over time. We observed that seven HLA groups showed significant frequency changes between ancient and modern populations. To evaluate whether these changes could be explained by genetic drift alone, we will use drift-only simulations, followed by tests for signatures of selection. This study provides critical insights into how pathogen exposure and evolutionary forces have shaped HLA diversity in Native American populations. More broadly, our temporal approach offers a valuable model for disentangling the complex drivers of immune gene evolution in human history.

Experimental evidence that balancing selection maintains sexually antagonistic genetic variation in a polygenic trait

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Genetic variation in fitness-related traits often persists despite ongoing selection, which is sometimes attributed to balancing selection. Sexually antagonistic selection (SAS), in which alleles have opposing fitness effects in males and females, has been proposed as one mechanism maintaining such polymorphism. However, how SAS influences genome-wide evolutionary responses during selection on polygenic traits remains unclear. Here, we address this question using an Evolve-and-Resequence experiment in the seed beetle Callosobruchus maculatus, manipulating the strength of sexual antagonism over body size and tracking genomic change.

We evolved replicated populations for ten generations under three regimes: sex-limited selection acting in a single sex, SAS (simultaneously favouring larger females and smaller males), and a relaxed-selection control. All regimes produced consistent phenotypic responses. Sex-limited selection resulted in the strongest divergence in body size, whereas SAS led to the greatest increase in sexual body size dimorphism.

Genomic responses contrasted markedly among regimes. Under SAS, allele-frequency changes were limited and genome-wide divergence remained low, despite ongoing phenotypic evolution. In contrast, relaxing sexual antagonism by selecting on only one sex produced large, repeatable allele-frequency shifts across populations. Loci underlying these responses were enriched for intermediate-frequency alleles and elevated Tajima's D in the ancestral population, consistent with long-term balancing selection. Functional annotation implicated developmental processes, particularly genes involved in BMP signalling, which diverged under sex-limited selection but showed constrained allele-frequency change under SAS.

Together, our results show that SAS can restrict short-term genomic divergence and preserve adaptive standing variation, reconciling persistent genetic diversity with ongoing phenotypic evolution.

Transcriptional Reprogramming as a Primary Driver of Long-Term Cold Adaptation in Wild Yeast

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How wild eukaryotes persist through prolonged periods of nutrient scarcity and extreme cold remains a fundamental question in microbial ecology. Specifically, it is unclear whether long-term adaptation to these conditions is driven by the classic selection of genetic mutations or by stable transcriptional rewiring. We addressed this by investigating the adaptive dynamics of the cryotolerant wild yeast Saccharomyces eubayanus during a 60-day chronological lifespan experiment at 4°C.

While aged isolates evolved a "specialist" phenotype with superior cryotolerance, whole-genome sequencing revealed a negligible genetic footprint with no fixed adaptive mutations, challenging the standard model of mutation-driven evolution. Instead, adaptation was underpinned by a massive transcriptional reprogramming. RNA-seq and network analysis identified a systemic shift from anabolism to a respiratory scavenging state, regulated by a rewired network involving Msn2/4 and HOG-pathway effectors. This physiological state, supported by mitohormetic ROS signaling and quiescent-like vacuolar reorganization, remained stable for ~40 generations under non-selective conditions. Crucially, this specialization occurred via an evolutionary trade-off, losing the cross-protection against other stressors observed in early adaptation. Our findings challenge the mutation-centric view of long-term microbial evolution, providing evidence that stable, transgenerational transcriptional states can serve as the primary driver for adaptation to persistent environmental stress. This work highlights the evolutionary significance of non-mutational plasticity in wild populations persisting in fluctuating extreme environments, such as the Patagonian Andes.

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What lives in, on, and around a lichen?

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Lichens are composite organisms in which filamentous fungi (mycobionts) and photosynthetic algae/cyanobacteria (photobionts) co-evolve to thrive in demanding habitats. In addition to the expected symbiotic organisms, lichens contain additional microorganisms, both prokaryotes and eukaryotes, found within the lichen, or on its surfaces. These organisms can help us expand our understanding of the ecology of the lichen and its interactions with the surrounding environment. Capturing this full biological complexity is possible by analysing lichen DNA sequencing data in a metagenomic framework.

At Tree of Life (ToL) at the Wellcome Sanger Institute we have generated high quality long-read sequencing data for 38 lichens. They are the result of collaborative efforts stemming from the Aquatic Symbiosis Genomics and the Darwin Tree of Life projects. We have explored the raw reads with k-mer based taxonomic profiling tools to identify organisms present, and we have assembled the data with the Metagenomeassembly pipeline, developed by ToL. Although DNA coverage limited the completeness of some eukaryotic assemblies, we recovered high-quality prokaryotic genomes and organellar sequences, as well as ribosomal DNA markers, enabling comprehensive taxonomic characterisation of the lichen symbiont communities. Moreover, complementary Hi-C data provided genomic interaction information, enabling additional insights into the organisation of lichen symbiotic communities and its interactions.

The session focused on hologenomics poses as the perfect stage to present our results, disentangling the complex community of organisms that were sequenced in each of our lichen samples, including insects, protists, and additional algae and fungi to the ones forming the lichen symbiosis.

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Not one Y, but five: evidence for mixed origins of Y haplotypes across the common frog's range

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In sharp contrast to the highly-degenerated Y/W chromosomes in most mammals and birds, most amphibians, many fishes and reptiles retain largely homomorphic sex chromosomes and undergo rapid turnover. The persistence of early-stage sex chromosomes without diversification is not understood. The common frog (Rana temporaria) is an exceptional system to understand it because multiple Y haplotypes coexist within and among populations and show variable X–Y differentiation. Utilizing chromosomal-level genome assembly, we generated RAD-seq data from 17 populations spanning the species range, representing three distintive levels of Y differentiation. We (i) quantify fine-scale X–Y differentiation within and across populations, (ii) reconstruct phylogenetic relationships and population-genetic dynamics of five Y haplotypes, and (iii) evaluate evolutionary scenarios with mixed origins across the species range. Across populations, X–Y differentiation is concentrated within a ~5 Mb sex-linked region encompassing the candidate sex-determining gene Dmrt1, or across the entire sex chromosome except the chromosome ends (~620 Mb), or there is no differentiation (XX males). Y-haplotype clustering broadly tracks the species' phylogeography, indicating strong coupling between Y variation and demographic history. Comparative analyses further suggest that the sex-determining region evolved after divergence from R. arvalis and Y haplotypes are best explained by two origins: four are consistent with a shared origin shaped by postglacial range expansion, while one Y-lineage has a distinct history. We speculate that introgression and/or recurrent sex reversals may contribute to the observed pattern. Our results reveal how demography and complex origins can structure early-stage sex chromosomes in non-model vertebrates.

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How and why genes survive on the human Y chromosome: Insights from telomere-to-telomere ape assemblies, long-read transcriptomes, and protein modeling

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The mammalian Y chromosome poses an evolutionary paradox: how do genes persist on this largely non-recombining chromosome prone to degeneration? Here, we address this question by integrating telomere-to-telomere Y chromosome assemblies from great apes with long-read transcriptomics and protein structure modeling.

Focusing on the seven canonical Y ampliconic gene (YAG) families (BPY2, CDY, DAZ, HSFY, RBMY, TSPY, and VCY), we resolve their full copy number, genomic organization, and evolutionary history at single-nucleotide resolution. We show that most YAGs are embedded within palindromes and tandem arrays that facilitate intrachromosomal gene conversion, driving concerted evolution and high sequence identity among copies, particularly those located on opposite arms of the same palindrome. Despite rapid structural lineage-specific expansions and contractions in copy number, our analyses reveal pervasive purifying selection on coding sequences, especially for CDY, HSFY, RBMY, and the RNA-recognition motifs of DAZ. Thus, structural dynamism coexists with strong functional constraint.

Using PacBio Iso-Seq from testis across great apes, we reconstruct isoform-resolved transcriptomes and demonstrate that gene survival is not merely genomic but functional: conserved structural isoforms—most strikingly for TSPY—are recurrently expressed across species, often supported by multiple sequence variants. Protein structure prediction further reveals that highly ordered domains are preserved despite extensive sequence and copy number variation.

In summary, Y-linked gene survival is enabled by palindrome-mediated homogenization, purifying selection, isoform conservation, and protein structural constraint. These findings illuminate the evolutionary scenario that preserves fertility-related genes on a non-recombining chromosome and offer new insight into the long-term persistence of the human Y chromosome.

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Molecular mechanisms of gene regulatory evolution revealed by in vivo genotype–phenotype maps

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Understanding gene regulatory evolution requires realistic genotype–phenotype maps that link regulatory DNA sequence variation to quantitative gene expression. Here, I present empirical in vivo genotype–phenotype maps for bacterial transcription factor binding sites (TFBSs), constructed using massively parallel reporter assays that quantify regulatory output for tens of thousands of sequence variants.

Across transcription factors with distinct regulatory scopes, these maps reveal highly rugged landscapes characterized by pervasive epistasis and thousands of local optima. Despite this ruggedness, evolutionary accessibility is structured rather than random: multiple high-function TFBSs can be reached from the same starting sequence, but the regulatory outcome attained depends strongly on mutational path structure and historical contingency.

By mapping regulatory landscapes for multiple transcription factors and explicitly characterizing their intersections—TFBSs that support regulation by more than one factor—we further show that regulatory innovation can proceed through molecular exaptation. Intermediate sequences frequently exhibit partial regulatory activity for multiple transcription factors, revealing transcriptional crosstalk as an intrinsic property of regulatory landscapes. Such intermediates can provide accessible mutational paths between distinct regulatory functions rather than constituting purely deleterious states.

Finally, comparing landscapes across regulators spanning local to global positions in gene regulatory networks demonstrates that regulatory scope is a key determinant of landscape architecture: local regulators evolve through clustered, accessible peaks, whereas global regulators are constrained by greater mutational robustness and slower evolutionary dynamics.

Together, these results identify general mechanistic constraints governing gene regulatory evolution and demonstrate how empirical genotype–phenotype maps inform the molecular basis and dynamics of regulatory evolution.

Plant terrestrialization: evolutionarily conserved mechanisms in UV acclimation in the closest algal relatives of land plants

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All land plants emerged in a singular evolutionary event: plant terrestrialization. During plant terrestrialization, the earliest land plants had to adapt to an array of rapidly changing terrestrial stressors. One of them was UV-B irradiation, which is filtered out to a large extent in the previously inhabited aquatic environments. We exposed one of the representatives of the closest algal relatives to land plants, the unicellular zygnematophyte Mesotaenium endlicherianum, to UV-B irradiance to elucidate its response to this major abiotic stressor. Integrating metabolomics, transcriptomics and physiological assessment, we comprehensively characterized the response of Mesotaenium to UV-B; we found that UV-B exposure induces the production of vacuoles containing UV absorbing compounds. To examine the composition of the metabolic response to UV-B, untargeted metabolite fingerprinting analysis was performed using an UHPLC-Q-TOF-MS system. We identified UV-B-induced metabolites such as phenolic compounds in profiling analyses. Extant land plants produce UV-protective phenolics sourced from the shikimate and downstream phenylpropanoid pathway. Homologs to enzymes involved in phenylpropanoid biosynthesis are also present within streptophyte algae and one, a homolog to 4CL, was found to be upregulated. Interestingly, it clusters closer to fatty acyl-AMP ligases, which could be involved in the polyketide pathway to produce the here identified coumarins. Our transcriptomic analyses reveal that homologs of expected UV-B response mechanisms such as the UV-B photoreceptor UVR8 and proteins of the photosynthetic machinery are differentially regulated. Contextualised with data from embryophytes, we infer the toolkit for diverse stress-induced mechanisms that likely constituted the functional core of the plant terrestrialisation toolkit.

Pervasive and convergent changes in the kynurenine pathway contribute to sugar-diet adaptations in bats

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While sugar-rich diets pose major metabolic challenges and can result in diseases such as diabetes and obesity in humans, several mammals adapt to feeding on natural sugar-rich food. Prime examples include bats in the New World family Phyllostomidae and the Old World family Pteropodidae, which convergently evolved fruit and nectar feeding. However, the genomic basis underlying these unique dietary adaptations remains unclear.
Using high-quality reference genomes of >100 bat species, generated by the Bat1K consortium to cover all recognized bat families, and state-of-the-art TOGA2 annotations of orthologous genes, we uncovered pervasive gene losses unique to fruit- and nectar-feeding bats, which severely impair the kynurenine pathway. The kynurenine pathway is responsible for ~95% of tryptophan catabolism in the liver of mammals, and plays key roles in immunity, neurodegenerative diseases, and metabolic diseases in humans. Transcriptomic data of liver samples representing 23 species revealed both convergent and lineage-specific expression shifts of kynurenine pathway genes in sugar-feeding bats compared to insectivorous bats. Furthermore, metabolomics revealed drastic differences in kynurenine metabolites in sugar-feeding bats, corroborating genomic and transcriptomic results. In particular, our data suggest that different sugar-feeding bats modulate the kynurenine pathway to either conserve tryptophan from protein-poor diets or to enhance the production of kynurenic acid, a metabolite linked to increased glucose oxidation and energy utilization. By combining comparative genomics, transcriptomics and metabolomics, our study discovered convergent remodeling of the kynurenine pathway in independently evolved sugar-feeding bat lineages, providing new insights into the genomic basis of adaptations in sugar and energy metabolism.

Maintenance of net deleterious mutations in polymorphism in fluctuating environments

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How non-neutral genetic variation is maintained in natural populations remains a fundamental question in evolutionary biology. Under environmental fluctuations, the fitness effect of a mutant allele may vary, shifting between beneficial and deleterious relative to the wild-type. If this fitness fluctuation is specific to individuals at a certain stage or age in the life cycle, it can give rise to negative frequency-dependent selection, leading to high levels of polymorphism. This impact of within-population heterogeneity under fluctuating selection is a key component of the diversity-promoting mechanism known as the storage effect. This study examines a general ecological scenario where fluctuating selection acts on genes determining the survival of the juvenile stage within an age-structured population that is also subject to demographic fluctuations. The results demonstrate that mutations with negative average fitness effects can nonetheless be maintained as polymorphisms. This counter-intuitive finding—the maintenance of net deleterious mutations—is explained by how the joint fluctuations of demography and selection modify the geometric mean fitness of a rare allele. Simple models of fluctuating phenotypic optimum predict that net deleterious mutations arise frequently. Therefore, this study reinforces the conclusion that significant non-neutral genetic variation is highly plausible in natural populations inhabiting fluctuating environments.

Disentangling Reticulate Evolution in the Mediterranean Wall Lizards with a Super Pangenome

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Wall lizards of the genus Podarcis form an abundant, diverse, and conspicuous clade in the Mediterranean. They exhibit remarkable phenotypic diversity, including convergent evolution of similar phenotypic syndromes alongside strong coloration divergence among closely related species and the emergence of island phenotypes distinct from nearby mainland populations. Their evolutionary history is reticulate, shaped by pervasive genetic exchange among lineages and resulting in mosaic genomes. We capture genomic diversity across the genus by constructing a super-pangenome using the pangenome graph builder (PGGB) and 15 high-quality, chromosome-level, haplotype-resolved reference genomes. Focusing on the shell component of the pangenome - shared by some but not all species - we quantify admixture-driven genomic mosaicism. Despite broad intrachromosomal collinearity and conserved gene content, the pangenome shows a three-fold increase in sequence length, largely driven by small variants (<50 bp). Larger structural variants (>50 bp) are enriched in transposable-element-dense regions and display a consistent positional bias toward one end of each acrocentric chromosome. We observe reduced cross-species diversity on the Z chromosome, indicating evolutionary dynamics distinct from autosomes and contrasting with elevated Z-linked diversity reported in avian species. Across species, approximately 20–25% of each genome comprises phylogenetically discordant regions, consistent with pervasive genomic mosaicism. Finally, we demonstrate the utility of the pangenome framework for characterizing the full spectrum of genomic variation and for resolving the evolutionary history of mosaic genomes.

Genomic and Phenotypic Differentiation of Cydia pomonella Populations Under Varied Pest Management Regimes in France

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Understanding pest adaptation to anthropogenic pressures is crucial when resistance enables population persistence under intensive management. In apple orchards, pheromone-based mating disruption (MD) has been widely adopted, releasing synthetic sex pheromones to prevent mate finding and reduce reproduction. However, declining MD efficacy has often led to increased chemical insecticide use, raising concerns about resistance evolution. Cydia pomonella, the codling moth, and a major apple pest, provides an ideal system to investigate the genetic basis of such unwanted evolutionary rescue. We first assessed phenotypic responses to MD. Flight tunnel experiments revealed altered orientation and landing behaviors in MD-exposed populations, while electroantennography showed significantly stronger antennal responses to synthetic pheromone, indicating changes in sensory perception and behavior that may facilitate persistence under pheromone saturation. To determine whether these phenotypic differences reflect underlying genetic divergence, we performed whole-genome resequencing of 95 individuals from three regions with contrasting management histories, revealing strong population structure with no admixture between distant populations and gene flow limited to neighboring populations. In the MD and insecticide–exposed population, three genomic regions exhibited reduced nucleotide diversity and elevated Fst and Dxy, consistent with high composite likelihood ratios from selective sweep analyses. Additional flight tunnel and Y-tube assays, GC–MS analyses of female pheromone blends, and transcriptomic comparisons of female pheromone glands and male antennae are ongoing. Together, these results suggest that resistance to MD and chemical insecticides likely involves polygenic adaptation and behavioral or regulatory plasticity, highlighting the complex genetic architecture underlying evolutionary rescue.

The Hidden Cost of Speed: A Molecular Conflict Between Light Damage and Visual Recovery in Human Evolution

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Reconstructing the evolutionary history of the visual niche has long relied on receptor kinetics (rhodopsin), where rapid active-state decay is assumed to facilitate fast pigment regeneration and visual recovery. This "kinetic-centric" paradigm posits that speed is the primary target of selection. We challenge this dogma via two discoveries. First, we demonstrate that slow rhodopsin kinetics are not adaptive for signal duration, but to protect cells against toxic accumulation of the chromophore, all-trans retinal. We identify this "Retinal Sponge" effect as a tunable, intrinsic property of the opsin scaffold. Secondly, we reveal that rhodopsin decay and chromophore clearance are functionally decoupled, such that decay does not predict visual recovery. We find that common human alleles with rapid decay kinetics paradoxically maintain high levels of trapped chromophore. This intrinsic sequestration acts as a competitive inhibitor for 11-cis retinal, effectively stalling pigment regeneration despite a "fast" kinetic signature. Strikingly, this trade-off appears to have driven convergent adaptation in humans. We map distinct "Constitutive" (African G51A) and "Inducible" (East Asian A299S) Sponge phenotypes to high-irradiance zones. Despite divergent molecular mechanisms, both variants convergently evolved to delay regeneration—sacrificing temporal resolution—to maximize cytoprotection. These findings expose a novel evolutionary axis: adaptations that enhance cytoprotection via sequestration necessarily compromise the metabolic speed of visual recovery, an acceptable trade-off favored repeatedly during human evolution. Furthermore, due to decoupling of decay rates from receptor recycling, we propose that many evolutionary transitions previously interpreted as optimizations for regeneration speed may instead represent adaptations that protect against light damage.

Copy That: Exceptional Retrocopy Abundance in Sloths and Xenarthrans

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Xenarthrans—sloths, anteaters, and armadillos—exhibit some of the most extreme morphological and physiological specialisations among mammals, including the exceptionally low metabolic rates that characterise sloths. Yet the genomic mechanisms underlying these distinctive traits remain largely unresolved. Genome plasticity driven by transposable elements can be a powerful source of evolutionary innovation, but its role in shaping long-term physiological specialisation is poorly understood. Using chromosome-level genomes including our new two-toed sloth (Choloepus didactylus) and the southern anteater (Tamandua tetradactyla) assemblies, we investigated how retrotransposon-mediated gene duplication has remodelled xenarthran genome architecture and adaptation. Comparative analyses across Xenarthra and 41 mammals reveal that xenarthran harbour the highest retrocopy burden reported to date, with pronounced lineage-specific dynamics. Anteaters and armadillos are characterised by predominantly ancient LINE-1 repertoires and older, species-specific retrocopy insertions. In contrast, sloth genomes retain abundant young LINE-1 elements and thousands of young retrocopies, together with a large shared cohort that originated from a burst of retroduplication in the lineage leading to their last common ancestor approximately 30 mya. Transcriptomes show that nearly half of retrocopies in C. didactylus are expressed, substantially exceeding levels observed in armadillos. Evolutionary analyses identify 38 sloth-only retrocopies with strong signatures of functional domestication, many derived from parental genes involved in mitochondrial function, energy metabolism, and cellular respiration. Together, these results implicate retrotransposition as a major driver of genome plasticity in Xenarthra and suggest that the extensive retention and functionalisation of retrocopies in sloths may have contributed to the molecular mechanisms underlying their uniquely slow and energy-constrained physiology.

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Using genomics to predict inbreeding depression risk: Case studies in Hawaiian birds

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Hawaiian birds are experiencing one of the most severe extinction crises of any vertebrate taxa, with only 25% of native species remaining. For many of the remaining species at or near the brink of extinction, a central problem is whether recovery will be limited by inbreeding depression. Leveraging recent genomic datasets from conservation breeding populations of imperiled Hawaiian birds, we show that the risk of inbreeding depression varies markedly among species. Focusing on two emblematic and critically endangered species, ʻakikiki and ʻalalā, we examined relationships between individual inbreeding—quantified as long runs of homozygosity (ROH)—and measures of survival and reproduction. While ROH are strongly associated with reduced fitness in ʻakikiki, we find little evidence for such effects in ʻalalā. Using genomic analyses and simulations, we further demonstrate that these contrasting outcomes can be predicted by the joint distribution of ROH and non-ROH heterozygosity, the latter serving as a proxy for masked recessive deleterious variation. Together, our results suggest a general genomic framework for predicting inbreeding depression risk based on ROH burden and non-ROH heterozygosity. We highlight the broad utility of this approach when applied to an additional diverse assemblage of bird and mammal populations, providing critical information to guide conservation decisions in cases where more direct measures of fitness are not available.

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New genome assemblies from neglected phyla illuminate the evolution of Ecdysozoa

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Ecdysozoa is the second largest clade within Metazoa and includes eight phyla. Little is known about the early evolution of the clade. Morphological features would group Priapulida, Kinorhyncha, and Loricifera into the clade Scalidophora. Moreover, the organization of the scalidophoran nervous system closely resembles that of Nematoda and Nematomorpha, leading to the proposal of the clade Cycloneuralia. Both hypotheses have been questioned by phylogenomic studies, opening a discussion on the evolution of ecdysozoan traits in relation to the inter-phyla relationships.

Previous phylogenies have mostly relied on transcriptomic data, particularly for phyla that are exclusively microscopic (i.e., Loricifera, Kinorhyncha and Tardigrada). For specimens smaller than 1mm, the DNA yields obtained after the extraction cannot meet the minimum requirements for long-reads sequencing. Therefore, long-reads high quality assemblies can only be achieved through amplification of the extracted DNA.

In this project we produced genome assemblies of six microscopic ecdysozoan: one Tardigrada (Florarctus antillensis), two Priapulida (Tubiluchus corallicora and Meiopriapulus fijiensis), two Kinorhyncha (Setaphyes dentatus and Echinoderes sp.) and two Loricifera (Armorloricus elegans and Nanoloricus valdemari), with the latter four being the first assemblies representing their phylum. For each specimen, the DNA extract has been amplified using two approaches, the long-range PCR and the multiple displacement amplifications. Combining the two methods, we achieved contiguous (N50 > 1 Mb) and complete (BUSCO > 90%) genomes from single microscopic individuals. With the inclusion of the new genomes, we will assess hypotheses such as Scalidophora and Cycloneuralia and characterize the evolution of pathways underlying key ecdysozoan traits.

Local genomic adaptation to rabies in raccoons

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Zoonotic diseases pose a major risk to human, domestic animal, and wildlife health, especially in an increasingly connected world. High-mortality pathogens act as a strong selective pressure and can drive local adaptation in wildlife reservoir species. Rabies virus is present in over 150 countries and is virtually 100% fatal in most mammalian species if left untreated. It is maintained by various bat and carnivore reservoirs including the raccoon, a reservoir for raccoon rabies virus variant (RRV) in eastern North America. Evidence suggests that eastern raccoon populations exhibit increased tolerance and survival of RRV after nearly 70 years of its presence in these populations. To investigate the genomic basis for adaptation to rabies in raccoons, we used whole-genome sequencing to test for genomic signatures of positive selection.We detected genome-wide evidence of selection in RRV-endemic populations, identifying 148 candidate genes under selection. Functional enrichment analyses revealed significant overrepresentation of pathways related to neuronal transport, viral entry and replication, translational control, and innate immune signaling. By revealing diverse molecular targets of selection, this study advances understanding of host–virus coevolution in natural populations and highlights how reservoir species may evolve resilience to highly lethal zoonotic pathogens, with important implications for disease maintenance and management.

Archaic Introgression in ancient Eurasians

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Archaic introgression, the DNA inherited from archaic humans, has been an important source of variation for the adaptation of modern humans outside sub-Saharan Africa.
Despite its significance, most of our knowledge comes from analyses of genomes belonging to present-day individuals, while only limited insights have been obtained from the large datasets of ancient genomes available so far.
When, and through how many events, modern humans encountered and admixed with Neanderthals and Denisovans remains an open chapter in our evolutionary history. Equally unresolved is how archaic introgression influenced past human adaptation and how these inherited regions evolved within modern genomes.
Imputation using a panel of present-day individuals is known to be a valuable way to improve ancient DNA quality. It has recently been shown to be highly effective at recovering genotypes within archaic introgression regions, thereby improving our ability to identify introgressed segments in the genomes of ancient individuals. We applied this approach to investigate a dataset of nearly two thousand ancient individuals from Eurasia. Our preliminary analyses reveal spatial and temporal patterns of archaic introgression across the continents and highlight genomic regions of archaic origin that appear to be over-represented in specific ancient populations.

High genomic connectivity and climate-linked demographic decline in the snowy owl

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Arctic ecosystems are undergoing rapid climate warming, providing an urgent opportunity to examine how molecular evolution, population connectivity, and demographic change interact under environmental stress. Here, we used whole-genome resequencing to assess population structure, genetic diversity, and recent demographic history in the snowy owl (Bubo scandiacus), a highly mobile Arctic apex predator recently reclassified as Vulnerable by IUCN. We analysed genome-wide data from individuals sampled across the species' circumpolar range, against a newly assembled chromosome-level reference genome. Population genomic analyses revealed an absence of detectable population structure, indicating extensive gene flow and near-panmixia across continents. Despite a modest global census size, snowy owls retain moderate nucleotide diversity and show limited evidence of recent inbreeding, with runs of homozygosity dominated by short tracts consistent with ancient rather than contemporary inbreeding. Our demographic inference revealed a sustained decline in effective population size over the past ~1,600 years, with pronounced reductions coinciding with historical warm periods and partial recoveries during cooler intervals. So, despite the current genetic robustness, the declining contemporary effective population size closely tracking climate warming raises concerns regarding long-term survival of the snowy owl. Our results demonstrate that high connectivity and retained genetic diversity do not necessarily buffer species against climate-driven demographic erosion. This study highlights the value of integrating whole-genome population genomics with temporal demographic reconstruction to disentangle genetic vulnerability from ecological decline, providing a framework for genomic monitoring and conservation decision-making in rapidly changing environments.

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The genomic consequences of introgression for an island-limited rail

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Small island-limited populations accumulate genetic load, reducing population fitness. Gene flow from more abundant populations has the potential to 'rescue' this effect, by increasing genetic diversity and providing new opportunities for selection against locally fixed harmful alleles. However, harmful recessive polymorphisms are far more abundant in large populations, and their introgression into a small island population could also increase genetic load. The long-term consequences of gene flow from abundant source populations to small sink populations are therefore unclear.
The Henderson crake, Zapornia atra, shows all the hallmarks of island life – increased body mass, flightlessness, a small census population size and reduced heterozygosity. The species is limited to a 37km2 island in the Eastern South Pacific, whilst its more widespread (flying) relative, the spotless crake, Zapornia tabuensis, occupies a vast range across Oceania and the South Pacific. Here we use whole-genome-sequencing data from modern samples and museum skins to investigate the demographic history of these species. We show that the Henderson crake has received migrants from the nearby (Eastern Pacific) race of spotless crakes, and that this gene flow occurred more recently than the bottleneck associated with island colonisation (<200kya), but far enough in the past for large admixture tracts to be broken down (>1kya). We then investigate the long-term consequences of gene flow by identifying small regions of the genome with strong signatures of introgression, and testing whether such regions carry an increase or a decrease in genetic load.

FAIRness of polymorphism data matters for plant demographic inference

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Many long-standing questions in population genomics (e.g. Lewontin's paradox, the prominence of adaptive evolution at the molecular level) can now be addressed through comparative analyses and by leveraging the vast amount of genomic data being generated. In the context of questioning the utility of producing such a large amount of genomic data, whether for ecological or economic reasons, we argue that data publication should be standardized to ensure long-term reusability. Based on a literature review and key examples, we emphasize that despite the growing volume of available data, the lack of methodological documentation and the absence of metadata make most published polymorphism datasets uncomparable, preventing the calculation of meaningful statistics. We stress that the standard Variant Calling Format (VCF) alone is insufficient to compute absolute statistics such as pairwise nucleotide diversity (π) or Watterson's θ. From a comparative analysis on plant demographies, we underscore the need for a systematic reporting of standardized statistics, coupled with transparent documentation of data processing steps, to ensure the reproducibility and comparability but also to isolate systematic bias from real biological signal. Finally, we propose guidelines and best practices to provide sufficient information to allow the proper calculation of standard statistics while accounting for sources of bias and misestimation frequently observed in the literature.

Genomic signatures of recent inbreeding are associated with rarity and habitat specialisation among flies of the UK.

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While monitoring programs have revealed dramatic shifts in population size and distribution in various focal insect species, the status of many insect populations remains unknown. Diptera (flies) are a ubiquitous and ecologically diverse order of insects, and while there is growing evidence of community-level declines, much of the knowledge we have on species-specific populations trends is anecdotal. At the same time, the growing availability of high-quality genomes offers new opportunities to investigate demographic history and evolutionary resilience in wild populations. Using reference genomes from the Darwin Tree of Life survey of eukaryotic genomes in Britain and Ireland, I examine patterns of genetic diversity in 150 UK fly species spanning the Dipteran phylogeny. I identify genetic variants within each reference individual and quantify genome-wide heterozygosity and runs of homozygosity (ROHs) as a measure of recent inbreeding. My analyses reveal that inbreeding is associated with observed species rarity and habitat specialisation, but not body size or trophic level, when accounting for phylogenetic relatedness. Forward-in-time simulations show that a demographic scenario of recent population decline can recapitulate genome-wide patterns of ROHs observed in several species. Together, these analyses demonstrate how single, high-quality genomes can provide valuable insights into the genetic status and potential evolutionary resilience of species across an ecologically diverse clade of insects.

Comparative genomics reveals chemosensory gene family evolution within a conserved genome architecture in Culex

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Culex mosquitoes are major vectors of West Nile virus and other pathogens affecting humans and wildlife. However, their evolutionary genomics, particularly genome-wide architecture and gene family evolution, remains poorly studied beyond Culex pipiens complex. Here, we apply a comparative genomics approach across Culex species present in the Mediterranean basin (Culex pipiens forms pipiens and molestus, Culex modestus, Culex perexiguus, Culex laticinctus, and Culex theileri) and other members from Culex pipiens complex (Culex quinquefasciatus and Culex pipiens pallens). We integrate phylogenomics, genome-wide synteny and comparative analyses of gene families to investigate genome evolution and chemosensory diversification.

Using eight high-quality reference genomes, we resolved their evolutionary relationships and clarified the placement of closely related members of the Culex pipiens complex. Synteny analyses revealed conserved chromosomal architecture with limited rearrangements between taxonomic units, indicating that diversification in ecological traits such as host preference have evolved against a stable genomic background. Chemosensory gene families showed interspecific variation in gene repertoires while maintaining similar genomic organization. Odorant-binding proteins (OBPs), olfactory receptors (ORs) and gustatory receptors (GRs) showed conserved clustered distributions but substantial differences in gene family sizes. Culex quinquefasciatus and Culex pipiens pallens exhibited the largest gene repertoires, while species outside the Culex pipiens complex consistently displayed smaller gene family sizes.

These results clarify evolutionary relationships within Culex and highlight the dynamic evolution of chemosensory gene families within a conserved genome structure. Our findings reveal gene family turnover as an important driver of diversification within Culex, offering new insights into sensory ecology and vector-associated traits.

Assessing dog introgression through structural variants in European refugial wolf populations

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European wolves have recently undergone a remarkable demographic recovery, however the potential conservation implications of wolf-dog hybridization across a broad range of genomic variation remains unclear. For example, wolf-dog hybridization can alter the adaptive potential of wild wolf populations, yet its genomic consequences have been inferred from single nucleotide polymorphisms (SNPs) alone. Here, we tested whether structural variants (SVs) capture patterns of admixture and introgression between wolves and dogs in three European wolf populations from glacial refugia (Dinaric-Balkan, Iberian, and Italian), where wolf-dog hybridization has been relevant over the last 30 years. Moreover, we included a broad representation of domestic dogs, plus Karelian wolves and three outgroup species to infer introgression. Admixed and non-admixed individuals were first identified using genome-wide SNP-based analyses, providing an independent reference to assess SV-based signals. Then, we characterized deletions, duplications, and inversions and implemented tailored dual approaches to identify putative recent and historical dog introgression separately within each wolf population and SV category. Deletions and duplications captured broad-scale population structure and revealed signatures of genome-wide admixture, although with lower resolution than SNPs, whereas inversions only distinguished wolves from dogs. We identified both putatively recent and historical dog introgression, highlighting heterogeneous dynamics across refugia. Gene ontology analyses of candidate introgressed SVs suggested potential functional roles that might have shaped physiology, behavior and ecology during population evolution and following recent admixture. Overall, our results show that SVs provide a complementary perspective to SNPs, adding an additional layer for disentangling the genomic impacts of wolf-dog hybridization.

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Genomic legacy of near extinction and intensive management in the pink pigeon

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Intensive management can rescue population size yet fail to rescue genetic diversity. The pink pigeon (Nesoenas mayeri), endemic to Mauritius, declined to 9-10 known wild birds in the 1990s but recovered to ~600 in the following decades through captive breeding, reintroductions, predator and disease control and supplementary feeding. Given the well-documented demographic trajectory and decades of monitoring, this species provides a powerful system for quantifying how intensive management shapes genomic trajectories in recovered populations. We generated 150 whole-genomes spanning 180 years, capturing before and after the population nadir. Using this time series, we quantified genome-wide and immune gene diversity, inbreeding, putative load, kinship structure, and demographic history.

We document a ~20% loss of genetic diversity between historical and 1990s individuals, accompanied by rising inbreeding, evidenced by an increase of medium- to long-length runs of homozygosity. Genetic diversity continued to decline during the period of most rapid demographic recovery, with no evidence of rebound between 1990s and contemporary individuals. Kinship analyses show strong early-recovery reproductive skew, with contemporary birds descending from only a few lineages, which could help explain the continued loss of diversity despite rising population size. Moreover, SLiM simulations show that gains from future genetic rescue will be limited, as the captive population has also lost substantial diversity.

Our results illustrate the challenges of restoring genomic diversity in severely bottlenecked populations and highlight the importance of evolutionary-informed management strategies that account for effective population size, lineage representation, and the timing and sources of reintroduction events in genetically depleted populations.

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Pollen tube competition is mediated by a gene subject to Positive Selection in Arabidopsis

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Genes expressed in flowering plant pollen tubes are predicted to evolve under positive Darwinian selection, due to competition for access to ovules, and this has been confirmed at the whole transcriptome level. However, no pollen tube-expressed gene under positive selection has been identified. Here, we demonstrate that an uncharacterised gene encoding a protein kinase is specifically expressed in Arabidopsis thaliana pollen tubes and is evolving under positive selection. This gene is required for correct pollen tube guidance both in vitro and in vivo: while knock-down lines still produce viable pollen and fertilize full seed sets when pollen is in excess, the competitive ability of their pollen is significantly impaired. This demonstrates that positive selection is associated with evolutionary competition between pollen tubes, in a manner analogous to mammalian sperm and in agreement with theories that sexual selection is a major driver of gametophyte function in flowering plants.

Improved Power to Detect Sparse Episodic Positive Selection: A Protein Language Model-Informed Branch-Site Approach

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Background: Episodic positive selection typically affects only a small fraction of sites (~1%) along specific lineages. However, standard branch-site likelihood ratio tests (BS-LRTs) have mostly been evaluated under dense positive selection (e.g., 20–40% of sites). We simulated fitness shifts at ~1% of sites (5 of 500 codons) using non-equilibrium, time-heterogeneous mutation-selection models, revealing a "power crisis": traditional tests have little power to detect adaptation in biologically realistic regimes, rendering most subtle fitness shifts statistically undetectable.

Innovation: We demonstrate that power can be substantially recovered by incorporating site-specific covariates into a mixture-model framework for BS-LRTs. In "oracle" simulations providing full to partial separation of shift from non-shift sites (3–5 of 5 correct), power reached 81% for large fitness-shift effect sizes (high Kullback–Leibler divergence between stationary distributions), compared to <5% via standard methods on the same data. To translate this approach to empirical data, we introduce a pipeline using the ESM-2 protein language model (PLM) to derive informative site-specific covariates by comparing sequence probabilities in foreground versus background clades.

Results & Application: Preliminary results using carefully constructed null distributions confirm that PLM-derived scores are significantly enriched at true shift sites, effectively mimicking the partial "oracle" conditions that restored power. We are completing BS-LRT power evaluations using PLM-derived covariates to quantify power gains relative to: a) standard; b) oracle (mixture model) methods; and c) site-specific LRTs. This work bridges protein representation learning with statistical phylogenetics, offering a scalable approach to identify the subtle adaptations that define lineage-specific biology.

Transposable element islands at the interface of 3D genome architecture and karyotype evolution in ants

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Karyotype diversification is a common phenomenon in evolution, yet how the underlying chromosomal rearrangements emerge often remains unclear. Here, we generated chromosome-level assemblies for ten species of Cardiocondyla ants and the outgroup Nesomyrmex wilda to investigate the genomic basis of karyotype diversification. Cardiocondyla species possess the smallest ant genomes reported yet exhibit extraordinary chromosome number variation (1n=8-32). Transposable Elements (TEs) in Cardiocondyla genomes are highly compartmentalized into dense TE Islands. These islands coincide with pericentromeric regions, are hotspots of structural variation, and frequently overlap chromosomal breakpoints, implicating them as anchors of Robertsonian fusions and rapid centromere turnover. 3D genome analyses revealed spatial clustering of centromeres embedded in TE Islands, providing a structural context facilitating repeat-mediated chromosomal rearrangements. Our results identify TE Islands as focal regions that both promote and record structural genome evolution, revealing a mechanistic link between TE compartmentalization, 3D genome organization, rapid karyotype diversification and genome compaction.

A statistical framework for DNA methylation repeatability in natural populations

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Epigenetic regulation is known to be influencing phenotypic plasticity and adaptation and may drive evolutionary forces if epigenetic variation is heritable. Wild populations are ideal for studying epigenetic variation where selection acts more realistically, but complicated natural systems exhibit more biological variation than in laboratory settings and needs careful measurements. Reduced Representation Bisulfite Sequencing (RRBS) enables genome wide profiling of DNA methylation in non model organisms, but technical noise and data processing choices can substantially affect inference in comparative and evolutionary analyses. In this work, we examine how reliable DNA methylation is across technical replicates, across two different wild avian species by quantifying the variance introduced from technical sources. We develop and apply a statistical framework in order to quantify and model DNA methylation repeatability. We evaluate key analytical steps, including post alignment SNP filtering, the use of technical replicates, and the estimation of per site repeatability metrics. Preliminary results show that repeatability varies widely across CpG sites and is strongly structured by genomic context and data quality features. We further identify predictors of repeatability, which enable the classification of CpG sites into reliable and unreliable regulatory signals. Finally, we assess how aggregation across genomic windows and functional regions alters data structure and downstream interpretation. Together, this framework improves the identification of robust methylation signals and provides a statistically grounded approach for modelling the evolution of gene regulation from population scale epigenomic data.

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Ancient Reconstructed Proteins, inferring ancient proteins from ancient metagenomics samples

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The de novo assembly of ancient metagenomics samples remains one of the most challenging computational problems. We have recently shown that ancient DNA damage is the most crucial problem to solve. However, its incorporation into an assembler called CarpeDeam enables us to retrieve longer contigs from ancient environments. In addition, we have released a tool called AdDeam, which allows users to validate which contigs are likely to be ancient in origin. We show that we can combine this methodology with AlphaFold to increase the protein repertoire by retrieving proteins annotated from ancient contigs, folding them and comparing them to modern orthologs. We demonstrate the potential of ancient reconstructed proteins by predicting 1,299 methane-related protein structures using the two-million-year-old datasets from the Kap København Formation in Northern Greenland. Our methodology could infer ancient proteins to reconstruct metabolic capabilities that have since gone extinct and facilitate the study of protein functions by increasing our protein repertoire.

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Convergent and divergent genetic routes to persistence under thermal stress in the yeast genus Saccharomyces

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Thermal adaptation is a central determinant of species distributions and evolutionary rescue under climate warming, yet the extent to which molecular responses are conserved across species remains unclear. Using the budding yeast genus Saccharomyces as a comparative evolutionary model, we combined long-term experimental evolution with whole-genome and functional analyses to dissect the phenotypic and genomic basis of adaptation to sustained temperature increases. We evolved populations of eight Saccharomyces species under constant and progressively increasing temperature regimes, exceeding ancestral thermal limits in several species, to assess their potential for evolutionary rescue under future warming. Thermal performance curves varied significantly among species, revealing two main adaptive trajectories with contrasting rescue outcomes. Warm-tolerant species evolved higher optimal growth temperatures and increased thermal tolerance, whereas cold-tolerant species evolved broader thermal breadth and higher upper thermal limits but exhibited reduced maximum performance. To identify the molecular basis of these responses, we performed whole-genome sequencing of 256 evolved genotypes. Across species, independent lineages repeatedly accumulated de novo mutations in conserved signaling pathways, particularly TORC1, PKA, and MAPK, revealing strong functional convergence at the pathway level. In contrast, species-specific fitness outcomes were associated with divergent regulatory rewiring, distinct gene expression responses, and frequent mitochondrial DNA loss in some lineages. Functional assays confirmed that mitochondrial state and signaling pathway modulation jointly shape thermal tolerance trajectories. Together, our results demonstrate that evolutionary rescue from sustained warming is driven by conserved molecular targets but constrained by lineage-specific physiological and mitochondrial differences, defining the limits of thermal adaptation across species.

Sex chromosome variation across vertebrate genome assemblies

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The mechanisms of sex determination, the system that determines whether an organism differentiates into male or female, vary extensively across vertebrate lineages. While birds and mammals have largely conserved genetic sex determination systems, other vertebrate clades, including squamate reptiles, turtles, ray-finned fish, and chondrichthyan fish, have multiple independent sex determination systems. This independent evolution made identifying sex chromosomes in whole genome assemblies challenging. Recently, researchers in the Vertebrate Genomes Project (VGP) have generated multiple haplotype-resolved genome assemblies and annotated sex chromosomes across the vertebrate Tree of Life. Using VGP's high-quality dataset, we analyzed sex chromosome biology across ~500 MY of vertebrate evolution, examining variation in relative sex chromosome size and repeat density. We defined pseudoautosomal region (PAR) boundaries using sex chromosome alignments to compare sex chromosome structure within and between taxonomic groups. We found that Z and X chromosomes are generally, but not always, larger than W and Y chromosomes, and the size ratio varies extensively within and between vertebrate clades. We further applied multiple approaches to identify previously unannotated sex chromosomes in the VGP genome assemblies, uncovering putatively novel chromosomal sex determination systems. Here we present our summary analyses, including novel approaches for annotating and curating sex chromosomes in haplotype resolved assemblies.

Balancing and Positive Selection Shapes the Spot Patterning Phenotype in the Masai Giraffe

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Masai giraffes have intricate spot patterning with highly variable shape and size. Spot patterning is heritable, and variation in spot patterning influences survivorship in both calves and adults. This suggests that natural selection may influence spot pattern variation in the Masai giraffes. Here, we sampled and sequenced 23 Masai giraffes from the Serengeti National Park in Tanzania, Africa, and 12 captive Masai giraffes to study how selection shapes genetic variation in these animals. After calling genetic variants, we characterized population structure among four wild populations and the captive individuals. We then performed multiple allele-frequency and haplotype-based selection scans to detect signals of both positive selection and balancing selection. These analyses, combined with functional enrichment analysis, identified several candidate genes involved in melanin production that may play key roles in spot patterning. One gene, putatively under positive selection, is essential for the development, survival, and function of melanocytes. Another gene, putatively under balancing selection, is involved in the degradation and trafficking of melanin. These results suggest that giraffe spot patterns are not merely aesthetic traits but are shaped by selection. Furthermore, spot patterning may have important implications for understanding unusual phenotypes and informing conservation strategies.

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Tracking the evolution of protein fusion entrenchment via genomic directed evolution

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The evolution of multi-domain proteins is often characterized by the fusion of previously autonomously folding domains. While the prevalence of multi-domain proteins is often attributed to adaptive benefits, this architecture can become irreversible simply because separating the domains becomes deleterious—a process termed entrenchment. We hypothesize that protein fusions can become "locked" in a fused state during co-evolution, where mutations accumulate that are harmless in the fused context but disrupt function if the domains are separated.

To capture the emergence of dependence on the fused state, we deployed a genomic directed evolution method to evolve the histidine biosynthesis enzymes HisI and HisE. Standard directed evolution relies on plasmids, but their uneven distribution and over-expression of proteins distort selection for dosage-sensitive metabolic enzymes. To avoid these artifacts, we employed a CRISPR-Cas9 editing system to evolve a Listeria innocua hisIE fusion directly within the E. coli His operon, maintaining native expression levels. We generated two libraries: one maintaining the fusion and one with forced fission by reintroducing stop and start codons before each round of selection. We evolve the fusion only, but measured the fitness of fusion and fission at every generation using pacbio. By tracking the fitness of the fusion relative to its non-fused counterpart, we can identify the specific mutations that enlarge the fitness differences between the two states.

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Evolutionary rescue via short-lived modifiers of genetic variation

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Evolutionary rescue depends on the availability of genetic variation. Empirical studies have shown that environmental change can promote the evolution of mechanisms that generate such variation, including increased recombination or mutation rates. To identify conditions under which this feedback facilitates rescue, we analyze a three-locus model consisting of two fitness loci and an unlinked modifier locus that alters either recombination or mutation rates. Using analytical approximations validated by stochastic simulations, we show that a rare modifier mutation—whether promoting recombination or mutation—can substantially enhance the probability of rescue. Our main finding is that this enhancement often occurs despite the modifier quickly assorting onto the wild type background and thus disappearing before the rescue process is complete. We consider modifiers arising from both standing genetic variation and de novo mutation, and we identify conditions under which recombination modifiers are more likely to promote rescue than mutation modifiers. Overall, our results suggest that short-lived changes in the genetic architecture of populations can play a decisive role in enabling evolutionary rescue.

Molecular phylogenetics directly from deep learning protein foundation models

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Protein foundation models (pFMs), also known as protein language models, are large neural networks trained on hundreds of millions of protein sequences, commonly implemented using the transformer architecture. pFMs are becoming a focal point for studies in evolutionary inference, leveraging extracted information about species relationships for myriad applications. In this context, we raise a fundamental question relevant to this symposium: What is the distribution of evolutionary information captured by different layers of the network for a given protein sequence alignment? We analyzed signals of species phylogeny across the layers of two state-of-the-art pFMs: MSA Transformer, trained on multiple sequence alignments (MSAs), and ESM-2, trained on unaligned sequences. We developed methods to convert transformer attention matrices, which quantify how strongly each sequence or residue position influences others in the dataset, into pairwise evolutionary distances. These distances were then used to construct neighbor-joining trees without relying on any explicit models of sequence evolution. Our findings indicate that phylogenetic information is uniformly distributed across the layers of MSA Transformer, while ESM-2 tends to concentrate learned species relationships in its earlier layers. Surprisingly, the species phylogenies generated by ESM-2 are often more accurate than those derived from MSA Transformer, even though MSAs are not used in ESM-2's pretraining or tree reconstruction. We will discuss possible reasons for this intriguing result. Additionally, we will compare the performance of classical phylogenetic methods with pFM-based phylogenetics to evaluate the advantages and limitations of deep learning models in reconstructing evolutionary histories.

Giant toxin genes, extreme genome variation, and repeated hybridization in harmful bloom-forming haptophyte golden algae

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As sequencing technologies become more accessible, genomes of previously neglected microbial eukaryotic lineages are reshaping our understanding of gene and genome architecture and evolution, pushing the boundaries of what was once thought possible. A compelling example comes from genome analyses of the toxic haptophyte Prymnesium parvum sensu lato (s.l., in the broad sense) also known as golden algae. Toxic blooms of P. parvum s.l. can cause catastrophic damage to aquatic ecosystems and human aquaculture. Although its members are morphologically indistinguishable and previously considered a single species, P. parvum s.l. is now recognized as a species complex harboring considerable genomic and biochemical diversity. Haploid genome size estimates among strains representing different chemotypes range from 115 to 359 Mbp, largely driven by rapid proliferation of transposable elements. Vegetatively haploid, diploid, and polyploid strains can be maintained in stable culture, and comparative genomic analyses suggest rapid evolution via mitotic recombination, loss-of-heterozygosity, and aneuploidy. P. parvum s.l. is also capable of repeated hybridization, as indicated by chloroplast cytotype differences among hybrid strains co-isolated from the same bloom. Golden algae produce prymnesins, giant hemolytic fish toxins that are among the largest known non-polymeric metabolites. Genome sequencing enabled the discovery of correspondingly massive proteins (~45k amino acids), encoded by record-setting modular polyketide synthase genes (PKZILLAs), responsible for prymnesin biosynthesis. Together, our analyses provide a robust phylogenetic, genomic, and biochemical framework for investigating the eco-evolutionary consequences of extreme genetic variation present in P. parvum s.l. and highlight the need for similar resources for other neglected microbial eukaryotes.

Cis and trans contributions to cell type–specific regulatory evolution in primates

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Understanding how gene regulatory programs diverged between humans and other primates remains a central challenge in evolutionary genomics, largely because regulatory mechanisms operate in a highly cell type–specific manner. We previously addressed this limitation by developing heterogeneous differentiating cultures (HDCs) from human and chimpanzee iPSC panels, enabling systematic, parallel profiling of matched cell types across species. Here, we extend this framework to directly interrogate regulatory architecture using single-nucleus multiomics.

Using paired single-nucleus RNA-seq and ATAC-seq data, we profiled 135,000 nuclei from 7 human and 9 chimpanzee HDCs, generating a high-resolution, cell type–resolved atlas of chromatin accessibility and gene expression in the two species. Among 695,945 orthologous open chromatin regions spanning 22 cell types, we identified thousands of regions with species-specific accessibility, approximately 20% of which overlap putative enhancers. To resolve the genetic basis of these inter-species regulatory differences, we profiled an additional 40,000 nuclei from a human-chimpanzee allotetraploid HDC line, enabling direct separation of regulatory divergence into allele-specific (cis) and shared (putatively trans) components.

By integrating chromatin accessibility with matched gene expression profiles from the parental lines and the allotetraploid model, we linked candidate cis-regulatory elements to their target genes and uncovered widespread cell type–specific regulatory activity. Transcription factor motif analyses further revealed coordinated divergence in TF expression and motif enrichment, consistent with remodeling of regulatory networks across species.

Together, these results provide a mechanistic, cell type–resolved view of primate regulatory evolution and establish a scalable experimental framework for dissecting the genetic basis of human-specific regulatory innovation.

Bagworm moths: a new model for studies of genome evolution across variable levels of sexual dimorphism, from mild to extreme.

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Sexual dimorphism is intriguing because each sex within a species shares the same genomic information while manifesting striking, sex-specific phenotypes. Although this topic has received substantial attention, inferences are often limited as most examined systems exhibit mere modifications of a shared body plan. Therefore, systems containing varying degrees of dimorphism are needed to clarify how sex-specific phenotypes arise. One such system is the Bagworm moths (Lepidoptera: Psychidae). In this conserved ZZ/Z0 system, females exhibit a continuum of body plans: fully winged, half-winged, wingless, and vermiform (which lack most typical adult characters). Males retain fully developed wings/ appendages. Paired with peculiar reproductive ecologies, Psychidae provide a powerful model for examining how variation in sexual dimorphism shapes genome evolution.

Here, we introduce Psychidae as a comparative system, present preliminary results, and outline efforts to characterize genomic variation using a phylogenetic framework. Leveraging publicly available data and in-house generated chromosome-level assemblies, we explore how shifts in female form relate to genome architecture, including structure, divergence rates, genetic novelty, and heterozygosity. Initial analyses reveal overall highly conserved synteny, with gene movement onto and off the Z chromosome largely confined to vermiform lineages. The Z chromosome also contains proportionally more novel genes than autosomes in highly dimorphic species. Expression patterns indicate increased female-biased novelty in the winged-to-wingless transition, while vermiform evolution involves novel genes expressed in both sexes. Together, this work highlights Psychidae as an integrative system for the examination of sex chromosome dynamics, chromosome rearrangement, and sexual dimorphism within a single evolutionary framework.

Ancient Genomic Analysis of a New Mycobacterium tuberculosis Lineage from Iron Age Britain

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Tuberculosis is the leading cause of death due to infectious disease in contemporary human populations, and evidence of selection on TB-associated variants suggests that the disease has afflicted Eurasian populations for at least 2,000 years (Kerner et al. 2021, Akbari et al. 2024). Beyond this human impact, a paraphyletic clade within the Mycobacterium tuberculosis complex (MTBC) evolved to specialize on a diverse array of domesticated and wild mammals. Several human-infecting lineages fall within the animal-infecting clade, suggesting a complex history of inter-species transmission and adaptation; however, both the antiquity of these animal-adapted lineages and the genomic underpinnings of host specificity within the MTBC remain poorly understood. We report the oldest whole-genome Mycobacterium tuberculosis data generated to date from a 20–25-year-old female Iron Age individual from the site of Wetwang Slack in East Yorkshire, United Kingdom (Burial 9, c. 400-50 BCE). Molecular dating analyses incorporating this basal lineage may help to resolve long-standing debates regarding the antiquity of tuberculosis in human populations. Interestingly, while Burial 9 exhibits no pathological alterations, contemporaneous remains from both humans and livestock buried at Wetwang Slack display lesions characteristic of tuberculosis infection (Wooding et al. 2022). Consistent with these observations, phylogenetic analysis of modern and ancient MTBC diversity places the Wetwang lineage basal to all animal-infecting MTBC strains. While further sampling and analysis is needed, osteological and genomic evidence suggests that the Wetwang strain may represent a previously unsampled host-generalist lineage, providing an opportunity to shed light on the evolution of host specificity within the MTBC.

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To purge or not to purge? How mating systems shape transposable element dynamics in Mimulus (monkeyflowers)

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The shift to self-fertilization (selfing) is one of the most common evolutionary transitions in plants and results in dramatic genomic consequences. Owing to reduced effective population size, selfing species often have increased homozygosity, reduced genetic diversity, and more deleterious mutations. However, empirical evidence of the impact of selfing on transposable element (TE) evolution is mixed, and evolutionary theory is similarly conflicted. While selfing lineages are expected to accumulate more deleterious mutations, such as new TE insertions, due to the reduced efficacy of selection, they are also theorized to purge highly deleterious TEs. Here, we investigated how transitions to self-fertilization impact TE dynamics in the genus Mimulus (monkeyflowers) using comparative genomics and pangenome TE annotations for three pairs of closely related outcrossing and selfing species representing three independent transitions to selfing. We have found that the selfing species differ in the distribution of TEs within their genome and accumulate fewer young TEs compared to their outcrossing relatives. Characterizing intra- and interspecific TE presence/absence variation has further clarified the evolutionary processes driving these dynamics in selfing monkeyflowers. Ultimately, this work provides powerful insights into the fate of TEs in selfing lineages, helping to reconcile the conflicting patterns seen in previous empirical studies and predicted by evolutionary theory. It also illuminates the evolutionary mechanisms that may be shaping the fate of TEs in selfing lineages.

BLInG: Enabling Genomic Studies of Unicellular Organisms to Illuminate Major Evolutionary Transitions with Single-cell Genomics

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Unicellular organisms are critical for understanding major evolutionary transitions, from the origin of eukaryotes to the emergence of multicellularity and complex symbioses. Recent discoveries of novel eukaryotic lineages, including uncultured protists that serve as sister groups to multicellular lineages, have revolutionized our understanding of these transitions. However, many phylogenetically pivotal unicellular organisms remain impossible to culture, creating a significant barrier to genomic characterization. While single-cell transcriptomics has advanced, single-cell genomics has lagged behind, limiting our ability to investigate genome evolution across evolutionary transitions.

To address this challenge, I am developing BLInG (Barcode Ligation for Intracellular Genomics), a novel single-cell DNA sequencing method that eliminates physical cell isolation. All existing single-cell genomic technologies require isolating individual cells into separate wells or droplets—a fundamental constraint incompatible with fragile protists, environmental assemblages, and symbiotic consortia. BLInG overcomes this barrier through a paradigm shift: instead of separating cells, we perform whole-genome amplification inside intact cells in mixed populations, then use combinatorial split-pool barcoding to assign unique molecular identifiers to each cell's amplified DNA. This enables simultaneous sequencing of thousands of cells while maintaining single-cell resolution, dramatically increasing throughput and reducing costs compared to isolation-based methods.

BLInG enables genomic analysis of previously inaccessible unicellular lineages, including uncultured protists and unicellular relatives of multicellular organisms. By enabling high-throughput genomic analysis, BLInG will facilitate comparative genomic studies essential for understanding genetic innovations underlying major evolutionary transitions, variations in genetic codes, and the evolution of cellular complexity across the tree of life.

Functional genomic diversity and migratory survival: implications for evolutionary management of a critically endangered parrot

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The orange-bellied parrot (Neophema chrysogaster) is a critically endangered migratory parrot endemic to Australia, facing an 87% chance of extinction by 2038. Following repeated population crashes in the wild, the species reached a low of just 3 wild-born females and 12 males in 2016. Despite intensive conservation efforts commencing in the 1980s, modelling has shown that juvenile survival during migration remains one of the top threats to population recovery. Using 94 resequenced genomes of wild (N=45) and captive (N=49) birds combined with a comprehensive meta-dataset, we investigated the genomic basis of migratory success. Using sequences from all possible unrelated wild-born individuals between 2015 and 2023, we investigated genome-wide associations to identify candidate genomic regions potentially linked with successful migration discovering 6 significant regions. We examined the presence and frequency of these candidate genotypes within the captive breeding population that provides individuals for release. Using these insights, we provide guidance for the recovery team on selecting the most suitable captive individuals for release, aiming to retain the successful migratory genotype while preserving overall genome-wide genetic diversity. This study provides a next-step critical framework in the field of conservation genomics for the management of threatened species whereby functional genomic data is associated with a known phenotype and used to inform management actions.

Characterizing HIF-pathway alteration across two early diverging metazoan lineages (Ctenophora, Porifora).

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Ctenophores and sponges are some of the earliest diverging metazoans, evolving in very low oxygen conditions 800 million years ago. Although there was little oxygen present, they still seemed to have parts of the pathway associated with oxygen homeostasis - the Hypoxia Inducible Factor (HIF). This pathway is considered highly conserved across all of metazoa, with only a few recent exceptions. Previous work has shown that the main HIF transcription factor (HIFa) is present in sponges and ctenophores; yet it is the canonical domain associated with oxygen sensing (oxygen degradation domain; ODD). Additionally, they are missing the primary repression genes in the HIF pathway (EGLN). This leaves the question of whether HIFa evolved de novo or if it was co-opted from existing machinery. Also, it is unknown if these differences in the basal metazoan pathway were present in prior lineages (choanoflagellates). Using publicly available genomes and transcriptomes, I analyzed a wider breadth of basal metazoans, as well as the closest outgroup, for the presence of various elements of the HIF-pathway: 19 species of ctenophores, 15 species of sponges and 19 choanoflagellate species. Ultimately, we confirm the presence of a “HIFa”-like in sponges and ctenophores with no similar member in choanoflagellates. Further investigation is needed to determine if “HIFa” in ctenophores and sponges have oxygen related functions. Investigating HIFa in ctenophores and sponges will elucidate what the ancestral function of this gene is and ultimately help us understand how animals adapted to the rise in oxygen concentrations during early animal evolution.

Decoding gene essentiality from cross-species transcriptional constraints

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Evolutionary constraint at the sequence level has long been central to understanding the genetic basis of disease. Measures of loss-of-function tolerance in human populations have proven powerful indicators of dosage sensitivity and essentiality, while comparative sequence conservation across species underpins most models of variant pathogenicity.
However, sequence constraint alone offers limited insight into the biological contexts, such as tissues or regulatory programs, through which genetic perturbations manifest as disease.
Gene expression provides a complementary view of evolutionary constraint by capturing the functional and regulatory environments in which genes operate. Variation in expression levels across tissues and species reflects how selective pressures shape phenotype, yet its relationship to gene essentiality remains poorly characterized.
Here, we develop a deep learning framework that integrates multi-tissue transcriptomic data across multiple vertebrate species to learn a gene-level manifold of evolutionary constraint. Genes are embedded using cross-species expression patterns while accounting for orthology and tissue structure, and these representations are used to predict sequence-based constraint metrics and gene essentiality in humans.
We find that conserved cross-species expression profiles are predictive of sequence constraint and loss-of-function intolerance, revealing a systematic coupling between selective pressures acting at the sequence and regulatory levels.
Beyond essentiality prediction, the framework enables prioritization of tissues most informative of disease relevance for individual genes, and suggests principled strategies for identifying compensatory or alternative paralogs as potential therapeutic targets.
Together, these results support a multi-dimensional description of evolutionary constraint involving both sequence and regulatory layers.

Evolutionary history of two X chromosome meiotic drivers and polymorphic Y chromosomes in Drosophila affinis

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Meiotic drivers are selfish genetic elements that bias gametogenesis to enhance their own transmission, cheating Mendelian segregation. When located on a sex chromosome, such drivers can skew progeny sex ratios, create a female-biased population and diminish average population fitness. In Drosophila affinis, two distinct X-linked meiotic drivers segregate at ~10% frequency in wild populations and are associated with diagnostic chromosomal inversions. The X chromosome of D. affinis is a neo-sex chromosome formed by the fusion of the ancestral X with a former autosome, placing ~40% of the genome under the potential influence of meiotic drive. Using whole-genome sequencing of wild-caught males with and without meiotic drive, we show that inversion polymorphisms linked to meiotic drive suppress recombination across the entire neo-X, leading to long-term divergence between the three X haplotypes (two driving and one non-driving).
D. affinis also harbors extensive Y chromosome polymorphism, including multiple morphologically distinct Y variants and fertile XO males. The two drivers differ in their resistance profiles in XO males, and resistance may trade off among Y morphs. Consistent with this, we find that polymorphic Y chromosomes are highly differentiated from one another, including genic content. Together, these analyses leverage a rare natural system with two distinct X-linked drivers and polymorphic Y chromosomes to test how meiotic drive shapes recombination, genomic divergence, and fitness across a newly formed sex chromosome.

Transcription start sites experience a high influx of heritable variants fueled by early development

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Mutations drive evolution and genetic diversity, with the most consequential mutations occurring in coding exons and regulatory regions. However, the impact of transcription on germline mutagenesis remains poorly understood. Here, we identify a mutational hotspot at transcription start sites (TSSs) in the human germline, spanning several hundred base pairs in both directions. Notably, the hotspot is absent in de novo mutation data. We reconcile this by showing that TSS mutations are significantly enriched with early mosaic variants, many of which are excluded from de novo mutation calls, indicating that the hotspot partly arises during early embryogenesis. We associate the TSS mutational hotspot with divergent transcription, RNA polymerase II stalling, R-loops, and mitotic—but not meiotic—double-strand breaks, suggesting a recombination-independent mechanism distinct from known processes. Our findings are reinforced by mutational signature analysis, which highlights alternative double-strand break repair and transcription-associated mutagenesis. We further show that the TSS hotspot is eroded by negative selection and biased gene conversion. These insights reveal a germline mutational phenomenon with evolutionary and biomedical implications, particularly affecting genes linked to cancer and developmental phenotypes.

When Social Structure Shapes Genomes: Modeling Demography and Genomic Signals in Reef Fishes

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Understanding how population dynamics impact genomic signals is a major challenge for population and conservation genomics. Many reef fishes exhibit complex social systems, such as size- or rank-based dominance, socially controlled reproduction, and sex change, yet most population genetic models and empirical sampling designs typically assume random mating and representative sampling.

Here, we present a spatially explicit, non–Wright–Fisher SLiM model developed to investigate the joint demographic and population-genetic dynamics of reef fishes under realistic social organization. The model explicitly couples social rank, reproductive access, sex-specific life histories, and site attachment across discrete habitat patches. Individual fate (growth, survival, sex, and reproduction) is determined by local social context, generating emergent deviations in reproductive success and non-random genetic contributions across generations. This framework enables the exploration of how social regulation alters effective population size, genetic diversity, and allele-frequency trajectories under stable and perturbed demographic conditions.

Beyond characterizing the genetic consequences of social structure itself, the model can also evaluate sampling scheme biases. We contrast population-genetic inferences derived from random sampling of individuals with those based on breeders only, rank-restricted samples, or uneven spatial sampling schemes. This allows direct quantification of how commonly used empirical sampling strategies may misestimate diversity, relatedness, or demographic history when social structure is ignored.

By linking demography, social behavior, and genetics in a unified simulation framework, we characterize how social systems can shape evolutionary responses and provide a controlled testbed for assessing the robustness of genomic indicators used in reef fish management.

An increase in chromosome copy number drives rapid adaptation in a cold-adapted bacterium

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Large genome rearrangements, such as alterations in the number of chromosomes (aneuploidy) and copy number variations, are a common mechanism for rapidly responding to stress in eukaryotes. Whether this is also the case in prokaryotes is not known, but at least one-tenth of bacterial species have genomes with more than one chromosome. To investigate bacterial adaptation to stress, we used the cold-adapted bacterium Pseudoalteromonas haloplanktis TAC125, which has two chromosomes (chromosome I, chromosome II). We adapted twelve populations of P. haloplanktis to severe nutrient stress for 200 generations. We sequenced 56 endpoint clones and identified two main evolutionary paths underpinning adaptation to the stress conditions: an increase in the number of copies of chromosome II, and mutations affecting outer membrane proteins. The increase in chromosome II copy number was very frequent and emerged independently in all populations, suggesting that it is adaptive. Chromosome II codes for the genes responsible for transporting and metabolizing D-gluconate, which is the only carbon source present in the medium. We hypothesize that an increased number of copies of chromosome II is beneficial because it increases the expression of genes involved in D-gluconate metabolism. Our results suggest that genome plasticity provides a rapid mechanism for bacterial adaptation to stress.

No evidence for recent selection on amylase copy number in humans

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Amylases catalyze the first step in the digestion of starches. Species that depend on starches have undergone independent duplications of the amylase gene, and often express it in saliva as well as the pancreas, resulting in increased energetic gain from their diet. In humans, increased AMY1 (salivary amylase) copy number (CN) is correlated with agricultural subsistence. This has been taken to mean that it has been under selection in human populations in response to the development of agriculture. However, previous studies have considered a limited number of populations in investigating this question, and have ignored the confounding effects of ancestry differences between populations.

Here, we revisit recent studies conducted using ancient DNA from Eurasia as well as global present-day data to test for CN differences by subsistence strategy and for selection. The correlation between subsistence and AMY1 CN in modern-day populations disappears in analyses with increased sample size, or if principal components of ancestry are included (P = 0.25 with both compared to original P=1.9x10-3). A time series analysis showing a significant increase in AMY1 CN in Eurasia over the last 10,000 years is also no longer significant once PCs are included (P = 0.14 compared to original P=7.4x10-5), and there is no evidence for selection. Our study illustrates the difficulties of detecting selection in populations with complex demography. In conclusion, while amylase copy number may have been adaptive at some point in human evolution, recent changes reflect neutral evolution rather than adaptation to agriculture.

New meiofaunal genomes reveal the diversity of animal Hox clusters

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The Hox cluster is a highly conserved group of developmental transcription factors involved in patterning along the primary body axis of most animals. Bilaterians share seven homologous Hox gene families, several of which underwent subsequent duplications following the splits between deuterostomes, spiralians, and ecdysozoans, such some constitute synapomorphies of these clades. This understanding was until recently based on surveys narrowly biased towards large, tractable model organisms. New genomes from early-branching, microscopic, and/or lesser studied spiralians and ecdysozoans now reveal instances of divergent Hox gene losses, duplications, and rearrangements, unveiling the complex evolutionary trajectory of bilaterian Hox clusters. We surveyed not only the Hox gene complement, but also the organization of Hox genes and conserved micro-RNAs known to regulate Hox gene expression in newly sequenced genomes from meiofaunal animals, to understand how cluster integrity and gene complement may reflect larger-scale evolutionary trajectories of animal body plan diversity and genomic organization. Several meiofaunal lineages represent instances of secondary miniaturization, some recent and others more ancient. Across independent events, species with more divergent body plans tend to have undergone more changes to their Hox gene clusters, though this varies with each instance. Furthermore, some species that share ancient body plan modifications, i.e., miniaturization, now show interesting differences both in body size and complexity and Hox gene complement. Our survey of Hox clusters provides several interesting new avenues to explore the relationship between the genetics underlying developmental patterning and body plan evolution in the future.

Divergent cis-regulatory haplotypes at Tlr2 are associated with immune responsiveness

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Positive and balancing selection on pattern recognition receptors (PRRs) is widely thought to target ligand-binding domains and affect the specificity of recognition of different pathogens. Well-established examples of selection for PRR specificity are, however, rare. Studies of a wild rodent (the bank vole, Clethrionomys glareolus) have shown that Tlr2—a lipoprotein-binding PRR—is highly polymorphic with divergent haplotypes and signatures of balancing selection, and that Tlr2 genotype is associated with susceptibility to Borrelia afzelii infection in the wild. To investigate if Tlr2 is an example of selection for ligand-binding specificity, we here perform integrated population genetic and functional analyses. Ex vivo infection experiments show that the protective Tlr2 haplotype produces a stronger proinflammatory response to B. afzelii compared to the haplotype associated with susceptibility. Tlr2 genotype has a similar, albeit not statistically significant, effect on responsiveness to the phylogenetically distant pathogen Streptococcus pyogenes. We find that the strongest signature of balancing selection is 4.6 kb upstream of the Tlr2 coding sequence, near a putative enhancer, and that Tlr2 exhibits allele-specific expression such that the protective haplotype is more expressed. Collectively these results indicate that balancing selection has primarily acted on cis-regulatory variation affecting the general responsiveness via Tlr2-signaling rather than on polymorphisms affecting Tlr2 ligand-binding specificity.

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A practical framework for identifying genetic subpopulations and ESUs: insights for IUCN assessments and broader management

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The International Union for Conservation of Nature (IUCN) Red List and Green Status of Species guide global conservation priorities by evaluating species’ extinction risk and recovery status. Although such frameworks are often thought to include genetic diversity information and are considered a proxy for genetic erosion risk by some, this aspect of biodiversity remains underrepresented in assessment criteria due to technical and historical constraints. Incorporating genetic diversity into IUCN assessments is vital to ensure accurate extinction risk estimates. However, to guarantee equitable access, steps toward this goal cannot rely on molecular data alone.

Here, we outline a flexible framework proposed by members of the IUCN SSC for Conservation Genetics that integrates molecular and non-molecular evidence to identify meaningful genetic units (IUCN-defined subpopulations and ESUs). Inclusion of such units in IUCN assessments could enhance representation of adaptive genetic diversity, better informing conservation planning and decision-making. Acceptance would also pave the way for the inclusion of genetic erosion–related criteria and realign IUCN assessments with the new genetic indicators within the Convention on Biological Diversity’s Kunming–Montreal Global Biodiversity Framework. We demonstrate the application of this framework to dozens of species with published Green Status of Species assessments, highlighting which information has been key to the successful reuse of molecular data, as well as the challenges faced.

Dissecting the genetic basis of the Paris SR meiotic drive system in Drosophila simulans

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In Drosophila simulans, X-linked meiotic drivers disrupt Y-chromosome segregation during male meiosis, producing a strongly female-biased sex ratio. This segregation distortion is caused by two X-linked elements acting together. The first is a dysfunctional allele of HP1D2, a young and rapidly evolving member of the heterochromatin protein 1 family. HP1D2 originated from a duplication of HP1D/Rhino and accumulates on the heterochromatic Y chromosome in spermatogonia. The second driver maps within a tandem duplication (DPSR) encompassing six genes and a junction region. Preliminary evidence indicates that the driver embedded within DPSR corresponds to Trf2. Trf2 produces two main protein isoforms: a long and a short form. Within the DPSR, the distal copy (Trf2d) appears wild type, while the proximal copy (Trf2p) is 5’-truncated and may therefore encode a truncated version of the long isoform. We designed four shRNAs to target both Trf2 copies and their isoforms. Preliminary RNAi experiments show that knockdown of the truncated long isoform from Trf2p restores a balanced sex ratio, supporting the hypothesis that Trf2p is the DPSR-embedded driver. We propose that Trf2p produces a dominant-negative Trf2 isoform that competes with the functional Trf2d product. Notably, in D. melanogaster, Trf2 interacts with Rhino to regulate transposable elements through the transcription of heterochromatic small RNA source loci. This suggests that HP1D2SR, together with Trf2p, mis-regulate Y heterochromatin, thereby causing Y nondisjunction during meiosis II. The Paris SR system constitutes an ideal model to investigate the regulation of heterochromatin during spermatogenesis and how its mis-regulation leads to meiotic failure.

Modelling the genetic control of phenotypic stochasticity in genotype-phenotype-fitness maps

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Biological systems are inherently stochastic, hence any trait varies stochastically even when genotype and environment are held constant. However, while the degree of stochasticity in the genotype-phenotype map —phenotypic stochasticity— has been shown to be under genetic control, we lack population genetic theory and experimental systems to study how it affects the adaptation process. To tackle this problem, we develop a novel population genetic simulator —HANOI (Heritable Additive NOIse)—, which implements genotype-phenotype-fitness maps with a genotype-dependent phenotypic stochasticity. Using this model under simple scenarios, we show that selection can act on phenotypic stochasticity when fitness at the phenotypic expectation is similar between genotypes. To empirically demonstrate our theoretical prediction, we establish a novel experimental system based on artificial selection. We compete low- and high-stochasticity alleles and follow the phenotypic and genetic trajectories across generations. For this, we take advantage of Drosophila melanogaster mutants of the circadian clock genes whose time of eclosion, or adult emergence, is more stochastic than wild-type. Our study corroborating novel theoretical and experimental approaches is one of the first attempts to shed light on the evolutionary conditions under which genetically-regulated stochasticity will benefit adaptive evolution, and to explore how phenotypic stochasticity can itself evolve.

Evaluation of a target capture approach for plant dietary identification from paleofeces

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Reconstructing ancient diets provides insight into past human lifestyles. In this study, we focus on paleofeces to reconstruct past diets using genomic methods. DNA contained in paleofeces originates from dietary plants and animals, providing genetic evidence relevant to evolutionary history and biodiversity. However, genomic analysis of paleofeces remains challenging because dietary DNA is extremely limited. Consequently, PCR-based metabarcoding methods are widely used to amplify taxonomically informative regions, although these approaches cannot detect damage patterns characteristic of ancient DNA.

To overcome these limitations, we introduced a target capture method using RNA probes to enrich dietary DNA fragments, by designing custom probes to target two informative chloroplast loci, trnL and matK, for plant identification. Because this approach has not previously been applied to paleofeces, we evaluated the applicability of the analytical workflow using modern fecal samples from humans and Japanese macaques with known dietary records, and found plant-derived DNA was enriched by 3,400- to 8,400-fold, and plant taxonomic assignment accuracy exceeded 90% at the family level, demonstrating robust dietary identification from fecal samples.

We then applied the validated workflow to paleofeces excavated from two prehistoric Japanese archaeological sites: Torihama Shell Midden (approximately 6,000 years ago), representing a hunter-gatherer society, and Mitani Archaeological Site (approximately 2,700 years ago), associated with rice cultivation. We confirmed the effectiveness of our enrichment strategy in paleofeces, achieving approximately two-fold enrichment. At Torihama Shell Midden, Fabaceae were frequently detected, whereas the Mitani site exhibited low inter-sample similarity in plant taxa, revealing clear dietary differences between the two sites.

Volcanic drivers of human demographic collapse and genetic divergence on New Britain Island

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Major changes in human demography and genetic diversity can be driven by diverse phenomena, including diseases, climate change, and disastrous events by natural hazards, yet causal links remain poorly understood, particularly in prehistoric times. Volcanic eruptions represent one of the most abrupt and severe environmental perturbations, with direct and indirect impacts on ecosystem, climate, and human populations. Here, we investigated the impacts of large eruptions using whole-genome sequencing data from the Baining and Nakanai populations of New Britain Island, Papua New Guinea, one of the most volcanically active regions on Earth. Population genomic analyses revealed a sever population collapse in the Baining, with an estimated ~94% reduction in effective population size, accompanied by divergence between the Baining and Nakanai ~6,000–5,000 years ago (ya). This period coincides with multiple major eruptions, including the Raluan eruption (7,290 ya) and the W-K1 eruption (6,200 ya). Using energy cone modelling and prior field data, we show that the emplacement of the Raluan Ignimbrite very likely swept at least 2,500 km2 of area associated with the Baining. Demographic modelling further indicates a prolonged population bottleneck lasting ~1,400 years before recovery began, resulting in remarkably reduced genetic diversity in the Baining. Together, our study provides genomic evidence linking large volcanic eruptions to prehistoric human demographic changes and demonstrated that extreme natural disasters can leave lasting signatures in the genomes of contemporary human populations. This study established an interdisciplinary framework for investigating the impact of volcanism on humans.

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An Exploratory Assessment of Opsins in Pleurobrachia pileus

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Opsins are photoreceptor proteins that bind light-reactive chromophores and initiate visual and phototactic signalling cascades in eukaryotes. While bilaterians possess four to nine paralogous opsin groups, opsin diversity in non-bilaterians remains poorly understood. Ctenophores are an early-branching non-bilaterian animal phylum, making them valuable for studying the evolution of photoreception. With only ten ctenophore species sequenced to date, this study focuses on Pleurobrachia pileus, an underrepresented species native to the UK and Ireland. We aim to generate and annotate a high-quality reference genome for P. pileus and use transcriptomic data to assess differential opsin expression and isoform usage and determine the evolutionary trajectory.

Using a novel assembly pipeline, we extracted high–molecular-weight DNA to sequence, assemble, and annotate the Pleurobrachia pileus genome, achieving reduced genomic duplication. We sampled surface and benthic P. pileus populations along the Scottish coast to assess differential opsin expression and observe isoforms. Finally, maximum-likelihood phylogenetic methods reconciled gene and species trees, allowing inference of duplication and loss patterns for differentially expressed opsin genes across evolutionary history.

Our results reveal variation in opsin expression associated with differing light environments and provide new insights into the evolution and diversification of opsin genes in non-bilaterian animals, contributing to a broader understanding of the origins of vision and phototaxis.

The role of Wolbachia in reproductive isolation and speciation in Drosophila paulistorum

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Symbiont-driven speciation may occur when endosymbionts that influence host reproduction persist within hosts over evolutionary timescales. Drosophila paulistorum is a Neotropical species complex of six geographically overlapping but reproductively isolated incipient species, whose biology is strongly influenced by Wolbachia. Most notably, it contributes to reproductive isolation among the semispecies by affecting female assortative mating behavior and male semispecies-specific pheromone signaling. Moreover, while most Drosophila species in the willistoni group are facultatively infected with Wolbachia, D. paulistorum harbors an obligate infection. These findings suggest that Wolbachia may contribute to the ongoing sympatric speciation in D. paulistorum, providing a unique opportunity to explore the role of endosymbionts like Wolbachia in driving this process.

We sequenced Wolbachia genomes from several D. paulistorum semispecies and related willistoni group species, together with their respective Drosophila host genomes. To investigate evolutionary relationships and the extent of co-evolution between host and endosymbiont, we combine comparative genomics, phylogenomics and divergence time estimates with a relaxed molecular clock model. Our results show that, although host and endosymbiont tree topologies are largely congruent, Wolbachia consistently appears younger than its hosts. This pattern indicates a higher turnover rate of Wolbachia than previously thought and reflects the combined effects of vertical inheritance and introgression shaping Wolbachia prevalence and persistence in Neotropical Drosophila. Together, these results advance our understanding of the interactions between bacterial symbionts and their hosts and provide new insights into the role of endosymbionts in shaping eukaryotic host evolution.

Environmental effects on the origin and establishment of Arabidopsis arenosa

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The effect of the environment on the establishment of polyploidy has been a long-term mystery, and it has been hypothesized that polyploids are better adapted to temperature extremes than their diploid progenitors. Given the increasing challenges that plants and animals face due to global warming, this study explores polyploids' molecular basis of their adaptation to thermal and precipitation fluctuations, using Arabidopsis arenosa from the family Brassicaceae as the model system. This species crosses multiple climatic zones along its distribution, and its various intraspecific lineages are adapted to diverse environmental conditions, including northern latitudes.

In this study, I utilized the first pan-genome of A. arenosa and genotype–environment association analysis with 250 genome-sequenced diploid and 473 tetraploid populations (total 723 individuals) to investigate the impact of harsh environments on the adaptation of A. arenosa, namely selected genes. Also, genetic offset was used to predict maladaptation comparing diploids with tetraploids.

Based on the findings from this analysis, significant differences in single nucleotide polymorphisms strongly associated with temperature and precipitation were observed between diploids and tetraploids. Our findings indicate that diploid climate adaptation is primarily associated with metabolic, stress-response and developmental pathways, including carbohydrate and lipid metabolism and hormone signaling. In contrast, autotetraploid adaptation is enriched for regulatory, epigenetic and cellular homeostasis functions, suggesting greater buffering capacity under environmental change. This may explain why tetraploids exhibit robust adaptation across broader environmental regimes, as reflected by lower genetic offset.

Heterogeneous evolution of effective recombination landscapes across percomorph fishes

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Recombination shapes how alleles are combined across the genome and plays a central role in adaptation and speciation. While recombination rates are known to vary and evolve, how recombination landscapes diverge through time and which processes drive this divergence remain poorly understood. Here, we use the Population Recombination Divergence Index (PRDI), an approach that controls for key confounders of LD-based inference, to quantify divergence in realized recombination landscapes in seven population comparisons across four percomorph fish lineages (cichlids, sticklebacks, killifish, and clownfish). We find that recombination landscapes evolve rapidly across this broad taxonomic set. Across comparisons, recombination landscape divergence generally increases with genetic differentiation and divergence time, but the rate at which divergence accumulates varies markedly among population pairs. To interpret this heterogeneity, we propose a conceptual framework in which divergent selection and gene flow interact to shape recombination landscape divergence. Although our dataset is limited, we observe a positive association between gene flow and the relative increase in recombination divergence per unit of genetic differentiation. Finally, we introduce a local version of PRDI (l_PRDI) to characterize genomic heterogeneity in recombination divergence, to examine how it relates to genomic differentiation, and how this relationship is modulated by gene flow. Together, our work provides new insight into the dynamics of recombination landscape evolution, highlights the importance of recombination divergence heterogeneity, and motivates theoretical and empirical efforts to integrate evolution of recombination into studies of adaptation and speciation.

Is genetic differentiation between species homogeneous across mammals?

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Speciation progressively reduces gene flow between lineages, leading to increasing genetic differentiation. In the absence of a widely accepted threshold for species delimitation, it has been proposed to use genetic differentiation observed among already recognized taxa as a comparative benchmark. However, this approach assumes that genomic divergence and population structure are reliable proxies for taxonomic rank and that such thresholds can be transferred across independent species complexes. To test this assumption, we examined how genetic differentiation varies across taxonomic levels. We compiled 69 publicly available whole-genome assemblies spanning eight mammalian genera. We estimated pairwise sequence divergence (Da and Dxy) and genomic differentiation using FST-like Index. Species-level pairs consistently exhibited higher FST, Da, and Dxy values than pairs belonging to lower taxonomic ranks. These results indicate that genomic differentiation metrics broadly track taxonomic rank and may provide an informative guide for species delimitation. We further applied this comparative framework to an emblematic taxonomic case, the black-backed jackal, Lupulella mesomelas, which includes two geographically disjunct populations in Eastern and Southern Africa. Our findings illustrate how genome-wide divergence metrics can help refine species boundaries.

Bacterial ecospecies: extraordinary new models for studying complex adaption.

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In my final outing as SMBE associate editor (16 years of service), I will present an overview of our recent discovery of bacterial ecospecies and explain why they are exceptional new model systems for studying complex adaptation. Bacterial evolution differs from that in outbreeding eukaryotes because of clonal evolution, meaning that fit genotypes can multiply via clonal expansion. This has previously led to the identification of recently arisen lineages with limited diversity and a distinct ecological niche, or in other words bacterial ecotypes. Bacterial ecospecies, by contrast, are differentiated at a small fraction of the genome but can be a similar age to the species and contain nearly its entire diversity. Their pattern of diversity resembles that in eukaryotic models of ecological adaptation such as sticklebacks, but with narrower differentiation peaks, allowing precise identification of coadapted loci. Moreover, the powerful tools of molecular microbiology can be used to dissect the role of each of the differentiated genes. I will illustrate these principles using our work on ecospecies in Helicobacter, Vibrio and Streptococcus.

Effects of habitat arrangement on gene flow and genetic diversity in a grassland-specialist butterfly (Cupido minimus)

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Loss of biodiversity is a global concern with many contributing factors, including human-driven land cover change and the resulting habitat loss. The impacts of habitat arrangement have also received much attention in recent years following a meta-analysis indicating that habitat fragmentation could have positive outcomes for biodiversity after accounting for the impacts of habitat loss. While the effects of habitat arrangement have been examined for variables such as species abundance and species richness, few studies have explored impacts on gene flow and genetic diversity. We address how habitat amount and arrangement influence functional connectivity and genetic erosion in pollinators, focusing on the grassland specialist butterfly Cupido minimus. This species exhibits population structure at distances of less than 8 km. Based on whole genome sequencing of 200 individuals collected from 40 sites in southern Sweden we estimate functional connectivity by assessing FST and clustering. We then compare the genetic distances between populations to the amount and arrangement of habitat separating them. We also assess the effects of habit amount and habitat arrangement surrounding each population on level of inbreeding, approximated by runs of homozygosity and accumulation of genetic burden (genomic inference of deleterious mutations). The insights gained through the landscape genomic methods in this study are important both for conservation planning in areas with finite space available for habitat, and for better understanding how landscape patterns can influence functional connectivity, with consequences for the prospects of population persistence.

Historical Genomes Reveal a Centuries-Long Competition–Colonization Trade-off in Plant-infecting Pseudomonas

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Microbial competition drives rapid adaptation, often forcing organisms to specialize in new ecological niches. Adaptations that improve competitive ability can reduce performance in other environments, creating evolutionary trade-offs. Whether such trade-offs persist in nature, or are eroded as lineages adapt through compensatory changes, remains largely unknown. Here we show that a trade-off between competitive ability and host colonization has been stably maintained in natural plant-infecting Pseudomonas populations for centuries. Wild plant-pathogenic Pseudomonas compete using tailocins—phage-derived molecular weapons that bind to specific cell-surface receptors. Genomic surveys and functional assays reveal that the most broadly lethal tailocins remain rare. While tailocin production increases competitive killing, it also compromises plant colonization. Crucially, herbarium-derived historical genomes spanning two centuries demonstrate that the underlying polymorphisms are not transient. These time-resolved data reveal that the competition–colonization trade-off has persisted for at least 10^5–10^6 generations, providing direct evidence that this constraint is evolutionary stable rather than transient. Together, these results show that in natural populations, a trade-off between competition and colonization is fundamental and not easily overcome. This stability suggests that tailocin resistance may come with predictable fitness costs, highlighting tailocins as a promising therapeutic avenue where resistance could weaken pathogens in natural or clinical settings.

HOGPROP: transferring functional annotation and reconstructing ancestral function

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The evolutionary history of gene families is shaped by complex processes, including gene duplication and loss, which challenge classical tree-based functional inference. While phylogenetic trees provide a powerful framework for modelling ancestry, the propagation of functional information across large, heterogeneous gene families requires models that can integrate multiple evolutionary relationships across diverse datasets. Here, we present HOGPROP, a scalable, phylogeny-aware framework for functional annotation transfer and ancestral function reconstruction based on Hierarchical Orthologous Groups (HOGs). HOGs represent gene family evolution as nested evolutionary units across speciation and duplication events, naturally forming a directed acyclic graph rather than a single tree. HOGPROP leverages this structure to propagate functional information across extant genes and ancestral nodes while explicitly accounting for orthology, paralogy, and evolutionary distance. The method integrates multiple layers of evidence within a unified scoring framework that enables probabilistic functional transfer and reconstruction of ancestral functional states. Using a dataset of more than 2,000 genomes spanning the tree of life, we demonstrate the utility of HOGPROP for functional inference in understudied species and for ancestral Gene Ontology enrichment analyses, illustrating how graph-based representations of gene family evolution enable robust and interpretable inference across deep evolutionary time.

Evaluating protein preservation in dental calculus from natural history specimens for dietary reconstruction

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Natural history specimens record past biodiversity and ecosystem transitions. To date, stable isotope and dental wear analyses have been widely used to reconstruct diets from these specimens. These approaches reveal broad dietary patterns but not specific food items.
Analysis of dental calculus offers an alternative approach that yields individual-level dietary information. Analysis of starch granules, phytoliths, DNA, and proteins preserved in ancient dental calculus can identify specific food items consumed. Proteomic analysis enables the identification of broad food categories at the plant and animal levels. However, natural history specimens undergo anthropogenic alterations during preparation that may compromise protein integrity. The degree of protein degradation in dental calculus from natural history specimens caused by the skeletal preparation procedures (e.g., boiling or chemical treatments) has yet to be elucidated.
To assess food-derived protein preservation in dental calculus from natural history specimens, we performed proteomic analysis on sika deer specimens (n=8) prepared by different treatments and analyzed carbon and nitrogen stable isotope values of sika deer hair. Dental calculus from boiled specimens showed reduced protein identification compared with raw dental calculus, but some plant-derived proteins were still preserved. However, dental calculus from specimens subjected to both boiling and chemical treatment, including protease and bleach, yielded almost no identifiable proteins.
Our findings suggest that proteomic analysis of dental calculus is a viable tool for dietary reconstruction even in boiled natural history specimens. Furthermore, this approach enabled us to infer causes of inter-individual variation in stable isotope ratios at the level of specific food items.

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Bayesian test of gene flow between sister lineages using genomic data

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Inference of interspecific gene flow using genomic data is important to reliable reconstruction of species phylogenies and to our understanding of the speciation process. Gene flowis harder to detect if it involves sister lineages than nonsisters; for example, most heuristic methods based on data summaries are unable to infer gene flow between sisters. Likelihood-based methods can identify introgression between sisters but the test exhibits several nonstandard features, including boundary problems, indeterminate parameters, and multiple routes from the alternative to the null hypotheses. In the Bayesian test, those irregularities pose challenges to the use of the Savage-Dickey (S-D) density ratio to calculate the Bayes factor. Here we develop a theory for applying the S-D approach under nonstandard conditions. We show that the Bayesian test of introgression between sister lineages has low falsepositive rates and high power.We discuss issues surrounding the estimation of the rate of gene flow, especially at very low or very high rates.We find that the species split time has a major impact on the information content in the data, with more information at deeper divergence. We use a genomic dataset from Sceloporus lizards to illustrate the test of gene flow between sister lineages.

Dissecting the factors underlying sequence evolution by disentangled representation learning

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The evolution of molecular sequences is driven by many factors, such as neutral evolution following phylogenetic history and natural selection for different functions or properties of a molecule. Dissecting the impact of these factors on sequences is a fundamental task in molecular evolution, providing us with insights into sequence evolution principles and the potential for modulating sequence properties toward specific functional goals. While conventional methods can detect site-level signatures of specific factors such as positive selection in sequence alignments, attributing more complex patterns to such factors is challenging. Here we propose a deep learning framework Deep Disentanglement Of Protein Sequences (DDOPS). Focusing on the PBP and MBL protein superfamilies with convergent evolution of β-lactamase activity, we constructed and trained a disentangled representation learning model. Consequently, different representation blocks were disentangled, being able to predict only the corresponding factors, such as superfamily assignment (phylogeny) or β-lactamase activity (function). In interpretation analyses, the function block reassuringly showed high attention on a loop structure essential for TEM-1 β-lactamase activity. Furthermore, the autoregressive decoder in the framework enabled sequence generation conditioned on specific combinations of factor states. Combining the phylogeny block of PBP and the function block from MBL β-lactamase, the model generated new proteins with high sequence and structure similarities to PBP β-lactamases. Most of these generated proteins also showed expected activity in antibiotic resistance assays. In summary, the DDOPS framework is able to disentangle and reconstruct complex sequence patterns driven by specific evolutionary factors.

The Tie That Binds Us? Challenging the Primacy of DNA in Kinship Studies and Re-Centering Community in Defining Human Connections

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Biological determinism continues to shape how kinship is defined, from research to repatriation proceedings. This privileging of biological relatedness reflects and reinforces dominant "Western" frameworks of kinship, often sidelining culturally-specific, Indigenous, and community-centered understandings of family and social belonging. Advances in archaeogenomic technologies today offer unprecedented insight into past human societies, and these advances have the potential to forge new, multivocal, and inclusive approaches to kinship. However, the application of ancient DNA risks reproducing power imbalances and epistemic hierarchies when genetic connections are assumed to be the primary or sole measure of social ties. This paper examines the conceptual and ethical implications of privileging DNA as a measure of kinship (in repatriation decisions, for instance), emphasizing how such practices can obscure complex social realities, undermine self-determination, and reify narrow and essentialist understandings of identity. We call for critical reflection about the agents and motivations of archaeogenomics research, on the role of genetics in defining relationships and urge that multiple knowledge systems be considered in studies of kinship, both past and present.

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Restoring Vulnerable Populations via Genomic Rescue

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Human-driven environmental change has left many wildlife species fragmented into small, isolated populations. Such populations are especially vulnerable to extinction, not only due to demographic stochasticity and environmental pressures, but also because of genetic factors: loss of diversity, increased inbreeding, and the accumulation of deleterious mutations. While the principles of drift, inbreeding, and mutation load are well established in molecular evolution, their combined role in determining extinction risk is less well understood.

Conservation interventions increasingly draw on genetic tools, including genomic rescue. Current practice often emphasizes demographic recovery or increasing diversity. Yet even when these targets are met, genetic load may persist, accumulate further and eventually become expressed, especially when both source and target populations share deleterious alleles. Thus, interventions aimed at increasing diversity can inadvertently cause harm if the underlying evolutionary processes and resultant genetic patterns are not carefully understood.

We have developed a molecular-evolutionary framework for genomic rescue, which integrates demographic history, standing genetic diversity, mutation load, and local adaptation to inform conservation strategies. We will highlight theoretical insights and showcase a high-profile real-world example, the melanistic tigers of Simlipal, where genomic data have informed decisions about translocations and population reinforcement.

By bringing together theoretical, empirical, and applied perspectives, we aim to connect molecular evolutionary principles with urgent conservation challenges. We argue that a genomic framework for population rescue will not only advance fundamental understanding of the vulnerability of small populations, but also improve the long-term outcomes of real-world interventions.

A dog is not a wolf – how tiny differences have shaped man's best friend

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The non-coding canine genome and the mechanisms behind selection on transcriptional regulation of genes have been explored in a limited manner for dog domestication due to a lack of epigenetic and genome-interaction datasets. In this study, we aimed to identify the genetics behind the earliest steps in dog domestication and combined RNA-seq data from prefrontal cortex and hypothalamus of 4 Mongrel dogs and 4 wolves with genome wide promoter-enhancer interaction data. Through targeted chromosome conformation capture (HiCap), we targeted 29.866 promoters of over 17.000 genes and detected over 60.000 interactions. Dogs gained 855 and lost 649 promoter interactions affecting 727 genes. These genes show a 2-fold enrichment for dosage dependent genes, suggesting functional consequences if their regulatory mechanisms are altered. Our analysis further revealed that alteration in promoters drive expression changes in evolutionary young, lineage specific genes, while enhancers mainly mediate species-species contacts with promotors of genes showing steady-state expression levels involved in embryonal and neural development. These genes were connected to enhancers with highly differentiated variants between dogs and wolves and enriched for genes impaired in neurodevelopmental disorders.

Our findings suggest, that during domestication, the cis-regulatory mode of genes in dogs has been altered through differential enhancer usage. This change achieved similar steady-state- gene expression levels in differentiated cells between wolves and dogs, while altered regulatory logic could lead spatiotemporal expression pattern during development. Our findings highlight an important genomic mechanism for adaptation and provide an explanation for the lack of marked differential expression changes between dogs and wolves.

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NS-QMaker: Non-Stationary Amino-Acid Substitution Models Facilitate Deep Phylogenetic Inference

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QMaker and NQMaker are widely used and efficient tools that estimate time-reversible and time-non-reversible models of amino-acid substitutions from a collection of multiple sequence alignments (MSAs). These tools are currently limited to stationary evolutionary models, assuming that amino-acid frequencies and exchangeabilities remain constant along the phylogeny. However, amino-acid frequencies are known to vary, especially in the context of deep phylogenies such as among Archaea, Bacteria and Eukaryota as well as plants, vertebrates, and animals. E.g., amino acid frequencies change with GC content, with environmental conditions, and with effective population size. Failure to account for these variations may lead to wrong trees caused by compositional bias.

To address these limitations, we introduce NS-QMaker, an extension of QMaker that allows for non-stationary models of amino acid substitutions, in which amino-acid frequencies and exchangeabilities may vary across different lineages of a tree. In addition, NS-QMaker can jointly estimate root amino acid frequencies between different trees inferred from different protein MSAs. We apply NS-QMaker to a cleaned dataset of Pfam domains to infer the root frequencies for the last archaeal and bacterial common ancestors (LACA and LBCA). Our results demonstrate that NS-QMaker enables the recovery of historical signals embedded in deep evolutionary processes.

Whole genome resequencing enables temporal reconstruction of purifying selection in a highly bottlenecked avian population

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Purging, whereby deleterious homozygous mutations are removed from gene pools by purifying selection, is believed to explain why small, inbred wildlife populations can persist despite depleted genetic diversity. However, while purging has been empirically demonstrated in wild populations, the process is not fully understood. Natural selection is less effective in small populations over short bottlenecks, during which genetic drift overpowers selection efficiency. Given the severity of modern wildlife declines, it is therefore not clear if and how purging can maintain persistence in small and endangered wildlife populations. Comparison of temporally spaced samples can contribute to understanding the dynamics of purging in wildlife populations by enabling reconstruction of evolutionary processes such as drift and selection. In Germany, the endangered Great Bustard (Otis tarda) declined by 99% in the mid-20th century. This closed, non-migratory population is an excellent model for temporal comparison. We conducted whole genome resequencing of 26 samples spanning 130 years to evaluate dynamics of diversity parameters including inbreeding and mutation load across the bottleneck. We found evidence for recent inbreeding, with greater frequency and length of runs of homozygosity (ROH) in the post-bottleneck population. We also found support for purging, with lower realized load of deleterious mutations after the bottleneck. Critically, however, we found a significant positive association between long ROH and quantity of deleterious mutations. Deleterious mutations present in the modern population include alleles associated with cellular structure regulation and immune system functioning. Further inbreeding in this population could result in fixation of these alleles, elevating extinction risk.

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The detection of selective sweeps associated with adaptation to lead (Pb) contamination in wild house sparrows

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Lead contamination is a serious issue on a global scale with well-documented negative effects on wildlife fitness. Chronic exposure to environmentally relevant lead concentrations is therefore expected to impose selective pressures, potentially driving rapid adaptive evolution. Wild house sparrows (Passer domesticus) living in urban areas of the Australian mining city of Broken Hill, Australia, have experienced intense lead contamination for approximately 140 years, and the population is ecologically insular, being surrounded by desert. Recent study of the population has revealed individuals surviving for extended periods with relatively high blood lead levels, suggesting some resilience. In this study we conducted whole-genome sequencing of 16 individuals from Broken Hill and compared them with 21 individuals from Adelaide, which is a relatively low-lead area, from which the Broken Hill birds originated. Combining both single-population (iHS, CLR, π) and cross-population (xpEHH, Fst) statistics, we identified multiple genomic regions that provide evidence of selective sweeps across the majority of these metrics. These hotspots of selection contained genes that have previously been associated with traits that may help to confer resilience to lead contamination. For example, an analysis of gene ontology identified cellular functions relating to metal transport. Our findings provide insights into the genomic mechanisms underlying adaptation to severe heavy-metal contamination and highlight the potential for rapid evolutionary responses to human-induced environmental change.

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A Baltic Cod pangenome for population inference

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Structural variants (SVs), including insertions, deletions, inversions, translocations and copy number variation, represent a major source of genomic variation with profound consequences for fitness and adaptation. Despite their relevance, most studies still rely on linear reference genomes, which often fail to capture large, repetitive, and structurally complex arrangements. Atlantic cod (Gadus morhua) genome exhibits these challenges, harboring extensive structural complexity, including four well-characterized megabase-scale inversions and high short tandem repeat (STR) content. These features frequently prevent accurate resolution of inversion breakpoints using standard approaches, limiting our ability to characterize SV diversity. While population-scale, high-quality genome assemblies are the most direct means to resolve these complexities, they remain rare in wild populations. To address this gap, we generated haplotype-resolved genome assemblies for five Eastern and four Western Baltic cod individuals via Oxford Nanopore Sequencing using ultra-long reads. These near telomere-to-telomere (T2T) continuity assemblies enable the construction of a regional pangenome for Baltic cod that resolves complex SVs inaccessible to conventional strategies. This allows us to track SV-driven genomic arrangements across populations, investigating how SVs are maintained and diverged in the wild Baltic cod populations. We further extended this graph-based pangenome framework to 131 short-read sequenced individuals, providing a foundation for population-scale graph genotyping and evolutionary inference in a structurally complex system. To our knowledge, this represents one of the first population-scale pangenome resources based on near-T2T assemblies in a wild vertebrate species, offering a powerful tool to study its evolutionary history including the genomic basis of adaptation to a unique environment.

TKF-based models with latent and hierarchical structure are competitive with parameter-heavy neural networks as models of protein sequence evolution

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Most statistical phylogenetic analyses rely on relatively simple continuous-time, finite-state Markov models of point substitution to describe molecular evolution. These models typically assume fixed sequence length, ignore insertions and deletions (indels), and make limited allowance for variation in selection pressures across residues. The simplistic assumptions of these models limit the realism of phylogenetics. We extend the TKF92 model - the canonical hierarchical model combining substitution and multi-residue insertion-deletion (indel) events - by introducing additional nesting and latent states. We compare these TKF92 extensions to two classes of neural seq2seq models. The first class fits site- and sequence-specific TKF92 rate parameters at each alignment column. The second directly predicts descendant sequences and alignments; evolutionary time is provided as an input feature, but a CTMC-based model is not enforced. We evaluate the per-character perplexities of all models on pairwise alignments curated from Pfam. A nested TKF-based model with only 32,000 parameters is highly competitive with neural networks containing tens of millions of parameters, outperforming all but two of the neural architectures tested. Our results indicate that approaches grounded in molecular evolutionary theory may be more parameter-efficient and provide a better fit to real alignments than unconstrained alternatives, supporting the incorporation of CTMC-based model structure within future neural phylogenetic approaches.

LLM Reveals: Viruses Copy Synonymous Cell-Type Specific Patterns of Human Coding DNA

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The extent to which synonymous codons are evolutionarily optimised–and the overlapping signals driving their selection–remains incompletely understood. Here, we investigate codon usage in human genes, its variation across tissues, and how these patterns are mirrored in human-adapted viruses. To this end, we trained a large language model (LLM) to predict codons from amino acid sequences while conditioning on transcript expression across 54 human tissues. The model dramatically outperformed frequency-based baselines, especially on proteins longer than 100 amino acids, suggesting the influence of broader constraints such as co-translational folding. Its advantage tracked GC content across human and viral genes, driven by the elevated use of rare codons in low-GC transcripts. Further analyses revealed that viruses tend to use codon patterns resembling those of their infected tissues. Strikingly, viruses displayed a consistent preference for codon patterns characteristic of cultured cell types and of tissues showing infection-related expression profiles–suggesting reciprocal adaptation between viral codon usage and the host cellular environment. These findings reveal unexpected complexity in codon usage and highlight the potential of LLMs to support codon optimisation, de-optimisation, and translationally informed sequence design.

Convergent evolution of genetic sex determination among species of stickleback fishes

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The evolution of sex chromosomes begins with the acquisition of a primary sex determination gene. Although sex differentiation is a remarkably conserved process among vertebrates, the primary sex determination gene that initiates sex differentiation can rapidly evolve across taxa. Stickleback fishes are an excellent model group to understand how newly evolved primary sex determination genes gain this function. The threespine stickleback (Gasterosteaus aculeatus) evolved a Y chromosome approximately 22 million years ago. Within the oldest region of the Y chromosome is a copy of anti-Müllerian hormone (Amh), which duplicated and translocated from autosome eight. We have shown this Y-specific duplication of Amh (Amhy) is both necessary and sufficient for male development. We are now comparing sex determination in the threespine stickleback with a closely related species, the brook stickleback (Culaea inconstans), which has an independently evolved Y chromosome at the early stages of differentiation. We have completed a genome assembly and discovered a 7 kb insertion on the new Y chromosome that contains a convergent duplication of Amh. In contrast to the threespine, the brook stickleback Amhy only has a handful of mutations that differentiate it from the ancestral autosomal paralog, indicating it evolved much more recently. Despite its recent origin, Amhy has already evolved multiple unique isoforms that are not detected from the ancestral autosomal locus or from the convergently evolved Amhy in the threespine stickleback. Both species will therefore offer unique insights into the different ways Amhy regulation can evolve to neofunctionalize as a primary sex determination gene.

Genome compartmentalization in a fungal insect pathogen reveals a second mating-type locus on an accessory chromosome

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The genomic diversity of many fungal pathogens is driven by rapidly evolving regions harbouring many transposable elements. Such genomic regions often contain genes important for pathogenicity and may be sequestered from the core genome on accessory chromosomes, which are chromosomes that are variably present among isolates of a species. Here we present a pangenomic analysis of a fungal insect pathogen, Metarhizium acridum, using seven chromosome-scale genomes from four different continents. We show that the pangenome of M. acridum exhibits functional compartmentalization, as the core genome contains carbohydrate-active enzymes, while accessory genes encode effectors located in gene-sparse regions. Furthermore, we identified the first accessory chromosome in M. acridum. This chromosome is enriched in functions related to sexual reproduction but does not encode known effectors or secondary metabolite proteins related to pathogen-host interactions as commonly found. Within the genus Metarhizium, M. acridum is one of few species considered to regularly reproduce sexually. We show that the accessory chromosome contains genes from both the MAT1-1 and MAT1-2 mating-type idiomorphs, in addition to the MAT locus found on the core chromosomes. Our findings suggest that the presence of this accessory chromosome facilitates sexual reproduction, possibly even primary homothallism, in the otherwise heterothallic M. acridum. Overall, our study presents a putative novel mechanism whereby fungal pathogens may undergo recombination by using an accessory chromosome.

Biodiversity genomics research practices require harmonising to meet stakeholder needs in conservation

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Loss of genetic diversity is increasingly recognised as a measurable risk factor to biodiversity and the bioeconomy, yet the routes by which genomic evidence informs policy and management remain poorly documented. Here, we synthesise insights from 20 applied genomic case studies coordinated under the Biodiversity Genomics Europe (BGE) project by the Swiss Institute of Bioinformatics (SIB), spanning diverse taxa, ecosystems, and decision-making context across Europe. These projects combine high-quality reference genomes with whole-genome and RAD sequencing to assess, among others, population-level genetic variation, species adaptability, and conservation status. We collated project deliverables and, where reporting allowed, harmonised a core set of commonly used genetic diversity metrics to meet stakeholder needs. Across most case studies, at least one metric suggested ongoing erosion within populations or among management units. Several projects explicitly linked these molecular signals to identifiable pressures aligned with EU biodiversity policy instruments, highlighting opportunities to slow or reverse biodiversity loss. We discuss how synthesis across heterogeneous genomic studies can support reporting, prioritisation, and evaluation of restoration, and how studying molecular evolution in eroded populations can inform both evolutionary inference and the development of policy-ready genetic indicators. Together, these findings illustrate how coordinated genomic monitoring can bridge molecular evolution, biodiversity assessment, and evidence-based governance.

Characterising and timing the four independent Denisovan admixture events in Asia and Oceania

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Modern humans had multiple encounters with Neanderthals and Denisovans during their global expansion. As a consequence, non-African genomes derive ~2-6% of ancestry from those archaic hominins. While Neanderthal ancestry originates from the same admixture event, Denisovan ancestry is more heterogeneous. Recent studies show that the ~0.1% component in EastAsians is from both a deeply-divergent Denisovan lineage from the sequenced Altai Denisovans and another more closely-related, whereas the ~4% Denisova component in Oceania and Island Southeast Asia (ISEA) stems only from the latter.

We scrutinise this by applying hmmix - a hidden Markov model approach that identifies archaic fragments without requiring archaic genomes - to ~3,500 non-African phased genomes from diverse populations, with a focus on ISEA and Oceania, where Denisovan ancestry is highest.

Our refined archaic ancestry map shows that the introgressed sequence spans most of the callable human genome, with over 80% containing Neanderthal and more than 75% Denisovan ancestry, while large deserts persist on the X chromosome. By comparing fragments to sequenced archaic genomes and across modern populations, we characterise contributing archaic groups. We find that the closely-related Denisovan ancestry in EastAsians also carries deeply divergent hominin ancestry, consistent with super-archaic contributions. With this resolution, we are able to distinguish different deeply divergent Denisovan groups that contributed to Oceanians and ISEA populations. Finally, improvements to hmmix yield more accurate fragment length distributions, allowing us to refine the timing of Denisovan admixture events during modern human expansion.

Biomedical and life science articles by female researchers spend longer under review

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Women are underrepresented in academia—especially in STEMM fields, at top institutions, and in senior positions. This is due, at least in part, to the many obstacles that they face compared to their male counterparts. There has been substantial debate as to whether the peer review system is biased against women. Some analyses—mostly based on thousands of Economics research articles—have shown that manuscripts authored by women experience longer peer review times (defined as the time intervened from submission to acceptance) than comparable manuscripts authored by men. Other studies, however, have found no effect of author's gender on acceptance delays, raising questions about whether the gender gap is specific to certain fields. We will present analyses of two separate sets of articles. By analyzing all articles indexed in the PubMed database (>36.5 million articles published in >36,000 biomedical and life sciences journals), we show that the median amount of time spent under review is 7.4–14.6% longer for female-authored articles than for male-authored articles, and that differences remain significant after controlling for several factors. The gender gap affects most disciplines, regardless of how well women are represented in each discipline; however, it is absent or even reversed in some disciplines (including Biology). By analyzing >49,000 research articles published in 11 Evolutionary Biology journals, we show that, in some of the journals, female-authored articles spent significantly longer under review; however, most of the observed differences vanish after controlling for the date of publication and the number of authors.

Molecular mechanisms involved in homologous and intramolecular recombination in Coronaviruses

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Recombination is crucial for coronavirus (CoV) replication and evolution, yet the precise molecular mechanisms underlying recombination in CoV remain poorly understood. Several studies have suggested a link to the unique proof-reading Exonuclease (ExoN) in Nsp14 of CoV, either as two complementary mechanisms of error correction on population level, or – conversely – through a direct mechanistic link.
To resolve this, we rescued a viable ExoN-knock-out mutant (ExoN-) of a highly replicative SARS-CoV-2 termed P100A. ExoN- has a 16-fold higher error frequency than parental P100A. Through a series of in vitro recombination assays, we determine the neutral recombination rate of SARS-CoV-2 to be 1.4x10-5/nt/generation, and show that treatment with a host-targeting antiviral leads to selection of recombinant virus within one replication cycle – in line with the concept that recombination facilitates epistatic mutation. ExoN- shows significantly decreased neutral recombination (5.3x10-6), suggesting that ExoN function is required for effective homologous recombination. Analysis of next-generation sequencing data reveals that ExoN- has lower levels of intramolecular recombination with more aberrant recombination products. We experimentally confirm that these can be explained by ca. 5 nt-long imperfectly paired heteroduplexes resembling transcription regulating sequence (TRS) that regulate the generation of viral subgenomic RNAs (sgmRNAs) during replication. This suggests that ExoN ensures accurate TRS utilization and suppresses aberrant sgmRNAs.
In conclusion, knock-out of ExoN decreases replication fidelity as well as homologous and intramolecular recombination in SARS-CoV-2, implicating a mechanism of recombination where the ExoN function both initiates and regulates recombination.

Signals of positive selection on transposable element control genes across structured human populations

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Transposable elements (TEs) are pervasive genomic parasites capable of disrupting gene regulation and genome integrity. To counteract their activity, organisms have evolved diverse molecular mechanisms of TE suppression. Comparative studies across vertebrates suggest that genes involved in TE control are frequent targets of positive selection, yet detecting such signatures within species remains challenging due to population structure, demographic heterogeneity, and departures from equilibrium assumptions.

Here, we investigate whether long-term positive selection has shaped genetic variation in TE suppression genes across globally diverse human populations. We analyse 59 autosomal protein-coding genes involved in TE regulation using whole-genome data from 828 individuals representing 54 populations of the Human Genome Diversity Project. Using a combination of population genetic summary statistics and comparisons with neutral expectations, we identify widespread departures from neutrality consistent with positive selection acting on TE control loci. Several genes show pronounced reductions in nucleotide diversity alongside an excess of high-frequency derived alleles. Importantly, these signals vary across populations: while some TE-regulatory genes exhibit shared signatures of selection, others display strong region-specific patterns, with particularly elevated signals observed in West Asian populations.

Our results demonstrate that meaningful signals of selection can be detected in highly structured, non-equilibrium populations using classical population genetic approaches. These findings highlight the evolutionary importance of maintaining effective TE suppression and underscore how selection can act both globally and locally despite complex demographic histories. More broadly, this work emphasises the value of incorporating underrepresented populations when studying adaptation in realistic biological systems.

A random forest classifier to retrieve Insertion Sequences carrying antibiotic resistance genes from wastewater samples.

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Horizontal Gene Transfer (HGT) of antimicrobial resistance (AMR) genes constitutes a key problem for public health as, thanks to it, such genes can spread rapidly among different bacterial hosts, making it very difficult to tackle such outbreaks.
Insertion sequences (IS) are the minimal HGT units responsible for moving AMR genes among different bacterial hosts based just on their physical proximity.
One of the most frequent environments where this physical proximity is achieved is wastewater processing plants. In fact, wastewater processing plants are likely hotspots of AMR genes dissemination through HGT.
Understanding the dynamics of mobile genetic elements and, in particular, of ISs, in wastewater processing plants might help to shed light on how AMR genes are spread and provide possible ways of preventing this from happening.
In this talk we will present a random forest IS classifier and its application to retrieve highly represented ISs in wastewater samples.
Using data from “The transposon registry” we will identify the most relevant features that enable a thorough identification of the ISs. These features cover gene content, order, physical characteristics and evolutionary features. We will use these features in a random forest classifier and show its accuracy on test data.
We will then apply the classifier on a wastewater metagenomic dataset collected in Wales (Knight et al 2024).

Comet, a genome from the dawn of cattle breeding

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Born in 1804, Comet was a bull that impressed. He was the first ever bull sold for £1,000 (the equivalent of £127,882/149,370€ today) and was widely regarded as a high quality bull. He was one of the foundational sires of the Shorthorn breed which was first developed in 18th century England and was later used to improve or develop as many as 40 other modern breeds. The legacy of Comet continues on in many modern developed breeds that are responsible for a large portion of the world's meat and dairy products.

For this project, the genome of Comet was sequenced to a coverage of 15X. This genome was used to investigate the legacy of Comet in modern developed breeds. Genetic continuity between Comet and modern Shorthorn individuals can be shown, across 200 years of selective breeding. Comparing runs of homozygosity between Comet and modern individuals shows changing approaches in livestock husbandry. Identity-by-descent segments shared between Comet and modern individuals reveals the extensive use of Shorthorns for breed improvement and indicate that some selected traits common in modern developed breeds can be traced back to this foundational sire.

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Genomic signal of local adaptation in UK silver birch (Betula pendula)

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Silver birch (Betula pendula) is an economically and ecologically important UK native tree species, thriving as a pioneer plant with resilience against wind and frost. Knowledge of the genomic basis of local adaptation in UK silver birch populations is limited due to the requirement for large-scale population sequencing, but may improve our understanding of the drivers of local adaptation to help inform planting, and promote growth for long-term survival under climate change. We sequenced the genomes of 2,054 silver birch trees from 20-year-old field trials at three locations in Britain, each site containing trees from the same 29 UK source populations. We performed a genome-environment association study on each genotype's source population, discovering single nucleotide polymorphisms (SNPs) associated with precipitation, wind, water flow, and frost. We used environmentally associated loci to predict the shift in allele frequency (offset) required for source populations to be adapted to trial sites, identifying a significant correlation between environmental dissimilarity and the predicted offset. This was driven largely by a northern trial site, outside of the environmental envelope of the source populations, with a significantly higher offset than that predicted for other sites, and even for each population to be adapted to the worst-case climate change scenario at their source locations. Comparisons of offset and performance of populations at each trial site highlighted that whilst individuals were smaller and broader at the northern trial site, trees are still surviving, suggesting large offsets do not necessarily indicate unviable populations.

Adaptive introgression from Pacific to Atlantic herring facilitates rapid niche exploration in the Baltic Sea

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Detecting signatures of local adaptation is often confounded by complex demography, particularly during rapid range expansions where genetic drift can obscure natural selection. The post-glacial colonization of the brackish Baltic Sea by Atlantic herring presents such a challenge. However, herring provide a powerful system to overcome this; their enormous effective population size minimizes stochastic drift, allowing selection to be the primary driver of genomic architecture ($s >> 1/Ne$).
In this study, we integrate high-coverage individual genomes, large-scale Pool-seq data, and transcriptomic profiles to characterize a striking case of adaptive introgression from Pacific into Atlantic herring. By synthesizing these multi-source data, we reveal that while Pacific introgression accounts for only 0.29% of the genome, these regions encompass 10% of the loci showing the strongest differentiation between Atlantic and Baltic herring. This concentration of introgressed alleles indicates that natural selection has effectively "filtered" the genomic landscape, favoring Pacific variants that promote adaptation to the brackish environment. We further incorporate RNA-sequencing data to validate the functional importance of candidate genes, such as THRB and SEC16B, in providing the physiological basis for visual and metabolic adaptation to the Baltic's low-salinity environment. Our findings demonstrate how interspecific gene flow, even when minimal in scale, can provide the raw material for rapid adaptation to novel environments, and how multi-modal genomic data can precisely identify selection in non-equilibrium systems.

Regulatory Plasticity as an Adaptive Strategy in Malaria Parasites

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One of the greatest global health challenges we face is understanding the mechanisms of rapid adaptation of pathogens to changing environments. Malaria parasites exhibit remarkable phenotypic and genomic plasticity, enabling rapid adaptation to fluctuating within host conditions. Although this plasticity is central to parasite survival and transmission, the regulatory mechanisms remain poorly understood. To fill this knowledge gap, we first produced high quality, chromosome level genome assemblies from field derived Plasmodium clones that retain their adaptive potential, leveraging long read PacBio HiFi sequencing. These assemblies provide a robust genomic framework for interrogating natural parasite variation, particularly within highly polymorphic gene families involved in host interactions. Building on this resource, we profiled and compared single cell transcriptomes of parasites from heterogeneous versus homogeneous transmission environments, and integrated these data with epigenetic profiles obtained through ATAC seq. This combined approach enabled high resolution dissection of transcriptional heterogeneity and the identification of gene regulatory networks and regulatory elements associated with plastic responses in the transmissible sexual stage, called gametocytes. Our analyses uncovered a set of genes that consistently exhibit transcriptional plasticity across biological replicates. Many of these genes encode known or predicted parasite surface proteins and mediators of host–parasite interactions. Their plastic expression supports a bet hedging strategy that is actively modulated during sexual differentiation, equipping parasites to cope with the unpredictable environmental conditions of transmission. Together, our findings provide new insight into the genomic and transcriptional bases of adaptive plasticity in eukaryotic pathogens.

A New Technique for Ultra-Fast Maximum Likelihood That Gives Exact Phylogenetic Gradients for Free

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Phylogenetic likelihood computations scale poorly with model complexity and data size, creating tension between biological realism and computational tractability. The fastest and most widely used approaches in maximum-likelihood phylogenetics require $O(N^3)$ matrix operations per branch for each free parameter (where N is the number of states in the model). For expectation-maximization (EM), this cost arises in computing sufficient statistics; for Quasi-Newton (QN) methods, in differentiating transition probability matrices along each branch to compute the phylogenetic gradient.

Here, we show how this dependency on the number of free parameters can be eliminated for both EM and QN with a single exact technique. Our approach, which we call the "inside-out likelihood sandwich," inverts the classical branch-specific likelihood construction by aggregating endpoint-conditioned expectations before integrating, rather than computing each parameter's contribution separately. The resulting E-step requires only $O(N^3)$ computations per branch, regardless of the number of free parameters--a substantial reduction from the previous best-case scaling of $O(N^3)$ per branch per parameter. Remarkably, this reorganization also allows the exact gradient to be obtained essentially for free, requiring only readout of precomputed quantities without costly matrix–matrix operations.

This work generalizes previous path-augmented likelihood methods for phylogenetic MCMC without approximation, eliminating a longstanding bottleneck that penalized attempts to fit more realistic evolutionary models. We demonstrate that implementations of the core techniques scale well to large phylogenomic datasets, reducing analyses that previously required hours to seconds. A Git repository with code and Jupyter notebooks demonstrating the core techniques will be made available alongside this presentation.

Parallel genomic adaptation promoting replicate range shifts of the blue-tailed damselfly, Ischnura elegans, in Scotland and Fennoscandia

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With climate change, range shifts to higher latitudes are now widely observed across plants and animals. Recent work has shown that range-expanding populations can rapidly adapt to new environments, fundamentally changing the expansion velocity and final range limit. However, the genomic changes underlying range shifts in the wild are still poorly understood, being challenging to detect due to complex interactions between gene flow, drift, and adaptation in spreading populations.

We overcome this challenge by studying four replicate range-shifting transects of the blue-tailed damselfly, Ischnura elegans, applying a recently developed statistical tool (PicMin) to detect parallel signatures of adaptation in the genome. We conducted low-coverage whole genome sequencing of 955 individuals from 81 sites spanning 1700km in Scotland, Norway, Sweden, and Finland, and analyzed the data using a genotype likelihood framework in ANGSD.

We found 61 genomic windows that showed significant association with the environment across all 4 transects, with annotations including the circadian clock, development and immune function. In a laboratory rearing experiment of Ischnura larvae, parallel outlier loci were more strongly associated with phenotypic performance than singleton outliers unique to individual transects, highlighting the greater confidence in parallel loci to detect signatures of selection under non-equilibrium conditions.

Finally, we modeled gene flow of neutral and putatively adaptive alleles across the landscape using divMigrate. Adaptive sites consistently showed greater asymmetry in gene flow than neutral sites, with increased northward movement of sites associated with adaptation to colder climates. Thus, adaptive gene flow could further fuel range expansion to higher latitudes.

Pathogen-Host Genomic Interactions as Drivers of Invasion Success

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The role of pathogens in species invasions has long been acknowledged, but rarely closely examined from multiple angles. The historical, ongoing, and future impact of invasive species coupled with the increasing impact of humans on biological systems makes it imperative to understand the influence of complex interactions between hosts and pathogens on species invasion dynamics. Rodents in New England provide an ideal system in which to study these relationships because of the relatively defined timeframe of invasive rodents' first introduction from Europe to the New England coast. To determine how pathogens influenced invasive rodent expansion into Vermont's native rodent territory over the past few hundred years, we combined analyses of population demographic change, inference of positive selection on pathogen-interacting proteins (PIPs) in native and invasive rodent genomes, and corresponding co-evolutionary changes in the pathogens of interest. To do this, we sampled 138 rodent skin museum specimens across 6 native and 2 invasive species to create a time transect spanning over a century. Sequencing of these samples provided an opportunity to estimate recent population demographic changes, identify positive selection on specific PIPs at a population scale, and screen these historic rodents for pathogens. Pathogens of interest were identified, characterized, and compared to investigate their evolutionary trajectory. Future work will include the addition of high-quality modern genomes and fine-tuned analyses to more accurately pinpoint selective sweeps in PIPs. The combination of these three angles of inquiry allows us to illuminate the broader picture of host-pathogen interactions in the context of species invasions.

A comparison of selection on autosomes and the young X chromosome in diploid Mercurialis species

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The evolutionary dynamics of proto-X and Y chromosomes during early divergence—when most genes remain functional but recombination is suppressed—have been explored theoretically. A recent model (the "slow-X" hypothesis) predicted that genes on young X chromosomes should exhibit lower adaptive substitution rates than autosomal genes due to their smaller effective population size and the 'masking' of their gene products by their Y-linked allelic homologs in males, while they remain functional. Accordingly, young X-linked genes should tend to accumulate deleterious mutations faster than autosomal genes. We tested these predictions in the dioecious plant Mercurialis annua and its sister species M. huetii, for which we are assembling a haplotype-phased genome. These species have young sex chromosomes with a large non-recombining region on the Y, where most genes are still intact, allowing us to evaluate the slow-X hypothesis. Although autosomal and young X-linked genes show similar divergence between species, X-linked genes segregate a higher proportion of non-synonymous polymorphisms. Selection tests indicate lower adaptive potential on the X chromosomes, and the distribution of fitness effects is skewed toward deleterious mutations with few or no beneficial ones. Overall, these results support the predictions of the slow-X effect.

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Whole-genome sequencing of Black Death victims reveals an immune gene under natural selection

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To identify genetic variants relevant to mortality during the Medieval Black Death, we sequenced more than 400 individuals from molecularly confirmed Central European plague mass graves. We successfully recovered whole-genome sequences at ~1.0× coverage, generating high-quality ancient human DNA data from the initial outbreak (1346–1353 CE) of the second plague pandemic. These data provide sufficient statistical power to detect allele-frequency changes at common variants and enable screening for pathogen-driven natural selection. We identify a major risk allele in an immune gene that plays an important role in the innate immune response to bacteria. Notably, this variant occurs at exceptionally high frequency in present-day European populations, suggesting a genetic contribution to the severe impact of the Black Death in West Eurasia. Our results provide evidence that natural selection acted on the human genome during one of the most devastating pandemics in recorded history and help to resolve long-standing debates about the genomic impact of the Black Death.

Pervasive lateral gene transfer among grasses as a driver of metabolic innovation

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Lateral gene transfer (LGT), defined as the acquisition of alien genetic material by means other than sexual reproduction, has been widely documented in grasses, including major crops. Despite the proven adaptive potential of certain laterally transferred genes, the extent to which LGT contributes to evolutionary innovation remains unclear. I scanned the maize pangenome for grass-to-grass LGTs and identified 22 laterally transferred protein-coding genes. These transfers appear to predate domestication, and variation among cultivars is likely a result of subsequent gene losses. Interestingly, some of these genes seem to have functions associated with important agronomic traits such as stress tolerance and seed oil content. Notably, half of the maize LGT were acquired from the same weedy grass species, Zuloagaea bulbosa, which naturally co-occurs with the progenitor of domesticated maize in Mexico. To test whether LGT was reciprocal between these two grasses, I generated a new genome assembly for Z. bulbosa and searched for LGT of maize origin. I found 31 LGT, 41% of which were acquired from close relatives of maize (Andropogoneae grasses). Despite this bidirectional exchange, most of the transfers do not appear to be reciprocal at the species level. Several laterally transferred genomic fragments contained metabolic genes, including genes which are part of biosynthetic gene clusters. In summary, LGT has contributed to genome plasticity by generating standing genetic variation, which the potential to facilitate metabolic innovation and rapid adaptation in grasses, including the ancestors of some of the world's most important crops.

Are Triallelic SNPs generated by trans-lesion synthesis?

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It has been shown that sites with 3 SNP alleles segregating in the human population are about twice as common as expected. It has been suggested that these might be due to a process, such as trans-lesion synthesis (TLS), that can generate two alternate mutations within the germline of a single individual. To investigate this, we conducted a comprehensive search of the literature for cases in which siblings and parents had been sequenced and de novo mutations discovered. Out of 333 siblings across 36 species, we found 3 cases in which siblings had different mutations at the same site. This is far more than would be expected by chance. However, they are sufficiently rare to suggest that they are either chronically underreported or that TLS is not the cause of triallelic SNPs. To investigate further we used Y-chromosome data from the 1000 Genomes Project. We test whether triallelic SNPs are over-represented and whether many of these originate within a single bifurcation of the tree as we would expect if mutations in a single individual cause triallelic sites.

Sex-chromosome evolution and speciation in the genus Salmo

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Species may arise through emergence of genetic incompatibilities that separate lineages of shared ancestry. These incompatibilities frequently arise in tandem with evolution of sex-chromosomes. Here we identify an extensive 20Mb chromosomal region exhibiting suppressed meiotic recombination that flank the sex determining loci in the Brown trout (Salmo trutta). We show that this extensive 'supergene' of tight meiotic linkage emerged through a double chromosomal inversion, separating S. trutta from its sister species in the genus Salmo, the Atlantic salmon (Salmo salar). By utilizing whole-genome sequencing we provide evidence that selection contribute to extension of the sex-supergene beyond the boundaries of the originating double inversion, a hypothesized trajectory in sex-chromosome evolution. Within S. trutta gradual repression of recombination between the sex chromosomes has resulted in formation of three evolutionary strata on the emerging Y chromosome that show different levels of divergence from the ancestral X chromosome.
A role of sex-chromosome evolution in speciation within the genus Salmo is supported by identification of incompatibility loci in derived evolutionary strata on the Y chromosome. We show that introgression between local populations is constrained by these incompatibility loci. Our study provides a novel case of sex-chromosome differentiation within the Salmonidae, and, demonstrate that sex-chromosome evolution may contribute to speciation in this highly diversified family of fishes.

The origins of domestic sheep and wool production in the Nordic Bronze Age

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The initial spread of domestic sheep into Europe began during the Neolithic, but the emergence of wool textiles occurred much later. By the Bronze Age, sheep assumed a central economic role, with wool becoming a highly valued and widely traded commodity, closely linked to the rise of early complex societies. However, the processes behind the transition to woolly sheep remain poorly understood.

The project Sheep, Wool and Landscape in the Nordic Bronze Age investigates the dispersal of domestic sheep and the development of wool production in Denmark. Despite the exceptional corpus of Danish Bronze Age textiles from the second millennium BCE, their provenance -local or imported- remains uncertain. To understand how local wool economies emerged, the project examines shifts in sheep husbandry from the Neolithic to the Early Iron Age. In particular, it explores whether the spread of wool was driven by cultural exchange, improvements in local sheep, or the introduction of new, woollier sheep types from the Pontic-Caspian steppes alongside human populations. We examine this question through proteomic and ancient DNA analyses of sheep bones combined with archaeological studies of settlements and landscapes.

Schistosoma mansoni single cell transcriptomics reveals recently duplicated genes specifically expressed in the host-parasite interfase.

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Gene duplication drives genome evolution, promoting functional innovation and regulatory diversification. In the human parasitic flatworm Schistosoma mansoni, recently duplicated genes appear to be retained due to increased dosage effects, showing high sequence conservation and correlated expression. Here, we integrate evolutionary genomic and 'bulk' and single cell transcriptomic analyses to study the fate of duplicated genes across different evolutionary timescales.

Homologous gene clusters were inferred from high-quality flatworms genomes available in WormBase ParaSite. Duplicated genes in S. mansoni were classified as species-specific, S. mansoni clade-specific, or ancestral duplications using a tree reconciliation approach with the ETE package. dN, dS, and dN/dS were estimated using YN00 and CODEML site models in PAML. Gene expression patterns and correlations between duplicated copies were analyzed using publicly available bulk and single-cell RNA-seq datasets, with random and neighboring non-homologous genes used as controls.

Recent duplications exhibit strong sequence conservation and highly correlated expression between copies. Both sequence similarity and expression correlation decrease progressively with duplication age, although ancestral duplications retain significant positive expression correlations. Control gene sets show marginal or no correlation. These patterns are consistent across bulk, pseudo-bulk, and single-cell RNA-seq data. Notably, recently duplicated genes show high and specific expression in the intra-snail stages. Moreover, these are tegumental-specific genes, revealing their tentative role in host-parasite interaction and hence relevant for species-specific adaptation.

Our results support dosage compensation as a key mechanism underlying the initial retention of duplicated genes in S. mansoni, followed by gradual divergence in sequence and function over evolutionary time.

Environmentally-driven asynchrony in genomic reconstructions of demographic responses to past climate change and human expansion across hundreds of bird populations

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Species-level genomic reconstructions of past population dynamics obscure how environmental change reshapes populations unevenly across geographic and climatic space. By reconstructing demographic histories for ~400 populations across diverse bird species worldwide, we uncover spatially-explicit divergence in population trajectories during a major late-Quaternary environmental transition. Specifically, the transition from the Last Glacial Maximum to the early Holocene—an interval characterized by rapid climatic warming and expanding human presence—was associated with widespread population decline, yet did not impose uniform demographic outcomes across populations within species. Although most populations declined between 21 and 10 thousand years ago, nearly one-third increased, and fewer than half of species exhibited declines across all populations sampled. Crucially, these divergent responses were geographically structured: populations experiencing similar local climatic trajectories, particularly temperature change, tended to respond synchronously, with intrinsic traits such as body mass modulating the scale of this synchrony. When placed within contemporary gradients of anthropogenic pressure and recent climatic change, populations occupying the highest-exposure regions are disproportionately characterized by low levels of genetic diversity, whereas populations with high genetic diversity are less frequently found in these regions. Together, these results show that climatic warming and increasing human pressure tend to coincide with population decline, while generating spatially structured divergence within species, such that future environmental change will likely impose widespread demographic pressure without uniform responses across populations, acting on genetic diversity that is already unevenly exposed.

Multiple Denisovan lineages shaped the genomic diversity of Asian populations

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Recent fossils discoveries in Asia, accompanied by the sequencing of Neanderthal and Denisovan genomes, highlight the complex hominin diversity and peopling history of this continent. However, investigations of Neanderthal and Denisovan in modern human ancestry have largely focused on European, East Asian and Oceanian populations, leaving Central and Southeast Asia comparatively understudied.

In this study, we investigated Neanderthal and Denisovan ancestry in Central and Southeast Asian populations. We estimated that Neanderthal ancestry proportions range from 2.5% to 2.8% across these populations. Using the f4-ratio statistic, Denisovan ancestry was undetectable in some Central Asian populations, while in other Asian populations it was in low amount (<1%), comparable to those observed in East Asian populations.

Using Sprime to further characterize Denisovan introgressed genomic fragments, we revealed that Denisovan ancestry in Asian populations clusters into distinct groups. Notably, Southeast Asian populations exhibit three distinct clusters of Denisovan introgressed segments, suggesting admixture with at least three genetically distinct Denisovan populations. In contrast, Denisovan ancestry in other Asian populations appeared to derive from only two Denisovan sources. The Sprime results were confirmed using an independent analysis using a CRF approach to identify introgressed segments.

These results shed a new light on the complex admixture history between early Homo sapiens and archaic hominins during the peopling of Asia and highlight the extensive diversity in these extinct populations.

Ancient-modern genomes reveal an impact-dependent erosion of functional diversity in Atlantic bluefin tuna

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Atlantic bluefin tuna (Thunnus thynnus) has supported the world's oldest commercial fishery and remains among the most valuable marine resources. Using high-coverage ancient (n = 34) and modern (n = 34) genomes from the eastern Atlantic, we detect a weak but consistent genome-wide signal of genetic erosion, in line with earlier work and the strong twentieth-century population contraction. Uniquely for a high-Ne marine fish, we quantify temporal changes in putatively deleterious variation using functional-impact proxies. While the genome-wide reduction in diversity is modest, temporal shifts are disproportionately concentrated at functionally constrained sites: modern genomes show a modest depletion at putatively neutral loci but a stronger depletion at variants predicted to be deleterious, scaling with inferred impact and broadly consistent with forward simulations in SLiM. Stratifying allele- and genotype-frequency contrasts by pre-bottleneck derived-allele frequency reveals that, although drift disproportionately affects rarer variants, higher-impact categories still decline more than lower-impact classes at matched starting frequency, supporting an additional role for purifying/background selection beyond drift alone. Together, these results advance empirical baselines for genetic-load dynamics in high-Ne species and reveal an impact-dependent footprint of recent decline on functional genetic diversity, with potential consequences for long-term adaptive capacity.

Molecular principles of iridescent color formation in bird feathers

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Structural coloration is widespread in nature and generates some of the most striking visual effects known, such as the bright blues of butterfly wings and the vibrant colors of the eyespot of peacocks. In birds, iridescent structural coloration arises within feather surfaces from nanoscale, periodic arrangements of keratin, melanin, and air that interact with light, producing angle-dependent, shimmering colors. Although avian iridescence is well characterized physically and anatomically, the genetic and molecular mechanisms that generate these photonic nanostructures, and modulate their optical properties, are basically unknown. By integrating genetic mapping, electron microscopy, and optical analyses of mutant breeds that arose during peafowl domestication, we show that feather photonic structures emerge through physicochemical self-assembly responsive to melanin biochemistry and melanosome biogenesis. Single mutations in melanogenic genes can induce gains, shifts, or losses of iridescence, without pleiotropic costs, explaining the evolutionary lability of avian structural coloration leading to its rapid diversification in nature. Single-cell RNA sequencing analyses of individual feathers displaying asymmetric structural color patterns uncovered extensive melanocyte regulatory rewiring associated with iridescence in wild bird species. This work establishes melanogenesis as a key pathway for the emergence and diversification of iridescent coloration in birds, and demonstrates how genetic control can leverage self-organizing mechanisms to create biological diversity.

Competition, compensation and inbreeding depression in the evolution of conifer polyembryony

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Gymnosperm reproduction differs from that of angiosperms in that it features a triploid endosperm and lacks carpel, the sporophytic tissue that can serve as a gatekeeper between pollen and ovule. Thus, gymnosperms are largely assumed to be incapable of having pre-zygotic self-incompatibility (SI) systems to avoid inbreeding. Interestingly, gymnosperms can have multiple ovules within a seed, sharing the same maternal haplotype and forming genetically distinct embryos (polyzygotic polyembryony) of which only one survives until maturity.

Our theoretical models show that polyembryony can evolve as a mechanism to compensate for inviable embryos, but also due to competition among embryos. Further, the model indicates that inbreeding depression acting during embryo development can be beneficial. As a result, recessive deleterious mutations accumulate under polyembryony essentially functioning as post-zygotic SI system.

To test these theoretical expectations, we collected spatially resolved seed gene expression (10x Genomics Visium) data from developing Scots pine (Pinus sylvestris), a conifer with high primary selfing rate (30%), and strong inbreeding depression. We have identified thousands of genes expressed in embryos across four developmental stages from fertilization to dominant embryo determination. We will use this data to identify the mutational target for early deleterious alleles, a crucial parameter in models of polyembryony and inbreeding avoidance evolution. Further, we will use population re-sequencing data to identify potential excess of rare deleterious mutations, a key prediction of our model.

Gene expression variation underlying local adaptation in silver birch (Betula pendula)

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Forest trees are excellent model species for understanding the genomic determinants of local environmental adaptation due to their broad distributions and hereditary, adaptive phenological differences among populations. Silver birch (Betula pendula) is an ecologically and economically important forest tree species in Northern Europe. While its phenotypic adaptation across latitudinal gradients is well established, the extent to which gene regulatory mechanisms drive these patterns remain largely unknown.

We conducted a large-scale growth chamber experiment with 1920 silver birch seedlings from four populations to investigate population-level transcriptomic and gene regulatory responses to photoperiod treatments. We sampled a time series of leaf material and conducted RNA sequencing from 214 samples and integrated these with ATAC-seq data from 24 samples to link gene expression with chromatin accessibility patterns. We analyzed time-resolved co-expression networks in addition to differential expression patterns across populations, treatments, and time points.

Variance partitioning indicated that sampling time (7.38%) and treatment–sampling time interactions (6.06%) explained the majority of gene expression variance, while population and related interactions together accounted for 2.72%. Consistently, co-expression network structure was dominated by modules associated with sampling time and photoperiod treatment. Population-specific modules were not identified. However, differential expression analyses identified over 600 genes related to population interactions with sampling time and treatment, as well as 81 genes specific to population–treatment–sampling time interactions. These results indicate that the mechanisms underlying local adaptation may rely on altering expression of individual genes that might be more flexible in their regulatory responses, rather than on altering an entire network.

Genomic fossils reveal hidden evolutionary processes underlying phylogenetic conflicts in avian radiations

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Phylogenetic conflicts in rapid radiations are often dismissed as stochastic noise from incomplete lineage sorting (ILS), yet emerging evidence suggests that some discordance patterns may preserve signals of specific evolutionary events obscured by recombination across most of the genome. Here we conduct the first genome-wide survey of long syntenic phylogenetic conflict (LSPC) across birds, analyzing 63,430 intergenic locus trees from published 363 bird genomes to systematically identify genomic regions where alternative topologies persist over megabase scales. We develop a quantitative framework partitioning phylogenetic discordance into ILS-driven and non-ILS-driven components, revealing fundamental differences between the K-Pg boundary Neoaves radiation (dominated by neutral ILS) and the Passeriformes radiation (shaped by selection). We identify 15 nodes with significant LSPC and classify them into four mechanistic types: localized signals from ancestral structural rearrangements, scattered signals from selection-mediated retention of introgressed haplotypes, genome-wide patterns from ancient gene flow, and chaotic signals from GC-biased gene conversion. We demonstrate that ancient introgression generated extended syntenic blocks selectively retained due to functional gene clusters, for example HOXD families in Columbiformes and ubiquitin ligase complex genes in ancestral Telluraves. Our results establish that LSPC regions function as "genomic fossils" recording evolutionary events otherwise erased by recombination, providing a framework for revealing hidden processes underlying phylogenetic controversies in rapid radiations across the tree of life.

Costs and benefits of genetic rescue of the critically endangered helmeted honeyeater from another subspecies

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Small, isolated populations rapidly lose genetic diversity, reducing adaptive capacity and increasing inbreeding and fitness loss. Genetic rescue—adding individuals from more diverse populations—can restore fitness. When sources of gene flow are ecologically similar and recently diverged from a recipient population, outbreeding depression and disruption of local adaptation—the common risks of gene flow—are unlikely. But when only more distantly related or differently adapted sources are available, adaptive genetic management can be used, with gene flow adjusted in response to measured fitness outcomes.

The critically endangered Australian helmeted honeyeater, a small and isolated subspecies of the yellow-tufted honeyeater, provides a rare case study of genetic rescue using migrants from a neighboring subspecies. We first conducted captive trials to test whether admixed pairs had higher reproductive performance than pure helmeted honeyeater pairs. Mixed pairs bred more readily, produced more nestlings, and showed less male-biased chick sex-ratio, indicating strong fitness benefits of admixture.

We then assessed whether the benefits persisted under the harsher conditions of the wild by monitoring field fitness across six breeding seasons. We examined whether variation in genetic diversity and inbreeding predicted survival and breeding outcomes. Preliminary analyses showed that more genetically diverse captive-bred chicks had higher survival in the wild, and that less-inbred wild birds were more likely to breed. These results support continued genetic augmentation and meta-population genetic management across remnant, reintroduced, and captive populations. More broadly, our results demonstrate that carefully monitored genetic rescue—even using moderately diverged sources—can substantially improve fitness in small, isolated populations.

Cell-Autonomous Adaptations in High-Altitude Human Populations

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High-altitude populations have evolved genetic adaptations to environmental stressors including hypobaric hypoxia and increased UV radiation. While well-established adaptations involve organ or tissue-level changes, such as Tibetans' EPAS1-driven blunted erythropoiesis, a critical yet overlooked layer occurs at the cellular level, which we term cell-autonomous adaptations (CAAs). CAAs are inherited genetic changes that improve individual cell survival under stress, thereby contributing to organismal fitness.

To systematically identify CAAs, we integrated functional genomics with evolutionary analysis. We performed a genome-wide CRISPR knockout screen in human skin cells under UV, a major high-altitude stressor, identifying 136 genes essential for cellular UV survival. To determine whether these genes show signatures of selection in high-altitude populations, we examined three populations: Tibetans, Andeans, and Papua New Guinea highlanders. This revealed candidate adaptive genes across multiple cellular maintenance pathways, including DNA-damage repair, chromatin regulation, and ribosomal function, suggesting adaptation targets fundamental cellular machinery.

However, a key challenge in interpreting selection signals is that they often span large genomic regions, complicating identification of causal variants and their target genes. To resolve this, we performed a massively parallel reporter assay (MPRA) testing the regulatory effects of ~12,000 candidate variants from the strongest selection signals across these populations, under hypoxia and UV. Integrating MPRA with CRISPR screening enables identification of variants that both alter gene regulation and are linked to genes essential for cellular stress survival, providing convergent evidence for adaptive alleles. Together, this approach establishes cellular adaptation as a critical, experimentally tractable component of human evolution in extreme environments.

Ancient HLA Variation and Predicted Immune Responses During Epidemics in Colonial Mexico

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During the colonial period in New Spain, interactions among Indigenous, European, and African populations led to major demographic and genetic changes. Between 1519 and 1600, successive epidemics caused a catastrophic decline in Indigenous populations, with mortality exceeding 80%. Differences in adaptive immunity, particularly within the human leukocyte antigen (HLA) system, may have influenced survival during these outbreaks.

To investigate HLA diversity and its potential role in immune responses during colonial epidemics, we analyzed ancient DNA(aDNA) from 59 individuals, including 54 from the colonial period and 5 from pre-Hispanic contexts. HLA regions were enriched using myBaits in-solution capture followed by next-generation sequencing. HLA genotyping was conducted using OptiType and TARGT. In addition, NetMHCpan and NetMHCIIpan were used to predict binding affinities between HLA variants and pathogen-derived peptides, providing insight into potential differences in immune recognition.

We obtained high-quality HLA data, achieving complete coverage of 26 HLA genes and an average sequencing depth of approximately 25× in high-quality libraries. Both HLA classI and classII alleles were identified, with allele frequencies broadly similar to those observed in present-day Mexican populations. Peptide-binding predictions revealed several HLA variants with strong affinities for pathogen-derived peptides. To assess the structural plausibility of these interactions, we performed molecular docking analyses of selected HLA–peptide complexes, which supported binding conformations.

Together, these results suggest that specific HLA variants may have influenced immune responses during colonial epidemics and provide new insights into the genetic factors underlying survival during one of the most severe demographic crises in the history of the Americas.

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Gene regulatory signatures of archaic introgression across human tissues and cell types

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Archaic humans, including Neanderthals and Denisovans, contributed to modern human genomes multiple times through a process known as archaic introgression. These introduced archaic DNA fragments have shaped human evolution and genetic diversity, and with the increasing availability of omics datasets, there is now an opportunity to infer the regulatory impacts of these fragments across many tissues and cell types. The existence of introgression deserts, regions strongly depleted of archaic DNA, suggests that some archaic genetic material is incompatible with modern human biology and potentially contributes to human uniqueness. Furthermore, as ancient DNA is preserved mainly from remains in colder climates, we may never be able to study the molecular profiles of archaic populations from warmer regions like South Asia. Here, we leveraged the large-scale sequencing efforts of GTEx (n=800) and UK Biobank (n=500,000) to generate maps of archaic introgression and introgression deserts. Using a reference-free method for detecting archaic introgression, we identify all archaic groups that contributed DNA to modern genomes. Using gene expression data for >50 tissues, scRNA-seq, methylation patterns, and H3K27ac data, we explored whether introgressed DNA and introgression deserts are associated with gene regulatory changes across specific tissues, including skin, testes, and brain regions, and cell types, such as T cells of the immune system and melanocytes of the skin.

Ancient Treponema pallidum genomes reveal phylogenetic diversity and lineage persistence through time in South American populations

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Treponema pallidum is a pathogen responsible for several diseases in humans around the globe. Its origin and spread have been subject of debate for centuries. Recently, the retrieval of ancient genomes has greatly deepened our understanding of T. pallidum evolution and global spread. Here, we expand on this framework by reporting additional ancient T. pallidum genomes from Peru obtained using a targeted pathogen DNA enrichment approach. These genomes span a broad time period and encompass various cultures, including the Moche and the Inca civilizations. Our results reveal a high phylogenetic diversity of T. pallidum in pre-Hispanic Peru, lending support to previous research conducted in several South American regions. Additionally, we increase the coverage of a previously reported ~5.500 years-old highly divergent genome from the Northern Andes by almost 10-fold, allowing for a deeper investigation of its genomic features and a more accurate estimation of its divergence from present-day subspecies. We demonstrate that this lineage survived up until the first centuries CE in Peru, suggesting a multi-millennial presence in South American populations. These results set the ground for a better understanding of the spread and persistence of treponemal diseases in South American populations through the millennia.

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Detecting Vulnerability Early: Genomic Signals from Fragmented Landscapes

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Even widespread and historically abundant species may be more vulnerable than commonly assumed. Several of the butterfly (Lepidoptera) species we study show genomic signatures consistent with early-stage genomic erosion, despite retaining relatively high nucleotide diversity. All species exhibit drastic recent declines in effective population size (Ne). This apparent mismatch may reflect a “drift debt”, where genetic drift acts more slowly in historically large populations with high standing genetic diversity, causing a lag in the loss of genetic diversity. Functional connectivity, i.e. the interaction between habitat connectivity and innate dispersal ability, plays a key role in mediating population genomic responses to habitat fragmentation. In this context, we examined seven species spanning a gradient of dispersal ability, Aglais urticae, Pieris napi, Gonepteryx rhamni, Maniola jurtina, Thymelicus lineola, Lycaena virgaureae, and Coenonympha tullia, across the highly fragmented Danish landscape. We assessed genetic diversity, population structure, inbreeding, genetic load, and historical Ne trajectories using genomic data. The population genomic patterns differ strongly among species and are shaped by dispersal ability. Species with low dispersal ability exhibit relatively higher levels of inbreeding and stronger population structure than highly dispersive species, indicating increased population isolation and reduced gene flow. By integrating life-history traits with genomic and spatial data, this study identifies early genomic indicators of population vulnerability and highlights the importance of functional connectivity and demographic history in shaping contemporary and future evolutionary resilience in fragmented landscapes.

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Adaptive Phylogenetic Tree Search via Machine Learning-Based Parameter Selection

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Phylogenetic tree reconstruction from genomic data is NP-hard, with search spaces growing factorially with the number of species. Current methods rely on heuristic search strategies. Each strategy uses a fixed set of search options to navigate the tree space, e.g., either defining neighbors according to either the nearest-neighboring interchange (NNI) or subtree pruning and regrafting (SPR) method. These search options were optimized to work well on average on benchmark datasets. However, they disregard dataset-specific characteristics, and they remain constant and predetermined along the entire course of the search progress.

Optimal search strategies inherently depend on context. Different alignments favor different configurations, and the optimal approach changes as the search progresses - for example, when a tree is already near-optimal, evaluating large-radius moves wastes computation, whereas broader exploration is beneficial early in the search.

Thus, we aim to develop a machine learning framework for phylogenetic tree reconstruction that allows search options to vary among datasets and within search stages, making it adaptive. Utilizing Deep Neural Networks, we predict optimal search parameters specific to each dataset and current state. Our preliminary results suggest that adaptive policies outperform static baselines that apply the single most frequently optimal configuration.

This research aims to lay the groundwork for next-generation phylogenetic software where tree reconstruction strategy adapts dynamically to each dataset and search stage.

Understanding the evolutionary dynamics of host and pathogen through comparative transcriptomics

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As natural reservoirs for emerging pathogens, bats represent a critical model for understanding host-pathogen co-evolution. Bats have adapted to pathogens through diverse mechanisms, including resistance—rapid pathogen elimination—and tolerance—limiting tissue damage following infection. In the Egyptian fruit bat (an important model in comparative immunology), several mechanisms conferring disease tolerance were discovered, but resistance mechanisms remain poorly understood. Previous studies suggested that elevated basal expression of innate immune genes may increase resistance. Here, we test whether such transcriptional patterns occur in Egyptian fruit bat tissues through single-cell and spatial transcriptomics of gut, lung, and blood cells, comparing gene expression between bat, mouse, and human. Despite numerous interferon loss and expansion events in the bat genome, interferon expression patterns are remarkably similar to mouse. In contrast, central complement system genes are highly and uniquely expressed in key regions of bat lung and gut epithelium, unlike in human and mouse. Interestingly, this unique expression in bat gut is strongest in the crypt, where developmental programs are highly conserved. Complement genes also evolve rapidly in their coding sequences across the bat lineage, and the bat complement system displays strong hemolytic activity. Together, these results indicate distinctive transcriptional divergence of the complement system, which may underpin bat resistance. Our findings demonstrate how comparative single-cell transcriptomics can reveal species-specific mechanisms of pathogen resistance and highlight the power of integrative methodologies to uncover how immune systems diversify under different evolutionary pressures—insights essential for predicting host responses to novel or shifting pathogen landscapes.

Uncovering previously unrecognized gene flow from modern humans into Denisovans

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Denisovan introgression has contributed genetic ancestry to present-day human populations, particularly in Oceania and parts of Asia, whether modern humans also contributed genetic material to Denisovans remains unclear.

We analyzed whole-genome data from 2,050 modern humans and two Denisovan genomes, Denisovan3 and the older Denisovan25, to test for human-to-Denisovan introgression. Using IBDmix, we identified on average ~3.3 Mb and ~6 Mb of Denisovan-like sequences per African individual based on Denisovan3 and Denisovan25, respectively, far exceeding the expected false-positive amount (~0.1 Mb/ind) estimated from simulations under a no-introgression model. Over 90% of these segments are shared with non-African populations, indicating inheritance from a shared modern human ancestral population.

Relative to Denisovan-derived sequences private to non-Africans, these modern-human-shared segments are enriched in high-heterozygosity regions of the Denisovan genome and segregate at higher frequencies in modern humans, a pattern consistent with introgression from modern humans into Denisovans. They also show significantly reduced overlap between Denisovan genomes, consistent with stochastic retention of introgressed human ancestry rather than Denisovan-derived variation. To control for potential confounding from Neanderthal ancestry, permutation tests show that Denisovans are significantly more similar to modern humans than to Neanderthals within these regions ($P < 0.01$). Simulations incorporating well-established summary statistics, including Rind and Rpop, further exclude ghost introgression and residual Neanderthal ancestry.

Together, our analyses support at least one episode of gene flow from modern humans into Denisovans at approximately 250–300 ka, contributing an estimated ~1–5% human ancestry and uncovering a previously unrecognized event in hominin evolutionary history.

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The contribution of epigenetic regulation to antimicrobial resistance phenotypes in Escherichia coli from antibiotic-free dairy farms

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Antimicrobial resistance (AMR) poses a major threat to human and animal health. Although commonly associated with antimicrobial use, resistant bacteria are increasingly detected even in the absence of direct antibiotic exposure. In a previous study, we investigated the genomic basis of AMR in Escherichia coli isolated from heifers raised on farms reporting no antimicrobial use. Despite the overall low prevalence of AMR, resistant and multidrug-resistant E. coli persisted across farms, seasons, and sequence types, a pattern not explained by resistance gene presence alone. To investigate additional mechanisms underlying this persistence, we tested whether epigenetic regulation contributes to resistance phenotypes. Using long-read sequencing, we analysed DNA methylation patterns in promoter regions. Differential methylation was enriched in promoters of multidrug efflux systems and envelope stress regulators, as well as resistance-associated genes. Notably, the mdtM promoter showed high GATC methylation exclusively in multidrug-resistant isolates carrying TEM-1 and floR, which were confined to a clonal lineage sampled repeatedly from the same animal across seasons. Our results show that identical genetic resistance determinants can be associated with distinct antimicrobial susceptibility phenotypes, consistent with variation in promoter methylation states. We identify associations between Dam/Dcm-mediated DNA methylation and resistance-associated gene expression, indicating that epigenetic modification contributes to phenotypic heterogeneity in AMR. These findings support the hypothesis that DNA methylation can function as a reversible, environmentally responsive regulatory layer, enabling E. coli to maintain resistance phenotypes in the absence of direct antibiotic selection and shaping AMR persistence in antibiotic-free environments.

Ancient DNA from birch tar artefacts: insights into population structure and gendered practices in Neolithic Alpine Europe

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Birch tar is emerging as an alternative source of ancient DNA, particularly in archaeological contexts where human remains are scarce or absent. As part of the AlpGen project, we have screened over 100 birch tar artefacts from Neolithic Alpine lake settlements to assess their potential for biomolecular analysis. In a region where skeletal material is largely lacking, birch tar provides a unique archive through which ancestry, population structure, and genetic relationships between communities can be explored. Many artefacts contain enough ancient human DNA for genetic sex determination, enabling new approaches to studying gendered practices in the production and use of birch tar. The recovered DNA also allows us to investigate ancestry and population structure among lake-dwelling groups, shedding light on the genetic makeup of Neolithic Alpine communities. The presence of oral microbial DNA helps identify chewed tar and supports the reconstruction of oral microbiome composition and past oral health, offering a potential alternative to dental calculus. In this paper, we present initial findings from AlpGen, showing that birch tar can preserve ancient biomolecules at a scale suitable for population-level research. These results underscore its value as a biomolecular archive for understanding the genetic and cultural landscapes of prehistoric Europe.

Pangenome-based investigation of genomic diversity in Kaolinonychus: A harvestmen lineage with deep admixture history and troglophilic adaptation (Arachnida, Opiliones, Paranonychidae)

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The Korean endemic harvestmen in the monotypic genus Kaolinonychus represents a compelling model for evolutionary dynamics, characterized by deep phylogenetic divergence and ancient admixture. Furthermore, spanning both cave-dwelling and surface-dwelling populations, it offers a unique system to investigate the genomic mechanisms of environmental adaptation. However, deciphering these dynamics between divergent lineages is challenging with standard linear reference-based genomics approaches, which suffer from reference bias and often fail to capture lineage-specific sequences and structural variants (SVs), which are increasingly recognized as pivotal drivers of evolutionary adaptation and speciation. To address these limitations, we employed a comprehensive pangenome strategy. As a foundational step to ensure representative coverage, we identified 5 major genetic lineages by analyzing 200 nationwide resequencing samples against a single reference genome. Guided by this framework, we sequenced representative individuals from each of the 5 lineages using PacBio HiFi reads, yielding 10 highly contiguous haplotype assemblies, which were subsequently integrated using the Minigraph-Cactus pipeline. The resulting pangenome graph significantly expands the genomic representation from 822 Mb (linear reference) to 1.27 Gb, capturing 445 Mb of novel non-reference sequences. This comprehensive topology explicitly encodes complex variation patterns, recovering over 17.8 million variants, including approximately 344,000 structural variants (≥50 bp) that were previously inaccessible. Furthermore, leveraging this graph substantially improved short-read mapping and variant calling sensitivity, particularly in divergent regions. Ultimately, this resource serves as a cornerstone for unraveling the species' reticulate evolutionary history and deciphering the precise genomic signatures of cave adaptation.

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Mapping the Local Biochemical Landscapes of TEM-1 β-Lactamase

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Understanding and predicting the effects of mutations on enzyme activity remains challenging due to pleiotropic impacts on multiple biochemical properties. Here, we developed a high-throughput approach that links bacterial growth to the catalytic activity of TEM-1 β-lactamase against ampicillin. By culturing E. coli expressing approximately 120,000 TEM-1 variants across 30 ampicillin concentrations and using deep sequencing to measure growth, we inferred in vivo catalytic velocities under each condition. Fitting these velocities to the Michaelis-Menten equation allowed estimation of Vmax and Km for each variant, enabling simultaneous quantification of fitness and kinetic parameters. Our results reveal widespread pleiotropy, with mutations exerting differential effects on catalytic constant, substrate affinity, and folding stability. The spatial distributions of mutations influencing these properties exhibit partial overlap,and long-range mutational hotspots distant from the active site exert significant effects on kinetic parameters. These findings provide a comprehensive mechanistic map of the TEM-1 fitness landscape, elucidating the complex sequence-structure-function relationships that underlie enzyme evolution and adaptation.

Unveiling the Evolutionary Dynamics of the X Chromosome in Aphids

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Sex chromosomes often display distinct evolutionary dynamics compared to autosomes. In many organisms, the X chromosome evolves faster than autosomes due to hemizygous exposure of recessive alleles and/or reduced effective population size. Disentangling the relative contributions of these two factors is challenging. However, aphids, with their XX/X0 system and cyclical parthenogenesis, offer a compelling model to examine these processes at broad phylogenetic scales. We conducted comparative genomic analyses across 53 aphid species, including four newly assembled high-quality genomes, to test whether faster-X evolution is a general pattern and to explore its underlying mechanisms. Despite remarkable macro-synteny conservation, X chromosomes exhibit significantly higher sequence divergence than autosomes across species, consistent with a pervasive faster-X effect. Strikingly, this elevated divergence correlates strongly with recent transposable element expansion and segmental duplication on the X. We identified abundant lineage-specific gene copies enriched on the X chromosome, many residing in regions shaped by TE activity, suggesting that TEs may contribute to the proliferation of these duplicates. Multi-species transcriptomic analyses further reveal that X chromosomes are consistently enriched for male-biased genes.

Our findings demonstrate that faster-X evolution is a wide phenomenon in aphids, associated with TE-related sequence turnover and the accumulation of lineage-specific duplicates on the X. The observed male-biased expression of these copies hints at functional differentiation, though the relative contributions of adaptive versus non-adaptive processes remain to be resolved. This work highlights the X chromosome as a potential hotspot for genomic innovation in aphids.

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Genome diversification and polyploidy in under-utilised, climate resilient millet crops in the grass genus Digitaria

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Select species in the grass genus Digitaria e.g. D. exilis (white fonio), D. iburua (black fonio), and D. sanguinalis (Polish millet) have enormous untapped agronomic potential as climate resilient millet crops. While D. exilis (a confirmed allotetraploid) has received increased research interest in the last decade, genomic resources across the genus are not readily available. Here we present whole genome assemblies for D. iburua and D. sanguinalis and provide a comparative framework for genomic diversity in Digitaria millets. Flow cytometry, chromosome counts, and assembly quality analysis (BUSCO and kmer spectra copy number) determined that both species are tetraploids (2n = 4x = 36), and that genome size and chromosome number are conserved across Digitaria millet species. Determining the mode of ploidy (auto vs allotetraploidy) in D. iburua and D. sanguinalis remains challenging due to low heterozygosity between respective sub-genomes in accessions sequenced, but the domestication of the three species was clearly independent. SEED-SHATTERING 1 (sh1) gene, a key gene underlying domestication associated with seed retention in multiple crops, including rice, has loss-of-function variant in D. exilis. In D. iburua, sh1 is duplicated in both sub-genomes i.e., four copies are present. Orthogroup analysis shows that exon1 is deleted in all four copies of sh1 in D. iburua compared to D. exilis and other Poaceae crops. However, phylogenomic analysis of sh1 orthologs revealed complex homology between duplicated genes in D. iburua and orthologs in D. exilis sub-genomes. These results facilitate efforts to modernise Digitaria millets and help meet food security goals globally.

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Testing the adequacy and the accuracy of models of amino-acid substitution across evolutionary timescales

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Models of amino-acid substitution are central to phylogenomic inference, yet their performance remains insufficiently tested. Here, we use simulation-based analyses to address two complementary aspects of model performance: model adequacy and phylogenetic accuracy. First, using empirical datasets spanning diverse evolutionary depths, we assess model adequacy with respect to across-site compositional heterogeneity, employing complementary metrics that capture both site-level diversity and the amino-acid frequency spectrum. In parallel, we perform targeted simulations to test the ability of widely used amino-acid substitution models to recover known topologies under varying degrees of compositional heterogeneity. When real datasets exhibit across-site compositional heterogeneity, site-homogeneous models consistently perform poorly in both adequacy and accuracy. Site-heterogeneous mixture models perform substantially better, with infinite-mixture models showing the best overall performance. Importantly, accuracy under infinite-mixture models remains high even when datasets are across-site compositionally homogeneous, due to their ability to effectively auto-tune toward simpler models. Together, our results demonstrate that evaluating both model adequacy and accuracy is essential for robust phylogenomic inference.

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Trophic specialization drives contrasting evolutionary dynamics of chemosensory genes in blowflies

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Transitions in feeding ecology are expected to impose strong selective pressures on chemosensory systems, yet their genomic consequences remain poorly understood in lineages with repeated origins of parasitism. Blowflies (Diptera: Calliphoridae) provide an interesting model to address this question, as closely related species span necrosaprophagy, facultative parasitism, and obligate parasitism. We investigated how trophic specialization shapes the evolution of three major chemosensory gene families, odorant-binding proteins (OBPs), gustatory receptors (GRs), and olfactory receptors (ORs), across a phylogenetically broad sampling of calliphorid genomes. Comparative analyses revealed extensive variation in chemosensory repertoires, with clear associations between gene family dynamics and larval feeding habits. Birth-and-death modeling shows that obligate parasites feeding on living tissues experience elevated gene loss rates, leading to net repertoire contraction, whereas necrophagous and flexible feeders display higher gene gain rates, particularly in OBPs and ORs. At the sequence level, ORs are largely conserved and evolve under strong purifying selection, while OBPs and GRs exhibit more heterogeneous selective regimes, including lineage-specific acceleration in parasites and necrophagous species. These contrasting patterns indicate differential functional constraints among chemosensory components.
Genomic organization further reflects these dynamics, as OBPs and GRs frequently occur in dense chromosomal clusters shaped by tandem duplication, whereas ORs are more often maintained as dispersed singletons, consistent with tighter regulatory constraints. Together, our results demonstrate that ecological specialization, especially the transition to parasitism, leaves a signature on chemosensory gene repertoires, molecular evolution, and genome architecture.

Non-coding RNA regulation in differentiating ZW sex chromosomes

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Sex determination is a fundamental developmental decision, yet its molecular basis varies strikingly across animals. Most insights into sex chromosome evolution and regulation come from a few well-studied XY systems, in which males are the heterogametic sex and sex chromosomes are old and highly differentiated. In contrast, young or partially differentiated ZW systems, in which females are heterogametic, remain understudied despite their potential to reveal early stages of sex chromosome evolution and dosage compensation.

Traditionally, research on sex determination has focused on protein-coding genes. However, growing evidence across animals indicates that non-coding RNAs (ncRNAs) can play decisive regulatory roles. Different classes of ncRNAs, including small RNAs, long non-coding RNAs, and circular RNAs, can interact through competing endogenous RNA (ceRNA) networks to modulate post-transcriptional gene regulation.

Here, we investigate the role of ncRNAs in Artemia franciscana, a crustacean with a differentiating ZW sex chromosome system and an unresolved sex determination mechanism. We generated Argonaute-enriched small RNA datasets capturing miRNAs, siRNAs, and piRNAs. These data reveal pronounced sex-biased and sex-specific expression patterns, with particularly strong differentiation in gonadal tissues and early development. Preliminary analyses further suggest a link between piRNA pathways and epigenetic regulation, consistent with findings in Drosophila and mice.

We are now constructing the first ncRNA atlas for A. franciscana, incorporating ceRNA networks, to identify candidate regulators of sex determination and dosage compensation. Beyond this system, the outcomes will inform general principles of sex chromosome evolution, dosage compensation, and ncRNA-mediated regulation across animals.

Deciphering Ion-Dependence of Fitness Effects of Protein Mutations

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Ionic environments critically influence protein evolution and function, yet their effects on genotype–phenotype–fitness relationships remain largely unexplored. To address this knowledge gap, we applied a high-throughput system linking bacterial growth to TEM-1 β-lactamase activity across 30 concentrations of ampicillin. By integrating deep mutational scanning and in vitro kinetics, we quantified fitness for 120,000 variants and inferred catalytic parameters for ~100,000 variants. This multi-layered profiling allowed us to systematically resolve how ions reshape global fitness landscapes and redefine mutational effects.

Our results show that Fe^{3+} and Ni^{2+} exert distinct and widespread influences on mutational tolerance and enzyme function. Fe^{3+} enhances variants with mutations near the active site and allosteric regions, whereas Ni^{2+} preferentially selects for N-terminal mutations while depleting those in central and C-terminal regions. Kinetic analyses further reveal that both ions alter catalytic efficiency particularly in loop regions, resulting in net activity enhancement for >30% of variants under Fe^{3+} and suppression for >50% under Ni^{2+}. These ion-specific modulations reshape epistasis and fitness landscape topography, thereby steering evolutionary trajectories under ionic stress.

Overall, this study provides a comprehensive and mechanistic map of how ionic environments sculpt protein fitness landscapes—linking biochemical parameters and cellular fitness—and offers new insights into environment-dependent protein evolution and engineering.

Integration and comparison of public single-cell RNA-Seq data for animals in the Bgee database and the scFAIR consortium

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Single-cell transcriptomics has become a widely used technology to study heterogeneous and dynamic biological systems. The complexity of these datasets makes them particularly challenging to find, access, and reuse; and to be integrated and compared over multiple experiments. In primary repositories such as the Sequence Read Archive (SRA), cell type information is mostly unstructured, and critical information for allowing reanalyses is often missing.
The Bgee database (https://www.bgee.org/) aims at standardizing scRNA-seq dataset annotations across experiments and species for improving data reproducibility and integration. It also aims at making the resulting expression data comparable between experiments and species. Moreover, Bgee is one the groups leading the scFAIR consortium (https://www.sc-fair.org/), to coordinate curation work and agree on best practices among major single-cell international resources (e.g., CELLxGENE, EBI Single Cell Expression Atlas). As a result, Bgee is recognized as a Global Core Biodata Resource and as an ELIXIR Core Data Resource.

In this presentation, we will describe the curation guidelines and best practices applied at Bgee and scFAIR in order to reuse public single-cell datasets. We will present the original statistical methods applied in Bgee to make these data comparable across experiments and species, and how to leverage ontology structures to reach common cell type information across species for gene expression comparisons. This work allows researchers to access highly structured FAIR data for reuse in their own analyses, and to provide simplified and easy-to-use gene expression information in cell types, comparable between species.

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Trinucleotide genome composition reflects context-dependent mutation spectra in plants

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Genome nucleotide composition is shaped by the interplay of mutation, recombination, drift, and selection. While GC-biased gene conversion (gBGC) drives intra-genome variation in GC content, it cannot fully explain the variation in multi-nucleotide composition observed across genomic regions or among species. Building on our previous observation of a strong correlation between CpG mutation rate and CpG content across 108 eukaryotes, we hypothesize that the multi-nucleotide composition of neutral genomic regions reflects the combined effects of gBGC and context-dependent mutation spectra.

By modeling the stationary trinucleotide composition under a given mutation spectrum using a discrete-time Markov chain, we found a significant correlation between the ratio of reciprocal trinucleotide mutation rates and their corresponding equilibrium abundance. This relationship is supported by the observed trinucleotide frequencies of reference genomes and mutation spectra inferred from genome-wide polymorphisms in multiple plant species, though gBGC weakens the correlation. Crucially, this relationship holds not only across trinucleotide pairs within a genome but also across species for the same trinucleotide pair.

Analyzing the trinucleotide frequencies in putatively neutral intergenic regions of 60 plant genomes, we uncovered remarkable inter-species variation, indicating differences in the underlying mutation spectra. Treating pairwise trinucleotide ratios as quantitative traits, we performed phylogenetic regression against DNA repair and methylation genes, thereby identifying candidate mutation modifiers in plants. Overall, this study demonstrates a strong connection between genome multi-nucleotide composition and context-dependent mutation spectrum, suggesting that a single reference genome can inform mutational patterns, even in species lacking polymorphism or direct mutation data.

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A cross-linking enzyme underlies the development of feather structural coloration in birds

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Birds are among the most colorful animals in nature. Plumages of birds serve important functions such as camouflage and social and sexual signaling. They use pigments and structural modifications to color their feathers. Combinations of these mechanisms have created highly diverse and striking colorations of avian plumage. While significant progress have been made in elucidating the genetic underpinning of pigment-based plumage coloration in birds, our understanding of the genetic basis of feather structural colors remains largely unexplored. Many birds have noniridescent structural plumage colors, which result from coherent light scattering caused by quasi-ordered β-keratin nanostructures and air within the medullary spongy layer of feather barbs, producing colors ranging from blue, violet, to ultraviolet. However, the molecular mechanism of how the nanostructures develop remains unknown. In this study, we investigated birds with mutations that affect their blue plumage colors. We first characterized the phenotypic difference between birds with and without the noniridescent structural plumage colors. We then combined genetic mapping and gene expression analyses to identify the gene underlying this phenotype. We uncovered a molecular mechanism that explains how a single enzyme modulates feather nanostructure development to produce noniridescent structural color. This mechanism underlies the remarkable phenotypic diversity observed in this vibrant group of animals, and identifying the genetic basis of structural coloration provides crucial insights into the evolution of avian diversity.

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Bayesian approaches to root phylogenetic trees under root uncertainty: evaluation using empirical and simulated ancient and modern pathogen data

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Accurately rooting phylogenetic trees is crucial for reconstructing the evolutionary and epidemiological histories of pathogens, yet it remains challenging when temporal signal is limited or outgroup information is uncertain. Here, we introduce a novel Bayesian framework for assessing statistical support for the root of phylogenetic trees that integrates molecular evolutionary models with sampling date information, aiming to robustly discriminate between alternative root placements. We benchmark the method using large-scale simulations under a range of evolutionary scenarios that are typical in ancient DNA studies, enabling us to systematically assess its sensitivity and specificity. To further explore its real-world utility, we validate the approach on well-characterized lineages of Yersinia pestis exhibiting both strong and weak molecular clocklike behaviour, as well as on empirical datasets from additional pathogens with unclear root placement. Preliminary results indicate that our method is broadly applicable and can provide improved root support and quantification of uncertainty, particularly in cases where standard root placement strategies are inconclusive. We discuss these findings and offer perspectives on the integration of this approach into future studies of pathogen evolution, highlighting its potential for enhancing confidence in evolutionary and epidemiological inference.

The Green Sahara genomic landscape: tracing ancestries across North Africa and Sahel through joint analysis of modern and ancient genomes

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Africa, the continent with the greatest genetic diversity, has long been underrepresented in large-scale genomic research, limiting our understanding of its demographic and migratory history. Recent advances in sequencing, bioinformatics, and interdisciplinary integration have enabled a more detailed reconstruction of African population dynamics. A key episode was the Last Green Sahara (12,000–5,000 years ago), when humid conditions transformed the desert into a fertile region that fostered mobility and interaction among distant groups. The subsequent aridification reshaped these connections, concentrating exchanges along different geographic axes, particularly the Nile Valley and the Sahelian belt.

In this study, 118 new high-coverage whole-genome sequences from Sahelian and North African populations were analysed alongside modern and ancient comparative data. Results show marked genetic continuity along the Nile Valley, confirming its role as a stable demographic corridor. At the same time ancestral components display a clear north–south gradient along the axis, reflecting a stratification shaped by both ancient and later historical events. The central Sahel displays strong genetic cohesion despite cultural and linguistic diversity, indicating long-term interaction and gene flow. An eastern ancestral component, introduced in the region at the end of the Last Green Sahara (around 4,000 years ago), is best represented today by the Nuba people of Sudan and serves as a genetic link between the Sahel and Nile systems. Finally, isolated populations such as the Copts of Sudan and the Berbers of the Siwa Oasis (Egypt) display strong local genetic identities, suggesting evolutionary trajectories divergent from the patterns observed at the regional scale.

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Evolution of recent autosomic translocations to the X of iconic neotropical bats

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While Eutherian mammal sex chromosomes are highly differentiated, their pseudo-autosomal region maintains recombination in males resulting in distinctive rates of evolution compared to their non-recombining genes. But how this shift in evolutionary rate first occurred is obscured by the age of this event. Here we analyze rates of evolution across the X chromosome of stenodermatine bats, a rapid bat radiation characterized by, among other traits, a large autosomal translocation to the X some 20 million years ago. Compared to other regions of the X, we find no evidence of recombination suppression (i.e., no gene loss) and rates of evolution similar to those of autosomes, consistent with ongoing recombination between this translocation and the stenodermatine -specific Y2. We propose this recent translocation is a sex-linked autosome.

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The Evolutionary Ecology of Color Vision in Krill: Comparative Genomics, Machine Learning and Analysis of Standing Genetic Variation in Opsins

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Do species exposed to similar light environments evolve comparable genetic solutions, and can machine learning (ML) help us understand how adaptive traits evolve? We address these questions through a comparative analysis of opsin genes in krill, a keystone group of marine macrozooplankton. Opsins mediate visual light sensitivity and frequently show adaptive tuning to environmental light conditions.

Building on the recent genome assembly of the Northern krill, which revealed a markedly expanded opsin repertoire and adaptive divergence in opsin alleles between populations, we extend analyses across more than 30 ecologically diverse krill species. Using transcriptomic data, we identified over 200 krill opsins and predicted their spectral sensitivity (λmax) with OPTICS, a machine-learning framework trained on the Visual Physiology Opsin Database (VPOD). OPTICS integrates multiple regression-based ML models to infer phenotypes from protein sequences while capturing epistasis and identifying key amino acid tuning sites.

Our results show that krill possess unusually large and diverse opsin repertoires, with parallel and pronounced expansions of blue-sensitive opsins in polar species, likely enhancing vision in seasonal and dim deep-water environments. Gene duplication and spectral tuning appear to have been major drivers of opsin evolution in krill. Lastly, we apply the framework to assess how much of the standing genetic variation in populations may significantly impact opsin function and have the potential to be adaptive under ocean change.

Overall, this study demonstrates how ML-enabled phenotype prediction can uncover repeatable molecular evolution and provides a generalizable framework for studying sensory adaptation and adaptive potential in non-model organisms.

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The effects of environmental stress on the genetic architecture of fitness

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Adaptation to stressful environmental conditions relies on the availability of suitable genetic variation. Interestingly, studies measuring variance in traits and fitness suggest that genetic variation is itself dependent on the environment, where stressful conditions can result in the release of 'cryptic' variation that is invisible under benign conditions. Being able to predict the ease and speed with which populations can adapt to a changing environment therefore requires an understanding of whether and how heritable variation in fitness changes with stress. Here, we address this question in highly replicated laboratory experiments in the fission yeast, Schizosaccharomyces pombe. Measuring growth under a range of conditions across a collection of mutation accumulation lines we show that genetic variance in growth rates varies with the level of stress. Genetic variation for relative fitness is highest at intermediate stress levels and reduced under both benign and extremely stressful conditions. But stress also affects stochastic variation in growth within strains and the way in which residual variance relates to strain-specific average growth rate: in more benign conditions, growth variation correlates positively with a strain's growth rate, while at high stress this relationship vanishes. Our result show that adaptive responses to moderate stress can be helped by the increased genetic variation and reduced stochasticity of growth, making selection more effective in increasing population productivity. Furthermore, they suggest a reinterpretation of cryptic genetic variation. Fitness variation under benign conditions is not the result of purifying selection, but rather due to inherently reduced mutational effects and/or increased mutational robustness.

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The genomic basis of hostplant usage in a rapidly radiating clade

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Niche expansion plays a major role in speciation. For phytophagous insects, one interesting aspect of their niche is their dynamic relationship with their hostplants. The genus Colias (Lepidoptera: Pieridae) consists of more than 80 species globally that are predominantly generalists on hostplants within the family Fabaceae. As Colias spread geographically, there have been multiple independent transitions to host species outside of Fabaceae. A recent hypothesis states that hostplant repertoire evolution is, to some degree, responsible for the rapid radiation experienced by Colias over the last ~3.5 million years. In order to gain insights into the functional basis of Colias host use, we implemented a comparative phylogenomic analyses to identify a set of potential candidate genes important for feeding on Fabaceae (e.g. both peptidase and trypsin genes were lost when shifting onto non-Fabaceae plants). We used CRISPR-Cas9 mutagenesis to test the effects of these potential candidate genes, finding that the loss of both peptidase and trypsin genes significantly reduced the fitness of Colias larvae on Fabaceae. Our results suggest that peptidase and trypsin genes are important for feeding on Fabaceae, which opens a new horizon of research into the coevolutionary dynamics between Colias butterflies and their hostplants.

Insights from ancient DNA into deep-time evolution of oral microbes in the Cusco region of the Peruvian Andes

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The Cusco region of the Peruvian Andes has a long history of human occupation and regional interactions, making it a valuable context for examining health and disease in ancient populations. Here, we employed ancient DNA and metagenomics approaches to investigate the evolutionary trajectories of oral microbes and pathogens across approximately 6,000 years of Andean history. Shotgun sequencing of dental calculus and tooth samples yielded ancient DNA for 23 individuals from four archaeological sites in the Cusco region: the Archaic-period (6,350-4,150 BP) hunter-gatherer site of Kasapata, the Formative-period (2,350-2,050 BP) village of Yuthu, and two Middle Horizon (1,350-950 BP) sites including the Wari colony of Hatun Cotuyuc and the nearby village of Ak'awillay. The Epstein-Barr virus, a ubiquitous modern pathogen associated with infectious mononucleosis, was detected in an Archaic-period hunter-gatherer, indicating its long-standing presence in this region. Partial genomes of opportunistic oral pathogens, such as the periodontitis-associated Tannerella forsythia, Treponema denticola, and Porphyromonas gingivalis, as well as the caries-associated Streptococcus mutans, were recovered from multiple individuals. Phylogenetic analysis of four Tannerella forsythia genomes revealed that the ancient Peruvian strains cluster within a lineage previously identified in pre-European Contact era individuals from the Americas and absent in modern-day individuals. Together, these findings demonstrate the utility of ancient metagenomics for reconstructing past health and disease ecologies and provide a framework for future investigations into long-term host-pathogen dynamics in the Cusco region.

From Sterility to Clonality: Linking Rapid Sex-Chromosome Turnover to Asexual Reproduction in a Vertebrate Hybrid Complex

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Interspecific hybridisation often triggers meiotic aberrations and the production of unreduced gametes, leading to asexual clonal reproduction. This outcome is strikingly sex-specific: hybrid males are typically sterile, while females reproduce via altered meiosis (e.g., premeiotic endoreplication). It remains an intriguing question whether this asymmetry stems from genome-wide incompatibilities or chromosome-specific conflicts, especially those involving divergent sex-determination systems. Answering this requires high-quality parental genomic references.
We therefore generated chromosome-level genomes for C. elongatoides, C. taenia, and C. tanaitica. Pool-Seq identified nascent, species-specific, sex-determining regions. This revealed rapid sex-chromosome turnover with XY systems on distinct chromosomes (Ch01 in C. elongatoides, putative Ch05 in C. taenia, putative Ch06 in C. tanaitica). In elongatoides-taenia F1 hybrids, species-specific Y-markers usually follow expected inheritance. Yet, we found notable exceptions, including females carrying one of the parental Y-markers and males lacking both—indicating ongoing turnover across lineages.
Critically, cytogenetic analysis in hybrid males shows severely disrupted meiotic pairing of these divergent sex chromosomes and autosomes. This failure directly links rapid sex-chromosome evolution to universal hybrid male sterility, creating the genomic conflict necessary for the switch to asexuality in hybrid females.
Our results demonstrate that hybrid meiotic behaviour is driven by chromosome-specific incompatibilities, as evidenced by variable bivalent formation, coinciding with rapid turnover of distinct sex chromosomes between species. This positions Cobitis as a valuable vertebrate model for linking parental genome architecture to the hybrid dichotomy of male sterility versus female clonality, uncovering a direct genomic pathway to asexuality.

Keywords: loaches, sex determination, chromosome evolution, hybrid sterility, (a)sexual reproduction

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Sex chromosome turnover: why some sex chromosomes never settle, and others never leave.

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Sex chromosomes have evolved countless times throughout the tree of life, yet the rate at which new sex chromosomes arise and replace the old ones varies dramatically across lineages. Some clades experience frequent turnover, cycling through largely homomorphic sex chromosomes, while others evolve long-lived and often heteromorphic sex chromosomes that appear to lose the ability to turnover. The diversity in turnover dynamics and the mechanisms leading sex chromosomes to lose this ability are often cited as some of the remaining mysteries in the field, but remain largely unexplored in theoretical models.

Using individual-based simulations, we explore how turnover dynamics are shaped by different modes of sex chromosome recombination suppression, by Y degeneration, by the evolution of dosage compensation, and by other processes such as spontaneous sex reversal.

Simulations uncover two distinct evolutionary regimes: a “turnover-prone” regime characterised by an endless replacement of sex chromosomes, and a “turnover-proof” regime in which turnovers are effectively halted. Transitions between the two are abrupt rather than gradual, indicating a bistable system. While mutation rates and the mode of recombination suppression modulate turnover frequency within the turnover-prone regime, the emergence of dosage compensation plays the key role in locking sex chromosomes into a stable, turnover-resistant state. Transitions toward turnover resistance are typically unidirectional; however, we identify rare conditions that can reopen a window for turnover, providing potential explanations for empirical cases in which lineages escape old and stable sex chromosome systems.

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Identifying noncoding contributions to life history evolution with machine learning

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During development, intricate changes in chromatin conformation expose small regions of the genome to a shifting set of molecules that regulate gene expression. The scale of these precise changes in open chromatin regions (OCRs) is enormous: on the order of 100-200 thousand OCRs are present at any given time during development, most of which are stage- or cell type-specific. Understanding the function of this vast set of putative gene regulatory elements, much less their contribution to trait evolution, presents an enormous challenge. The small size of OCRs (typically 100-500 bp), coupled with our inability to identify precise boundaries, pose further obstacles. Machine learning provides an attractive set of tools to explore how changes in chromatin configuration and their underlying sequence interact to contribute to trait evolution. Working in non-model organisms (camarodont sea urchins with distinct life histories), we show that neural networks can predict some aspects of OCR function based on sequence alone, including putative core promoter vs distal element and cell type specific accessibility. Neural networks can also predict which OCRs are likely to contribute to differences in gene expression among species. These approaches identify an unbiased set of putative regulatory elements that may contribute to life history evolution, providing novel candidates for experimental analysis.

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Disentangling Ghost and Reciprocal Introgression in Four-Taxon Genomic Datasets

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Hybridization and introgression generate reticulate evolutionary histories that challenge traditional tree-based models of diversification. Although four-taxon tests and related summary statistics are widely used to detect introgression, they implicitly assume simple, unidirectional gene flow among sampled lineages, limiting their ability to resolve more complex genealogical processes. Here, we examine two cryptic forms of introgression—ghost lineage introgression and reciprocal introgression—that systematically bias inference under tree-based frameworks and motivate the need for richer graphical models of evolution.

First, we introduce ghostbuster, a statistical approach that distinguishes introgression involving sampled lineages from introgression originating in unsampled (ghost) lineages using patterns of sequence divergence. Coalescent simulations show that ghostbuster accurately identifies ghost lineage introgression across a wide range of demographic and introgression scenarios, with reduced power only when divergence events are tightly spaced. Applying this framework to genomic data from Brassicaceae reveals that a previously inferred introgression event is more parsimoniously explained by ghost lineage introgression, revising evolutionary interpretations in this important plant family.

Second, we investigate reciprocal introgression, in which alleles are exchanged simultaneously in both directions at a single locus. Using theoretical expectations and coalescent simulations, we show that reciprocal introgression generates phylogenetic signals opposite to those expected under unidirectional gene flow, diluting true introgression signals and even producing spurious support for introgression events that never occurred.

Together, these results demonstrate how heterogeneous genealogies produced by complex introgression processes undermine single-tree representations of evolutionary history and highlight the importance of graph-based models for accurately capturing reticulate evolution across genomes.

plAIgue: An Artificial Intelligence Framework for Detecting Microbial Species in Ancient Human DNA

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We introduce an artificial intelligence (AI) model, plAIgue, which accurately assigns a probability of whether an ancient human DNA sample came from a person who died while infected with a microbial species. Detecting pathogens which circulated in the blood of ancient humans has emerged as a new window to understand diseases which afflicted our species in bygone eras and to study pathogen-host co-evolution. Existing methods to detect pathogens in ancient skeletal remains, however, require a series of ad hoc filters and do not quantify detection uncertainty. We propose plAIgue to overcome these limitations. We evaluated plAIgue's ability to detect the Black Death pathogen (Yersinia pestis) in DNA sequencing data from ~200 ancient humans. Depending on data curation stringency, plAIgue achieved 87-97% accuracy, 0.36-0.05 binary cross entropy loss, 1.0 sensitivity, and 0.95 specificity in our validation set. A state-of-the-art screening tool, the MEGAN ALignment Tool (MALT) followed by Heuristic Operations for Pathogen Screening (HOPS), achieves 0.27-1.0 sensitivity, and 0.47-1.0 specificity (depending on the HOPs step to which we compared) on the same dataset. These results suggest that plAIgue has the potential to perform as well or better than the gold standard method in a fraction of the time, with less human labor, and with quantification of detection uncertainty. Interpretability analyses show plAIgue uses variables and genomic regions indicative of Y. pestis infection when diagnosing true positives. We will generalize our method to other pathogens. Finally, analysis of more than 20,000 ancient individuals provides an opportunity to benchmark our model's capabilities.

1109

An updated perspective: what genes make a tree a tree?

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We learn early on how to tell trees apart from other plants. However, it has proved hard to distinguish trees from other plants at the genetic level, and it is believed that there are no unique 'tree genes'. With the rapid increase in available tree genomes, we can perform new comparative and evolutionary analyses of plant life histories and growth forms. Here we provide a fresh perspective on the genetic foundation for woodiness and perenniality in angiosperms by analyzing selection pressures and gene family evolution in the rosids using genomic data. We examine genes distinguishing trees from herbs and discuss future directions for uncovering the genetic factors that define a tree in this new era of tree genomics.

1113

Hybrid zones and a deadly fungus: adaptive selection and microbiomes in Bombina toads

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Amphibians are the vertebrates with the most severe population declines and species extinctions globally. The spread of the deadly chytrid fungus Batrachochytrium dendrobatidis) is one of the main threats this group of animals is facing. As few individuals survive infection, chytrid fungus exerts a strong selective pressure on affected populations. The skin microbiome appears to play an important protective role in amphibians who catch the fungus, for example by delivering anti-fungal molecules. Those few individuals that survive are therefore expected to have an exceptionally protective microbiome, genetic variants that help in the immune response to the disease, or a combination of those.
In hybrid zones, where two species meet and reproduce, new combinations of gene variants coming from the two parental species are made. These new combinations may be very good for adaptation to new circumstances, like the arrival of a new disease. Therefore, the hybrid zone of the fire bellied toad (Bombina bombina), the yellow bellied toad (Bombina variegata) in central Europe is the ideal study system. The two species have very different ecologies that would predict a very different relationship with chytrid fungus. We studied transcriptomes of individuals from natural populations to see if hybrid individuals get sick less often than parental individuals, and if their genomes or microbiomes show traces of the selective pressure the disease exerts in these populations.

1115

Evolution of mutation rate in a simulation system with an explicit genome representation and a complex genotype-to-phenotype map

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Mutation is the ultimate mechanism that produces genetic novelty, and thus a central ingredient of evolution. An organism mutation rate is therefore often thought to be finely tuned by natural selection to optimize a delicate balance between the generation of adaptive diversity and the accumulation of deleterious mutations.

As this selection happens over very long time scale, simulations have been a powerful tool to understand how mutation rate evolves and which factors influence it. Classical simulation studies are nevertheless limited by the oversimplicity of the adaptive landscapes they feature, and by the difficulty of incorporating a realistic cost or trade-off for having a low mutation rate.

We propose to use a modified version of Aevol, an evolutionary simulator with a realistic genome structure and a complex genotype-to-phenotype layer: we incorporated a mutation rate that can be reduced when organisms acquire genes coding for a higher replication fidelity, and thus the mutation rate is self-evolving. Because of the explicit genome representation inherent to Aevol, a lower mutation rate comes with the trade-off of a larger genome to encode the genes improving replication fidelity.

We first found that fidelity systems are selected in a large parameter zone, even when they do not seem to accelerate fitness improvement. Secondly, we highlight the effect of genetic drift and mutational supply on the evolution of mutation rate.

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The Brassica super-pangenome uncovers novel exploitable genetic resources for crop breeding

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Crop Wild Relatives (CWRs) represent a valuable reservoir of genetic variation since they have not undergone domestication bottleneck. Analyzing genetic diversity in CWRs is crucial to unveiling novel alleles for crop improvement. Despite the agricultural and economic importance of Brassica crops, comprehensive genomic studies of its wild relatives remain limited. Within the framework of the EU funded COUSIN project, we assembled the telomere-to-telomere genome for five wild Brassica oleracea complex species (Brassica incana Ten., Brassica drepanensis Caruel, Brassica rupestris Raf., Brassica macrocarpa Guss., Brassica villosa Biv., n=9), with genome size ranging from 575.74 to 644.84Mb and the number of annotated protein-coding genes ranging from 56,361 to 60,888. We integrated this novel resource with 38 previously reported B. oleracea genomes to construct a super-pangenome of Brassica. We analyzed the pan-proteome and traced the evolutionary dynamics of gene families. We found that gene families associated with abiotic stress resistance were significantly expanded in wild species. We delineated the landscape of structural variants (SVs), most of which resulting from the recent activity of LTR-retrotransposons. Further analyses of SVs and SNPs in a panel of 225 WGS accessions provide new light into Brassica domestication and uncover candidate regions for crop improvement.

1117

How informative is demographic inference from genomic data for conservation?

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Demographic inference methods can produce biased results if the model assumptions are distant from the true scenario. This raises a fundamental question: to what extent can demographic inference tools effectively inform conservation strategies? We address this question using whole-genome sequencing data from 28 humpback whales sampled in Madagascar, which experienced a very recent bottleneck caused by industrial whaling. We conducted a critical comparison of non–model-based and model-based frameworks relying on either the site frequency spectrum (SFS) or linkage disequilibrium (LD). Our analyses reveal major guidelines for the use of demographic inferences for conservation purposes. First, including population structure not only improves the fit to the observed data but drastically reduces the estimated intensity of the bottleneck in LD-based methods. Second, the SFS has low power in distinguishing between alternative scenarios, being strongly dependent on the user's settings (not always recovering the bottleneck). More concerning, inferences under the SFS could not reproduce the observed LD and vice versa. Hence, limited convergence among demographic methods complicates the translation of genomic inference into conservation outcomes, despite its considerable potential. The importance of uncovering the most likely scenario is finally demonstrated using forward simulations, highlighting strong dependence of the evolution of the mutation load and ROH trajectories on the simulated scenarios. Even under identical census observations and equivalent future population growth, fitness evolution differs markedly depending on past historical demography. These findings urge a reappraisal of evolutionary investigations in species of conservation concern and call for an integration of SFS- and LD-based approaches.

1118

One Hundred Years of West Nile Virus Envelope Protein Adaptation

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The structural proteins of flaviviruses are subjected to complex selective pressures given they balance fitness in vertebrate and arthropod hosts. Of these pathogens, West Nile virus (WNV) is the most common in the United States. Recent results have demonstrated adaptation to different hosts as the virus has spread globally, but these findings only extend to very recent evolutionary history since the advent of public health surveillance. To better understand how adaptation has occurred over longer timescales, we applied ancestral sequence reconstruction to a key WNV protein, the Envelope (E) protein extending across the recent century of evolution. We produced all 184 intermediate sequences reaching from a common ancestor to multiple contemporary strains. Performing a competition assay on mosquito, bird, and human cells, we demonstrated that as these ancestral viruses accumulated historical mutations, the lineage that went on to cause a large outbreak in the Americas increased fitness in bird and human cells. Further, ancestral fitness is preserved across most derived genotypes with the exception of select terminal isolates that often have decreased fitness on one or multiple cell lines, likely disrupting the transmission cycle. Our preliminary results have already systematically demonstrated the dynamic nature of host preference over recent evolutionary history. Such insights will improve our understanding of how novel genotypes have previously emerged and how future genotypes may arise.

1120

Tracing the origin and evolution of early smallpox in South America

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Soon after European contact and throughout the Columbian exchange, Indigenous populations of the Americas experienced catastrophic demographic collapse driven by multiple factors, most notably infectious diseases. Among the most devastating and highly contagious of these pathogens was smallpox. Historical records identify repeated smallpox epidemics as a major contributor to Indigenous population decline and, consequently, to European colonial dominance across the continent. Yet the genetic identity of the smallpox strains responsible for these epidemics remains unknown. Here, we report two cases of smallpox infection from an Inca/Early Colonial-era community in northern Chile, including the first near-complete single contig assembly (~220×) of an ancient Variola virus genome from the Americas. These genomes form a now-extinct lineage diverged in the early 12th century, after the diversification of early medieval European lineages but prior to the emergence of 17th–18th century European strains that ultimately gave rise to all 20th-century smallpox. Using the high-coverage genome as a temporal anchor, we detect elevated disruptive mutation rates during the 16th–18th centuries, a period when colonial activity intensified globally. These findings provide the first direct molecular evidence of smallpox introduction to the Americas through European contact and uncover how its evolution was accelerated by widespread transmission among previously unexposed populations.

1121

Comparative analysis of eukaryotic protein complex orthologs

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Protein complexes are essential for cellular biology. Comparative analyses of eukaryotic protein complexes typically use protein interaction data from few available reference species. Furthermore, these studies are often scattered across the literature, limited both by a small number of protein queries and under-representation of microbial eukaryotes.
Here I show the rationale, compilation and a demonstration of a tool that integrates orthology and protein interaction data to compare protein complexes across eukaryotes and find significant duplications and reductions of complex-forming proteins. By mapping proteins of experimentally verified complexes to orthogroups of proteins spanning 31 diverse eukaryotes, I determined that proteins within complex-harbouring orthogroups are retained and distributed more evenly across taxa than other orthogroups. I identified 184 universal orthogroups that included orthologs of known protein complex components from all 31 eukaryotes, consistent with a conserved, minimal protein complex repertoire of the last eukaryotic common ancestor (LECA). I generated the protein complex orthology cartographer (PCOC) suite to compare the number and distribution of proteins in universal orthogroups across and between eukaryotes. This revealed both multi-copy and notably single-copy proteins, in all queried species, from some key complexes. Finally, I used PCOC to map putative duplications and reductions within protein complexes of Naegleria gruberi and Guillardia theta.
This tool provides a systematic and reproducible framework for proteome-wide prediction of complex component proteins in reference and non-reference eukaryotes. These methods can be applied to additional sequenced eukaryotes, enabling consistent prediction of protein-complex repertoires and associated functional diversity across the eukaryotic domain.

Characterisation of a male Neanderthal from Prado Vargas, Spain, via enamel paleoproteomics

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In the absence of aDNA, enamel paleoproteomics offers an alternative approach to characterise ancient species and populations in a molecular framework. Among its applications, the analysis of peptides derived from AMELX and AMELY genes —transcribed from the X and Y chromosomes, respectively—has proven especially valuable to determine the chromosomal sex of tooth remains. This study aims to analyse the protein content of a Neanderthal tooth excavated at the Prado Vargas site, Spain, to infer the sex and corroborate the taxonomy assigned to this individual. The sample was morphologically identified as a Neanderthal deciduous lower-left first molar (Ldm1); ancient DNA (aDNA) recovery was not possible due to clear evidence of resorbed roots. The tooth is dated to approximately 54.7–39.8 ka and likely belonged to a child who lost it ante mortem at around 9 to 10 years of age. After LC-MS/MS peptide identification and protein sequence reconstruction, we confidently identified 14 proteins and detected AMELY-specific peptides featuring the 59-Met insertion, a variant exclusive to AMELY and not present in AMELX. Additionally, we assess the potential to differentiate hominin lineages using enamel proteomics by analysing 176 high-quality primate protein sequences, including ancient sequences from Neanderthals and Denisovans. However, it was not possible to tell the Prado Vargas tooth as a neanderthal due to unidentified sequences that were not experimentally recovered. These findings highlight the potential of enamel proteomics to test hypotheses in archaeological and paleontological contexts, particularly for immature individuals and isolated remains, whose morphology provides limited insight.

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Drivers of primary sex ratio bias in dwarf willow

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Deviations from Fisher's equal sex ratio at birth or seed production (primary sex ratio) can be due to meiotic drive or allelic incompatibility. The resulting sex ratio selection is proposed to contribute to the fast evolution of sex chromosomes. Yet, empirical studies on primary sex ratio bias are challenging and only limited data is available, particularly from natural populations. We investigate mechanisms leading to sex ratio bias in the dwarf willow Salix herbacea that has ZW sex determination, strongly female-biased sex ratios at the population level and variable sex ratios among families. We used pooled whole-genome re-sequencing to track allele transmission from parents to female, male and non-flowering offspring in six within-population crosses with a wide range of sex ratios. We further examined the inheritance of sex ratio bias over two generations. Our results suggest a dominant mechanism of maternally controlled sex ratios with biased transmission of autosomal alleles from different chromosomes to the rare sex, as expected under a scenario of W-chromosome drive with autosomal restorers in females. Moreover, we detected evidence for structural variation on the sex chromosomes. Overall, our findings are consistent with an evolutionary arms race situation leading to W-drive with multiple autosomal restorers. Our study is thus supports an important role of sex ratio selection for the dynamic evolution of sex chromosomes.

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Spatial and temporal patterns of genetic variation in Northern European pedunculate oak populations

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Long-lived forest trees are challenged by the speed of the ongoing climate crisis. Local adaptation versus options and limitations for gene flow, both natural and assisted, are therefore important to explore. Studies of genetic variation within and between tree populations across environmental gradients can provide insight into this. The degree and outcomes of provenance transfer during the past two centuries can be inferred from genetic characterization of population origins. Provenance transfer can have positive implications for the adaptive potential of forests facing extreme climate change. Using population level whole genome data, we estimate population structure across the northern range of the ecologically and economically important pedunculate oak (Quercus robur). We compare allele frequencies at loci found to be significantly associated with climatic variables in two age classes, very old veteran trees and trees in "present day" timber producing stands, to characterize potential genetic consequences of provenance transfer. Our results support widespread population structure and local adaptation in present day oak forests. While the general level of genetic differentiation within Danish oaks is low, certain regions of the genome show signs of fine scale differentiation between neighboring populations. We discuss to what extent patterns of genetic diversity could be the result of presumed post-glacial recolonization routes intersecting in Denmark. Our results highlight the importance of comparing contemporary gene pools across large distribution ranges as well as between age groups to get a better picture of how species and populations will respond to future changes in their local environments.

1130

Eukaryote-like evolution of Asgard archaeal genomes

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The emergence of eukaryotes roughly two billion years ago is one of the most enigmatic evolutionary events. The closest prokaryotic relatives of eukaryotes are a group of archaea called Asgard archaea. During eukaryogenesis the genomic repertoire of eukaryotes vastly expanded due to numerous gene duplication, transfer, invention and fusion events. In this study, we use the expanding repertoire of Asgard archaeal genomes, including several closed genomes and genomes from novel groups, to improve our view on Asgard archaeal genome evolution, including how different genetic innovations have shaped the genome content of Asgard archaea and, potentially, that of early eukaryotes. By applying recently developed phylogenetic models capturing site and branch heterogeneity and a novel tool that removes compositionally biased sites, we robustly resolved the Asgard archaeal phylogeny. Using gene tree-aware reconciliation methods we reconstructed the genome content of archaeal ancestors and illuminated their evolutionary genome dynamics. These analyses show an elevated rate of gene duplications and gene fusions and a lower rate of gene transfers in Asgard archaea compared to other archaea. This suggests that the mode of genome evolution of Asgard archaea is reminiscent of that of eukaryotes, providing a window into eukaryogenesis.

Comprehensive Characterization of Inversions across the Human Population using Strand-seq Pooled and Long-Read Sequencing

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Inversions are major contributors to human genomic diversity, yet significant knowledge gaps persist. These copy-number–neutral structural variants are often flanked by highly identical repeat sequences and frequently associated with disease-linked microdeletions and microduplications, making them exceptionally challenging to detect using conventional genomic technologies, necessitating integrated approaches.

We generated data from all 1000 Genomes Project population cohorts, enabling systematic characterization of inversions at population-scale and investigation of their frequencies and functional associations. We integrated single-cell template strand sequencing (Strand-seq) from 728 genomes with paired Oxford Nanopore Technologies (ONT) data generated as part of the IMP/MARVL study. The dataset maximizes global genetic diversity through balanced representation across five continental ancestries and 26 populations, with emphasis on African individuals. Strand-seq captures DNA strand directionality, enabling sensitive detection and genotyping of inversions >50 kbp even in repetitive regions. We combined Strand-seq with lymphoblastoid cell line pooling for high throughput, while ONT provided complementary detection and validation.

Our analysis revealed 465 inversion regions, including 247 previously unreported loci and 44 novel multi-megabase events; notably, a complex 57 Mb pericentromeric inversion in a Yoruba individual overlapping neurodevelopmental disorder loci. Population stratification revealed striking patterns: population-specific heterozygous variants at low frequencies and inversions showing over two-fold enrichment in specific population groups, particularly African and American ancestries. These events span genes involved in neurodevelopment, skeletal formation, and immune regulation, consistent with heterogeneous evolutionary histories. Our study provides the most comprehensive population-scale inversion callset to date, advancing understanding of inversion polymorphisms in human genome diversity and evolution.

1140

A macroevolutionary gene network reveals diapause evolutionary dynamics beyond the circadian clock and predicts microevolution

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Diapause is an alternative developmental pathway evolved independently in many insects to synchronize life cycles with resource abundance. While subsets of this essential phenotype have long been studied at a single species level, the genomic basis of the full diapause syndrome remains poorly understood. Remaining unknown is whether convergent diapause syndromes employ shared mechanisms. This paucity of insights has fueled a long-standing debate about how life cycle synchronization evolves. Using a comparative genomic analysis spanning diverse diapause transitions in butterflies, we identified a large network of coevolving genes unique to diapausing species. The network is composed of functional modules spanning circadian regulation, metabolism, and cell cycle control. We tested whether this macroevolutionary scale network predicts microevolutionary dynamics, finding that allelic variation in the diapause network is significantly enriched in signatures of local adaptation across latitudes, but only in diapausing species. Thus, we empirically show that diapause evolves through modular, coevolving gene networks, components of which regulate species/population specific diapause phenotypes. This novel perspective on this complex phenotype opens a new horizon of inquiry for understanding seasonal adaptation across evolutionary scales, while demonstrating the power of using comparative genomics to dissect polygenic phenotypes.

1144

Convergent molecular evolution of thermal tolerance in mammals

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Mammals vary in their ability to tolerate heat stress. Reproduction is especially sensitive; just a few days of elevated temperatures around the time of implantation can significantly impact fertility. We have gained some insights into molecular responses to heat stress in model species such as mice, pigs and cattle, but broader patterns across the wide diversity of mammals are not known. Right across the extant mammal phylogeny we observe multiple independent origins of heat tolerance. We wish to determine whether the convergent trait of heat tolerance is underpinned by convergent molecular adaptation.

We have collated genomic data from 18 heat tolerant mammal species from diverse lineages, classified according to climate data across current distributional ranges (temperature of warmest month > 30°C), and 69 mammals that occupy cooler environments. These 87 species include pairings of close relatives that differ strongly in typical maximum environmental temperatures encountered (e.g. barbary sheep Ammotragus lervia 39.6°C, bighorn sheep Ovis canadensis 29.3°C, diverged around 6 million years ago). Using branch-site models of selective pressure variation, we have identified gene families that have undergone convergent positive selection in heat tolerant species but not in other lineages. Incorporating data from our model system, the pig, we identify genes under convergent positive selection that also show differential expression during periods of acute heat stress in pregnant pigs. These results demonstrate convergent molecular mechanisms for heat tolerance across mammals and highlight pathways that underpin variation in susceptibility to heat stress, yielding important insights for species conservation.

1145

First ancient genome of Streptococcus pyogenes from a pre-Columbian Bolivian mummy reveals its presence in the Americas before European contact

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Streptococcus pyogenes (Group A Streptococcus; GAS) is a major human pathogen responsible for diseases ranging from pharyngitis to severe invasive infections. Despite its clinical importance and recent global resurgence, the evolutionary history of GAS remains poorly understood, particularly its presence in ancient human populations. To date, no genomic data from ancient S. pyogenes strains have been reported, leaving unresolved whether the pathogen has long coexisted with humans or emerged more recently in association with major historical events.

Here, we report the first genomic evidence of S. pyogenes in the pre-Columbian Americas. We analyzed a tooth sample from a naturally mummified individual dated to the Late Intermediate Period (1283–1383 cal AD) from present-day Bolivia. Shotgun metagenomic sequencing and de novo assembly enabled near-complete reconstruction of an ancient S. pyogenes genome.

Functional characterization using modern typing frameworks reveals close similarity between the ancient strain and contemporary GAS lineages associated with pharyngitis. The genome harbors core virulence determinants, although prophage regions lack streptococcal pyrogenic exotoxins.

Phylogenetic analyses position the ancient Bolivian strain near the base of modern S. pyogenes diversity, and Bayesian dating suggests that most extant GAS lineages diversified globally within the past ~5,500 years.

These findings substantially extend the known temporal and geographic range of S. pyogenes, providing direct evidence that the pathogen circulated among Indigenous populations in the Americas prior to European contact. Overall, this study offers new insights into the long-term evolutionary dynamics and persistence of virulence in a globally important human pathogen.

1148

The regulation of evolutionarily new genes

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Understanding how gene regulation evolves is central to explaining the emergence of novel genes and lineage-specific traits. While gene birth and death are continuous and dynamic processes during evolution, the regulatory architectures enabling the expression and persistence of evolutionarily young genes remain poorly understood. We combine single-cell transcriptomics and computational regulatory inference to investigate how transcriptional regulation evolves to accommodate newly emerged genes in the Drosophila lineage. Using single-cell RNA-sequencing data, we identified transcription factors associated with the expression of evolutionarily young genes and reconstructed their putative regulatory networks. We find that regulatory control of young genes is highly non-uniform: a small subset of transcription factors accounts for a disproportionately large fraction of regulatory associations, with three factors—Vis, Achi, and Jra—linked to the expression of ~28% of young genes analyzed. Notably, two of these transcription factors, Vis and Achi, originated via tandem duplication within the D. melanogaster species complex, suggesting that transcription factor duplication and subsequent regulatory diversification may facilitate the integration of new genes into existing regulatory networks. We experimentally tested these regulatory relationships by generating transgenic lines with altered Vis and Achi copy number, allowing us to assess how changes in transcription factor dosage impact young gene expression. Together, our results illustrate how modification of existing regulatory components can drive regulatory evolution, enabling the origination, stabilization, and expression of young genes. This work highlights the power of integrating single-cell data, comparative evolutionary frameworks, and functional genetics to dissect the mechanisms underlying the evolution of gene regulation.

Palaeogenomic insights into late Quaternary African faunas

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Palaeogenomic data from African taxa are relatively scarce. This talk will present four case studies providing novel insights into extinct species, past distributions, and genetic shifts: From the highlands of Ethiopia: (i) We sequence the nuclear genome of a 42,000 year-old wildebeest molar (Connochaetes sp.), the oldest sub-Saharan African aDNA to-date, and identify it as a previously unknown, extinct lineage; (ii) Via palaeogenomic analysis of a ~40,000 year-old ibex tooth (Capra sp.), we identify the presence of its predator, the brown hyaena (Parahyaena brunnea), which today is found only in southern Africa. From South Africa: (iii) We sequence for the first time the DNA of a previously-described extinct African Pleistocene species, the long-horned buffalo (Syncerus antiquus), and explore its phylogenetic relationship with its closest extant relative, the African buffalo (S. caffer); and finally (iv) Using the first South African faunal population-level palaeogenetic dataset, we show that the Cape grysbok (Raphicerus melanotis) has lost unique mitochondrial diversity during the Holocene. We illustrate that in Africa, palaeogenomics can be used to study extinct Pleistocene taxa, and identify range contractions and temporal genetic dynamics of extant taxa. This improves our understanding of evolution and can guide conservation decisions in the present day.

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Disentangling drift and selection in an endangered plant using temporal genomics and language models

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Recent advances in machine learning enable genomic constraint and genetic load to be predicted directly from sequence context, providing new opportunities to study short-term evolutionary dynamics where signals of selection are often obscured by drift. We applied population genomics to two locally endangered plant populations of Arabidopsis lyrata in southern Germany, sampled two decades apart during a period of regional warming and reduced snow cover. Genome-wide SNP data revealed stable differentiation between sites and minimal temporal stratification within sites, allowing direct allele-frequency comparisons across time. Using Waples' temporal method, we inferred population-specific effective population sizes, indicating differing levels of genetic drift. Leveraging language model–based genomic constraint estimates integrated with classical conservation scores, we assessed genome-wide signatures of negative and positive selection. Derived allele frequencies were consistently lower at highly constrained sites, indicating pervasive purifying selection and recapitulating established patterns of deleterious load. To identify candidate targets of positive selection, we compared observed allele-frequency changes to Wright–Fisher simulations parameterized by site-specific effective population sizes. While most changes were consistent with neutral expectations, a small subset of loci exceeded the simulated envelope. Functional enrichment analyses of these loci suggested involvement of metabolic and stress-related processes, though these signals were modest and should be interpreted cautiously. Overall, short-term genomic change in these populations appears dominated by drift and purifying selection. Importantly, our results demonstrate that LLM-based constraint metrics provide a scalable and complementary framework for interpreting genetic load and evaluating selection in temporal genomic data when classical signals of adaptation are weak.

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Two centuries of genetic diversity change in rice at different spatial scales

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For decades, researchers have warned of the drastic diversity decrease in staple crops. While a critical loss of local crop varieties has been well documented, some argue that genetic diversity has been replenished by using exotic gene pools in breeding. We investigated the genetic diversity change in rice at three spatial scales, using genotype and phenotype data. We compare whole genomes of 450 rice samples sequenced from museum and herbarium specimens, and collected contemporarily at the historical sampling locations. On a continental scale, we observed a loss of multiple rice lineages and homogenization of varieties cultivated contemporarily. On a regional scale, dense temporal sampling in the Mekong Delta revealed genetic continuity of rice populations between 1869 and 1957. In 1960s and 70s, the Green Revolution initiated a major overhaul of rice agriculture in Asia, which is detectable in our data with a complete genetic ancestry replacement by 2023. Contemporary rice populations in the Mekong Delta maintain genetic diversity levels observed in historical populations, however, exhibit closer kinship measured by sharing of large haploblocks. We also observed a significant increase in kinship among individual plants taken from the same field, compared to historical fields, where such kinship is virtually indetectable. The close relatedness in contemporary varieties substantially limited breeding pool and diversity in key adaptive loci. Overall, these findings showcase the complexities in genetic diversity changes in rice, where on a regional scale, net genetic diversity of rice has not decreased, but their evolutionary potential has diminished.

1158

The Toll-like receptor signalling pathway repertoire of cartilaginous fishes: loss of TLR4-LPS signalling as a case study

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Cartilaginous fishes (sharks, rays, and chimaeras) represent the earliest-diverging lineage of jawed vertebrates relative to mammals. Studies of their immune gene families have differentially shown both conservation and rapid evolution on both the level of sequence similarity and repertoire diversification through duplication and loss. Until recently however, fragmented genome assemblies have complicated both annotation and cross-species comparisons. Toll-like receptor (TLR) 4, which is an essential receptor for mammalian recognition of the lipopolysaccharide on the outer membrane of gram-negative bacteria, has previously been suggested to be absent from the elephant shark genome. Here, taking advantage of newly available chromosome-level genome assemblies from representatives spanning the major lineages cartilaginous fish lineages, and taking the TLR4-LPS pathway as a case study, we evaluate whether a TLR4-LPS signalling pathway is present in cartilaginous fishes. Employing careful homology searches, phylogenetics and synteny analyses we construct a TLR backbone tree and classify TLR orthologs and copy-number variations across vertebrates. We also examine the repertoire evolution of TLR signalling components in cartilaginous fishes compared to other vertebrate lineages. Our findings suggest that TLR4 and associated LPS-specific signalling molecules are absent in cartilaginous fishes, whereas many other signalling molecules and TLRs appear present. This has important implications for our understanding of the cartilaginous fish immune system and possibly for the perceived importance of LPS recognition for vertebrates. We are performing complementary functional analyses and are applying our approach to other immune gene families.

1159

Farming termites and microbial symbiont: enzymes and natural products in an evolutionary ecology context

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Fungus-farming termites have coevolved with a basidiomycete fungal cultivar (genus Termitomyces) that is maintained in external fungus gardens (combs) on a substrate of dead plant matter that passes through the termite gut before deposition in fungal combs. The association originated 30 MYA in sub-Saharan Africa and has diversified to include more than 330 described termite species, 40 described Termitomyces spp., and complex co-adapted gut bacterial communities. Collective functions of holobiont member properties allow for near-complete degradation of essentially any plant substrate, without appreciable infectious disease challenges. I will review recent progress in our understanding of how these termites accomplish efficient monoculture farming on diverse substrates without being compromised by crop diseases. I will further discuss putative defensive roles of secondary metabolites discovered in the symbiosis, and outline future research needs to understand the molecular underpinnings of these carefully-managed enzyme and secondary metabolite blends

1160

Programmed DNA elimination as a source of genomic plasticity in free-living nematodes

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In most organisms, all cells contain the same genetic material; however, some species break that rule through a process called Programmed DNA Elimination (PDE). In that process, parts of the DNA in the somatic cells are deleted during early embryogenesis, resulting in differences between the genomes of germline and somatic cells.
PDE was first discovered in parasitic nematodes in the 1800s. It has since been observed in a variety of eukaryotes: songbirds, fungus gnats, hagfish, among others. Despite being absent from the free-living model nematode Caenorhabditis elegans, PDE has been recently discovered in free-living nematodes from the genera Oscheius, Mesorhabditis and Caenorhabditis (suborder Rhabditina). In addition, the sites of DNA elimination were found to be highly precise and contained a short palindromic motif that likely recruits a nuclease to induce double-strand breaks, which are subsequently healed by de novo telomere addition.
These recent discoveries raise questions about how widespread the phenomenon is across Rhabditina and how the features of PDE differ across taxa. Here, we analyse the genomes of over 50 species and find PDE to be widespread across free-living members of Rhabditina and we discover that motifs differ in sequence and structure between clades. The amount of eliminated DNA also seems to vary and most of the eliminated genes are multi-copy, but some are highly conserved genes with important functions specific to germline development. PDE is a striking example of genomic plasticity within a single organism, and our work shows that it is much more widespread than previously thought.

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Genetics of repeated ecotype separation in Malawi cichlid genus Labeotropheus

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Over the past decade, a series of genomic studies in East African cichlids has identified the primary drivers of their divergence during adaptive radiation. Analysing the genomes of hundreds of species established a phylogenetic framework and revealed that both gene flow and structural variation play an important role. Despite these advances, it remains challenging to identify adaptive variants under selection in the face of wide-spread non-adaptive divergence. Here we address this using population-scale genome sequencing to associate allele frequency differences with adaptive phenotypes in the genus Labeotropheus. With two traditional described species, Labeotropheus is among the most widely distributed cichlid genera at the rocky lake shores, likely due to a key trophic innovation. By sequencing 900 whole genomes and generating chromosome-level assemblies from diverse locations across Lake Malawi, we show that a better description of the genus is that a morphologically derived deepwater ecotype has repeatedly evolved from the ubiquitous shallow-water lineage. Exceptional morphological convergence masked the non-monophyly of the deepwater ecomorph which was thus considered a single monophyletic species for many decades. We leverage the natural replication of the system to identify genomic regions underlying adaptive divergence and identify variants associated with derived male breeding colors, suggesting reinforcing sexual selection as a key facilitator of cichlid diversification.

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Likelihood-free inference of phylogenetic tree posterior distributions

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Phylogenetic inference, the task of reconstructing how related sequences evolved from common ancestors, is a central objective in evolutionary genomics. The current state-of-the-art methods exploit probabilistic models of sequence evolution along phylogenetic trees, by searching for the tree maximizing the likelihood of observed sequences, or by estimating the posterior of the tree given the sequences in a Bayesian framework. Both approaches typically require to compute likelihoods, which is only feasible under simplifying assumptions such as independence of the evolution at the different positions of the sequence, and even then remains a costly operation. Here we present the first likelihood-free inference method for posterior distributions over phylogenies. It exploits a novel expressive encoding for pairs of sequences, and a parameterized probability distribution factorized over a succession of subtree merges. The resulting network provides well-calibrated estimates of the posterior distribution leading to more accurate tree topologies than existing methods, even under models amenable to likelihood computation. We further show that its edge against likelihood-based methods dramatically increases under models of sequence evolution with intractable likelihoods

1165

Genome size: Did flight loss relax genome size constraints in birds?

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Genome size and its role in genome evolution have long been debated in evolutionary biology, with distinct trends emerging across taxonomic groups. Birds exhibit a particularly conservative range of genome sizes, often attributed to the energetic demands of flight. Here, we investigate whether the loss of flight relaxes this constraint on genome size. For this, we compiled short-read sequencing data of 61 bird species across 27 families, including 28 flightless and 33 flighted species, representing nearly 50% of extant flightless birds. Genome size was estimated using GenomeScope2, and Phylogenetic Generalized Least Squares (PGLS) analyses were used to evaluate predictors of genome size across the phylogeny. Genome size showed a strong phylogenetic signal (lambda = 0.715) and no correlation with body mass. Flightless birds had genomes ~0.048 Mbp larger on average than flying birds, although this trend was marginally non-significant (p = 0.052), and largely driven by ratites. To assess flight loss in a clade with multiple independent transitions, we focused on Rallidae (n = 17; 10 flightless, 7 flighted), where little genome size variation was detected. Comparisons of closely related flightless and flighted species also revealed no significant differences, suggesting that substantial evolutionary time is required for detectable genome size change. Finally, we observe a notably weak correlation between genome size estimates and assembly, indicating that these metrics are not interchangeable.

1170

Reproductive morph specialisation facilitated by a maternal sex determining region in a fungus gnat (Bradysia coprophila)

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Sexual reproduction promotes the evolution of specialised gametes and sexes with divergent reproductive roles. The resulting, cyclical relationship between selection for sexual dimorphism and the structure of sex determining regions shapes sex-chromosome evolution and helps explain the evolution and stability of mating systems.

Black-winged fungus gnats (Family: Sciaridae) are a group of Dipteran insects with maternal genetic sex determination, a unique system where maternal genotype - instead of zygotic genotype - determines zygotic sex. Within this, split-sex ratios have repeatedly evolved, where some females produce all-female broods while others produce all-male broods. In Bradysia coprophila, female reproductive morph is determined by a large X-linked inversion, which is present only in female-producing females. This relatively young (<0.5 Mya), morph-determining and non-recombining region offers an informative parallel to the evolution of sex-determining regions and sex chromosomes. Does this maternally-acting region accumulate deleterious mutations, or facilitate specialisation into female-production?

Using B. coprophila as a model, we observe that female morphs diverge significantly in phenotype and gene expression, in functions other than offspring sex determination. Despite signatures of degradation and reduced expression of homologs on the inversion, the fitness of female-producing females is maintained. Combined with analyses of rates of molecular evolution on X-linked genes, this suggests specialisation into distinct reproductive roles, which we hypothesise can partly explain the rapid turnover of mating systems in this family. We speculate on potential drivers for specialisation and show that sex-specific maternal provisioning could be involved.

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Ancient Epstein-Barr virus genomes from Mesolithic and Neolithic birch tar reveal early viral diversity and immune escape

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Epstein–Barr Virus (EBV) is a ubiquitous human oncovirus with two main genotypes (type 1 and type 2), exhibiting distinct geographic distributions and disease associations. The long-term evolutionary dynamics of EBV remain poorly understood due to the lack of ancient EBV genomes. Here, we report the oldest ancient EBV genomes sequenced to date, recovered from Mesolithic and Neolithic chewed birch tar in Europe. We demonstrate that both types of EBV already circulated in prehistoric Europe. Phylogenetic analyses reveal that ancient type 1 EBV strains fall basally with contemporary Asian lineages, suggesting a deeper shared ancestry with Asia and strain replacement occurred within Europe. To investigate functional evolution, we examined coding variations previously implicated in pathogenesis. One ancient strain carried two out of three high-risk variants within BALF2 associated with nasopharyngeal carcinoma. Besides, we identified the E201Q mutation in glycoprotein 350 to be under positive selection, associated with immune escape. Finally, we evaluated the ability of ancient EBV to evade cellular immunity by predicting MHC class I peptidome and testing CD8+ T cell recognition of ancient and modern EBV peptides using enzyme-linked immunospot (ELISpot) assays. Together, these data demonstrate that key adaptations influencing viral infectivity and oncogenicity were established early in EBV's history, and they provide direct genomic evidence for deep-time EBV diversity and lineage dynamics in Europe.

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A Landscape Genomic story of the olive tree in the western Mediterranean : insights into local adaptation and future (mal-)adaptation

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In the Mediterranean Basin, the average temperature is rising at a rate 20% faster than the global average. This climate change poses a substantial risk to the survival and distribution of species in the region. Understanding and forecasting species adaptive responses to environmental changes is thus crucial for enhancing conservation efforts, both for cultivated species and their wild relatives. Recent developments in the field of landscape genomics, especially regarding the forecast of (mal-)adaptation patterns to altered environments, a.k.a. genomic offset, have become an invaluable tool-set.

A set of spontaneous olive trees (Olea europaea subsp. europaea) from a 13 degrees latitudinal gradient in the western Mediterranean was used to investigate patterns of local adaptation. We performed a capture sequencing of more than 400 putatively wild trees together with a set of cultivated varieties, interrogating more than 50 000 predicted genes from an olive tree reference genome. We led a structure analysis to decipher purely wild derived genotypes from those resulting from hybridization with the cultivated compartment. Genotype Environment Analysis was carried out on the genuine wild oleasters and the model was used in conjunction with future climate projections to estimate their genomic offset.

We propose to extend this analysis to predict patterns of (mal-)adaptation to unlocalized genotypes, e.g. cultivated trees or hybrids for which the environment could not be assessed. Despite not being formally validated by field trials, the patterns of offsets found for varieties from the northern or southern shores of the Mediterranean are consistent with their putative geographic origins.

Co-isolation of ancient DNA and RNA from non-formalin-fixed lung specimens reveals host-pathogen interactions during the Industrial Revolution in Great Britain.

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Advances in the field of ancient pathogen genomics have expanded our ability to understand microbial sources of past epidemics, primarily through the study of ancient DNA (aDNA). While reconstructed historical genomes provide insights into pathogen evolution, there is limited information about host-pathogen interactions and their contributions to disease due to limitations in ancient RNA (aRNA) recovery. In this study, we successfully co-isolated aDNA and aRNA from eleven non-formalin-fixed lung samples with a record of respiratory disease from three museums across Great Britain, with collection dates spanning c. 1740-1939 C.E., a period marked by a rise in population density and spread of infectious disease, driven by industrialization. This protocol allowed for the reconstruction of pathogen genomes and recovery of both host and pathogen transcripts, including Human rhinovirus A, Streptococcus pneumoniae, Moraxella catarrhalis, and Haemophilus influenzae. We detected expression of putative virulence-associated bacterial genes and host immune response genes, revealing potential contributors to disease. Notably, the S. pneumoniae capsule polysaccharide (cps) locus was associated with a serotype targeted by contemporary vaccines, and transcripts for genes involved in immune modulation, exotoxin production, and stress survival were identified. The integration of genomic and transcriptomic data goes beyond pathogen discovery, allowing detailed interrogation of host–pathogen interactions, reshaping our understanding of host response dynamics in historical epidemics, and enabling direct comparisons with modern microbial infections.

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Tripling known fungal mitogenomes through large-scale public data reuse

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Many fungal sequence datasets are generated for different scientific purposes and are deposited in public repositories, yet their mitochondrial genome remains largely unexplored. Fungal mitochondrial genomes are critical for understanding phylogenetics, evolution, and ecology of the Kingdom Fungi. Public sequence repositories therefore provide a large resource of genomic data. We developed a reproducible workflow for retrieving and assembling mitochondrial genomes from 12,902 fungal short-read sequencing datasets publicly available in the Sequence Read Archive (SRA), resulting in complete circular genomes representing 2,695 unique species. This effort expanded fungal mitochondrial genome diversity by nearly 3X. The new dataset contains novel yet undescribed mitochondrial genomes at numerous taxonomic levels, including 15 classes, 64 orders, 178 families, and 544 genera. Taxonomic analysis showed wide-ranging ecological representation, including human pathogens, plant pathogens, edible mushrooms, and industrial species. We faced different layers of challenges while working at a public repository scale, including variable sequence quality, lack of metadata information, incorrect taxonomic annotation, and cases where the same species appeared under different names or taxonomic IDs. Our workflow integrates filtering and validation steps that enable mitochondrial genome recovery. By leveraging underused SRA sequencing data, this study demonstrates that public genomic repositories can serve as a powerful platform for data mining, expanding genomic resources while reducing the financial and environmental costs of generating new data. The resulting dataset provides a substantial resource for fungal phylogenetics and evolutionary studies and highlights the potential of large-scale public data reuse in genomic research.

Phenotypic plasticity shapes genetic variation and patterns of inbreeding and extinction risk

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Phenotypic plasticity is a major mechanism of adaptation to changing environments. When it alters an individuals' dispersal capacity it can modulate gene flow, shaping connectivity between populations and genetic diversity within them. The water strider Aquarius najas exemplifies this dynamic. Across Europe, it presents a latitudinal cline in wing frequency: Southern populations are wing-polymorphic and can disperse, while Scandinavian populations are wingless and sedentary, making it an ideal system to study how plasticity-mediated dispersal shapes genomic vulnerability at large geographical scales.

We sequenced >700 individuals and discovered extreme inbreeding in Northern populations, being characterized by low genetic diversity and strong isolation-by-distance, with no gene flow between rivers. Contrastingly, Southern polymorphic populations have ten-fold higher diversity and low differentiation between distant sites from different water basins, indicating flight-mediated dispersal. While ecological and genetic models partially explain the cline in diversity through Southern glacial refugia followed by successive Northern bottlenecks, the connectivity between distant polymorphic populations highlights the direct effect of wing polyphenism on diversity.

This study integrates population genomics, demographic inference and ecological models to reveal a highly fragile species facing different threats at each distribution edge. Southern populations, while genetically rich, face increasing habitat instability due to climate change-induced droughs; Northern populations are genetically eroded and isolated due to a complete loss of dispersal capacity. Our findings demonstrate how plasticity modulates dispersal patterns and therefore acts as an important mechanism that shapes genetic diversity and thus alters the equilbrium between mutation, drift, gene flow and selection across a latitudinal gradient.

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Assessing adaptive potential in Scandinavian populations of Willow ptarmigan (Lagopus lagopus) using temporal genomics

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Predicting species' responses to rapid environmental change is challenging but is especially important for cold-adapted species having limited capacity to shift ranges or adapt physiologically. For these species, genetic adaptation may be crucial for long-term survival.
One powerful tool to determine if species can adapt to rapid changes in climate is the usage of historical specimens. By comparing the genomic sequences of historical specimens with modern descendants, we can track evolutionary trajectories to determine the response to recent climate change and predict their future adaptive capacity. Here, we focus on willow ptarmigan (Lagopus lagopus), a Scandinavian species vulnerable to climate change. Reduced snow cover disrupts seasonal timing and causes camouflage mismatches, leading to lower survival and population declines across Scandinavia. The impact of these population declines to current levels of genetic diversity and degree of genomic erosion remains unstudied. Here, willow ptarmigan acts as a system to understand adaptation to environmental change in seasonal environments by documenting recent decline in populations with temporal genomic approaches combining museum archives and modern sampling.

To study recent demographic trends and adaptive potential, we conducted population genomic analysis across a temporal scale using approximately 400 modern and historical samples of Scandinavian willow ptarmigans. These genomes were combined with available genomic data for willow ptarmigan from Siberia, Scotland, North America to further contextualize levels of diversity in Scandinavia. This comprehensive spatial and temporal genomic dataset will be combined with demographic modelling and population viability analysis to assess the future evolutionary potential of willow ptarmigan.

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Four centuries of commercial whaling eroded 11,000 years of population stability in bowhead whales

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Bowhead whales were heavily exploited during commercial whaling between the 16th-20th centuries. Current and future climate warming poses a new threat. Assessing bowhead vulnerability to climatic change remains challenging, due to insufficient knowledge regarding responses to past climates and pre-whaling population dynamics. We integrate palaeogenomics and stable isotopes (δ13C and δ15N) of 201 Holocene bowhead fossils from the Atlantic Arctic with palaeoclimate and ecological modelling based on 823 radiocarbon dated fossils, including 140 from this study. We find long-term resilience of bowheads to Holocene environmental perturbations, with no detectable changes in genetic diversity or population structure. Simulated commercial whaling genetic and fitness changes found that population subdivision and loss of genetic diversity are unlikely to be fully realised, despite nearly a century since whaling ceased. Furthermore, even in simulated complete population recovery scenarios, overall fitness did not return to pre-whaling levels, potentially compromising the future resilience of bowhead whales.

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Genomic Consequences of Translocations: Lessons from the Critically Endangered Pyrenean Brown Bear

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In the face of the biodiversity crisis, translocations are a key conservation tool, yet their high costs often limit the number of individuals translocated. The critically endangered Pyrenean brown bear population, comprising only 10 genetic founders after reinforcement, exemplifies these challenges. Since reinforcement, fitness data and the pedigree of all individuals have been then tracked.
Using whole-genome sequencing of 32 bears, we assessed runs of homozygosity (ROH), genetic diversity, and mutational load. We compared these metrics to the long-isolated Apennine brown bear population in Italy, which has a similar census size. Our results reveal that the Pyrenean population exhibits greater variance but lower values in ROH size and realized load among individuals compared to the Apennine population.
We further quantified the impact of inbreeding depression on individual fitness using reproductive success data for the Pyrenean population. The reproductive success is negatively correlated with both ROH-based inbreeding coefficients (FROH) and realized mutational load, with a stronger effect observed for the latter. These results contrast with the long-term persistence of the Apennine population despite its higher load, suggesting a complex interaction between historical demography and selection in shaping genetic variation.
Finally, forward simulations for the Pyrenean population using SLiM projected future trajectories of ROH, mutational load, and genetic diversity under alternative management scenarios. Simulations predict increasing FROH over time, leading to the unmasking of recessive deleterious mutations and further threatening population viability.
Our results highlight the genetic debt of some translocation programs and emphasize the need to integrate genomics into conservation planning.

Temperature-Dependent Biochemical Landscapes of TEM-1 β-Lactamase

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Temperature profoundly shapes enzyme evolution, yet the mechanistic links between catalytic kinetics, protein stability, and fitness remain poorly understood. To address this gap, we implemented a high-throughput approach that links Escherichia coli growth to the catalytic activity of TEM-1 β-lactamase in the presence of ampicillin. By integrating this system with deep sequencing, we quantified the growth of approximately 120,000 TEM-1 variants across seven temperatures (18–45 °C) and multiple ampicillin concentrations, enabling inference of in vivo catalytic velocity under each condition. From these data, we derived the kinetic parameters Vmax and Km for each variant at every temperature. Our results reveal widespread temperature-dependent pleiotropy: individual mutations differentially affect catalytic constant, substrate affinity, and folding stability across thermal environments. The spatial distribution of functional mutational hotspots shifts significantly with temperature, and elevated temperatures tend to exacerbate the deleterious impact of mutations on substrate binding. This systems-level analysis establishes a mechanistic framework for thermal adaptation in TEM-1, revealing how temperature modulates sequence–structure–function relationships through alterations in biochemical parameters.

Humans as reservoirs: Historical microbiomes uncover hidden zoonotic pathways

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The rise in emerging and re-emerging infectious diseases encourages deeper investigations into human-animal-environment interactions. Zoonotic disease transmission events are most frequently recognized within the terrestrial environment in a single direction of transmission from nonhuman animals to people. However, these human-mediated epidemiological events include marine ecologies. Historical alterations to the marine biome linked to disruptive human activities (e.g., upland conversion, pollutant runoff, and exploitation of marine species) have shaped modern marine mammal populations such as California sea lions (CSL) (Zalophus californianus). Using dental calculus (n=60) subsampled from CSL housed at the Santa Barbara Natural History Museum and at the Smithsonian Institute we reconstruct CSL oral microbiomes and link microbial diversity to anthropogenic alterations. Metagenomic analysis reveal that CSL have maintained a stable and unique oral microbiome signature that is different from other mammalian species; suggesting the oral microbiome may be less prone to alterations than the gut microbiome. CSL host DNA was regularly recovered. We also recovered Klebsiella pneumoniae, a human associated pathogen linked to mortality events in CSL populations. Eight K. pneumoniae-positive samples underwent genome enrichment, yielding 71.17% coverage of the K. pneumonia reference genome at 1X depth in one sample. We provide a novel approach in using dental calculus as a sentinel for documenting shifting historical ecologies. Our analysis demonstrates the potential for recovering pathogen genomic data from marine mammal dental calculus, offering valuable insights into epidemiological events of marine mammals using museum specimens. Incorporating such analyses can open the door in developing datasets to identify unrecognized zoonotic pathways.

Mining Public Metagenomic Archives Reveals Deep-Time Evolution and Hidden Diversity of the Human Oral Microbiome

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The human oral microbiome reflects long-term interactions between host biology, diet, hygiene, and environment, yet its deep evolutionary history remains incompletely understood. In our study we aimed at reconstructing temporal changes in oral microbial communities from Neanderthals to modern humans using ancient dental calculus metagenomic datasets publicly available in different public repositories. A total of 840 ancient DNA datasets were analyzed across multiple host species, geographic regions, and historical periods. Community-level analyses revealed clear temporal structuring of the human oral microbiome. Ancient samples exhibit substantially higher levels of uncharacterized diversity, with Neanderthals showing a median of ~70.5% unknown taxa, compared to ~15% in modern humans. Compositional analyses identify significant shifts across historical periods (PERMANOVA $R^2 = 0.2225$, $p = 0.001$), displaying highly significant temporal variation. Supervised machine-learning models demonstrated that microbial composition contains a measurable temporal signal, achieving 80% accuracy in classifying samples by historical period. Genome-resolved metagenomics generated 6,638 genome bins, dereplicated into 850 non-redundant metagenome-assembled genomes (MAGs). Only 40% of which could be assigned at the species level, leaving nearly 60% completely unclassified. Notably, approximately one third of these unclassified MAGs belonged to the Candidate Phyla Radiation (CPR), with a strong enrichment of Patescibacteriota, particularly Saccharibacteria. The prominence of these ultra-small and poorly characterized lineages underscores ancient dental calculus as a reservoir of previously unexplored oral microbial diversity. Overall, this work demonstrates the importance of mining the public datasets and highlights the value of open research in answering seminal questions related to human oral microbiome evolution over millennia.

Evolutionary consequences of recombination suppression: the case of a chromosomal inversion in the seaweed fly

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Chromosomal inversions, which oppose recombination and form blocks of linked genes, are increasingly recognized for their role of “supergene”, protecting adaptive combinations of alleles. They are frequently involved in local adaptation, sometimes maintained over large spatio-temporal scales through balancing selection, and often forming parallel patterns across distant locations. However, the lack of recombination also limits the purging of deleterious mutations, raising multiple questions about the underlying functional, demographic, and selective mechanisms associated with large polymorphic inversions. We investigated the evolutionary dynamics of a large inversion - Cf-Inv(4.1) - harbored by the worldwide-distributed seaweed fly Coelopa frigida, which displays parallel latitudinal clines of frequencies in Europe and North America, suggesting a role in adaptation to an environmental gradient. With experiments, we found a significant impact of Cf-Inv(4.1) on egg-to-adult survival and fecundity, partially interacting with temperature. We speculate that inversion fitness may be shaped by subtle life-history differences whose relative advantage depends on climate. Next, we uncovered the evolutionary history of the inversion and the evolution of its sequence. Combining long- and short-reads from America, Europe, and Japan, we reconstructed the demographic history of Cf-Inv(4.1), inferred an ancestral recombination graph, and investigated the conservation of its structure across continents. Lastly, we performed simulations to elucidate how the clinal distribution of the inversion affects the purging of deleterious mutations and compared the results with empirical data. Overall, this study provides an empirical example that illustrates the contrasting evolutionary impacts of recombination suppression, highlighting both its possible adaptive and deleterious effects.

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Evaluating GWAS Power Using SLiM Simulations in Structured Populations

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The identification of the genetic basis of adaptive traits in wild populations is relevant to prevent biodiversity loss. However, finding these genes does not depend only on abundant sampling, and studies have often failed to identify major-effect genes.
The goal of this research is to understand how a population's evolutionary history and the characteristics of the trait influence detection power, and to provide recommendations for conducting GWAS. We used forward genetic simulations in SLiM to test two main scenarios: a single-population model, and a multi-population model in which the trait evolves in one population and spreads to another via gene flow. Within each model, we varied key factors such as population size, divergence times between populations, migration rate, the mode of gene flow (continuous versus episodic migration), and the genetic architecture of the trait.
In this study, we show especially the effect of population structure and gene flow on the power of GWAS to detect monogenic and polygenic traits, and we provide recommended sample size ranges to identify the genetic basis.

A preliminary look into the paleogenomics of Anatolian big cats

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Big cat species such as lions and leopards, once widely distributed across Eurasia, are now either extinct or in severe decline across much of their historical range. Despite their ecological and cultural importance, little is known about the changing historical population dynamics and demographic histories of big cats of Western Asia. To better understand both present-day and past population dynamics, and to shed light on changes from antiquity to present, we sequenced whole genomes from 30 ancient and historic big cat specimens from Hattusa (8 samples), Kültepe (9 samples), İnönü Cave (4 samples), Köşk Höyük (1 sample), Karain Cave (4 samples), Kela Henma (2 samples), and Ege University Museum (2 samples) spanning the Middle Paleolithic to modern period in Anatolia and Western Asia. We obtained adequate genomic data from 8 individuals (0.01-0.2 coverages), including five tentative lion samples and three tentative leopard samples. By integrating temporal genomic data with archeological and historical context we aim to understand changes in genetic diversity, population dynamics and inter-population relations of big cats through time.

Genera: An Integrative AI Framework for Conservation Management using Comparative Genomics at Scale

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Background: Genomic data provides a critical window into how species adapt to environmental pressures. In prior work (PMID: 37104572), we developed machine-learning(ML) models that predict mammalian extinction risk using genomic variables, demonstrating that genomic variables are predictive of extinction risk and outperform ecological variables alone when used in combination. Notably, these models enable risk prediction for species classified as data-deficient by the IUCN. However, translating these genomic insights into actionable conservation management practices remains a significant bottleneck.

Approach: Supported by the Bezos Earth Fund, we present a technical outline and conceptual framework for "Genera," a generative AI assistant designed to bridge this gap. Our roadmap scales previous ML models trained on 240 short read-based mammalian genomes (Zoonomia consortium) to incorporate 581 high-quality vertebrate genomes (Vertebrate Genome Project Phase 1) and next-generation AI models. We are building a multimodal deep learning architecture that integrates genomic foundation models with Large Language Models to jointly process DNA sequences, inbreeding metrics, and ecological metadata. This framework aims to translate high-dimensional genetic data into actionable management insights by generating interactive, natural-language conservation reports that evaluate simulated genetic rescue strategies based upon predicted extinction risk and genomic drivers of vulnerability.

Outcomes: Currently in the pilot phase, Genera aims to serve as a decision-support tool for practitioners -- assisting in breeding strategies, translocations, and reintroduction planning. We present our architectural roadmap and invite community feedback to co-develop this resource over the next two years, ensuring it meets the needs of the global conservation and evolutionary biology communities.

Characterization of archaic ancestry in 63,000 Japanese individuals from the Tohoku Medical Megabank

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Biobanks that provide genetic information and phenotypes for large cohorts have been used to explore the impact of introgressed Neandertal DNA on phenotypic diversity and disease susceptibility in present-day people. To date most studies have focused primarily on European populations who carry Neandertal introgressed DNA. We have characterised Neandertal and Denisovan introgression in 63,000 Japanese individuals from the Tohoku Medical Megabank Organization (ToMMo) biobank using a reference-free Hidden Markov Model (hmmix). We describe the set of Denisovan and Neandertal haplotypes in ToMMo and assess their relationship to the high-quality genomes of four Neandertals and two Denisovans. We confirm that Denisovan ancestry in Japan derives from two pulses of introgression from genetically distinct Denisovan populations, and find a negative correlation between Jomon and Denisovan ancestry using modern Japanese genomes. Using GWAS summary statistics, we investigate the impact of archaic introgression on SNP-heritability on traits from Biobank Japan. We also identify regions enriched for Neandertal and Denisovan DNA and describe high-frequency archaic haplotypes in the Japanese population that have significant replicable associations to human health outcomes in multiple East Asian biobanks.

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Holo-omic insights into host–microbiome dynamics during starvation and compensatory growth in zebrafish

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Host-associated microbes are increasingly recognized for their role in shaping adaptive phenotypes in vertebrates. Compensatory growth is an accelerated growth phase in fish that occurs when favorable conditions are restored after starvation. While several studies have identified host adjustment underlying this response, less is known about the microbial contribution. Given its role in digestion and nutrient processing, we applied a holo-omic approach to investigate the microbial dynamics in the zebrafish gut during starvation and refeeding, aiming to uncover hologenomic adaptations linked to compensatory growth.

We performed holo-omic extractions on whole gut samples from 108 zebrafish followed by long-read DNA sequencing and short-read RNA-seq. Most DNA was of zebrafish origin; however, co-assembly of unmapped reads followed by binning recovered 19 high-quality and 24 medium-quality Metagenome-Assembled Genomes (MAGs), including core taxa of the zebrafish microbiota. Relative to the zebrafish genome, microbial coverage decreased during starvation, but increased again during refeeding, reflecting a dynamic microbial fraction of the hologenome. Notably, the coverage of specific MAGs, including Aeromonas veronii and Pseudomonas sp. exceeded zebrafish genomic coverage, suggesting that bacteria may outnumber host cells in the gut.

Epigenomic data from long-read sequencing, together with paired RNA-seq, revealed genome-wide changes in host DNA methylation and gene expression during starvation and refeeding. Integrating these host responses with microbial gene functions highlighted a holo-omic interaction in dietary chitin degradation: host genes dominated initial breakdown, whereas microbial genes dominated downstream utilization. Notably Aeromonas veronii expressed high levels of chitin-utilization genes, consistent with enhanced chitin metabolism in the zebrafish gut.

Selection on sexual chromosomes and circadian genes during speciation in two Amazonian butterflies

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Sexual chromosomes in heterogametic species are predicted to have a disproportioned role in local adaptation and speciation. Detecting selection on sexual chromosomes in heterogametic systems is however challenging due to their lower effective population size (Ne) and the more efficient purge of mildly deleterious alleles. Here, we studied the selective regime in a pair of butterflies living in sympatry in the Amazon basin: Morpho helenor and M. achilles. In the sympatric zone, M. helenor is known to fly earlier in the day, which reduces reproductive interference and may contribute to the speciation process, according to theory. By performing field observations and selection analyses, we explored how selection promoted speciation in our system. We observed that M. helenor flies later in the day in geographic areas where M. achilles is absent. Using a GWAS approach, we then uncovered an association between the timing of daily activities and several circadian genes, many of them being located on the Z (sexual) chromosome. To measure the strength of selection on the Z vs. the autosomes and overcome the biases due to Ne and mildly deleterious mutations we relied on the software grapes implementing a dn/ds measure corrected using a population genetic model based on the SFS. We detected a slow-Z effect, consistent with a higher efficacy of purifying selection, and a higher adaptive evolutionary rate on the Z in the sympatric populations, consistent with a significant effect of the reinforcement process.

Understanding the diversity of adhesive proteins in sea stars (Echinodermata, Asteroidea)

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Marine invertebrates produce strong adhesive secretions to attach to the sea floor, particularly in intertidal environments characterized by strong current forces. Beyond substrate attachment, marine adhesive secretions may also serve for food capture, locomotion, building or protection purposes. Because biological adhesives consist mainly of proteins, 'omics technologies have been used extensively to characterize adhesive protein (AP) repertoires from diverse marine species. The wealth of public genomic data has also been increasing over the years. In sea stars, abundant data is now available, allowing to investigate AP diversity and evolution.

Our study covers and integrates three aspects of adhesion evolution in sea stars: the general asteroid phylogeny, the AP repertoire diversity, and the morphological and ecological traits relevant to adhesion. First, 26 publicly available genomes were gathered and annotated, using EviAnn. An evolutionary framework of the asteroid clade has been established using phylogenomic approaches (orthology inference, single-gene trees and supertree building and, alternatively, supermatrices), indicating basal Velatida, followed by a dichotomy between Forcipulatacea and other asteroid orders. Hierarchical orthologous groups were then mined to retrieve homologs to the adhesive proteins from two reference species, Asterias rubens and Asterina gibbosa. Corroborated by extensive HMMER searches, our analyses show that some APs are species-specific or lineage-specific, whereas others are ubiquitous among sea stars. In parallel, morphological and ecological metadata, such as habitat, role of adhesion, podia morphotype and adhesive cell types were mapped onto the evolutionary framework. Finally, AP phylogenies were reconciled with the species tree and ancestral gene repertoires were inferred.

Co-option of long terminal repeats mediates endogenous retrovirus dysregulation in cancer

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Human endogenous retroviruses (HERVs) are remnants of ancient retroviral infections which have become fixed in the human genome over millions of years. HERVs, typically under strict epigenetic repression, are known to be expressed in cancer. The long terminal repeat (LTR) region of HERVs, which regulate viral expression during exogenous infection, are rich sources of transcription factor (TF) binding motifs. Accordingly, previous studies have demonstrated the role of LTRs in an array of transcriptional programs including development, innate immune response, and others. Nonetheless, the regulatory potential of most LTRs remains obscure. Here, we leverage our standardized, comprehensive database of HERV loci, HERVdb, along with publicly available ChIP-seq datasets accounting for 1031 TFs to systematically identify novel co-options of LTRs for gene regulation. We identify 80 potential LTR-TF regulatory pairs across 13 LTR families, defined by significant enrichment of TF binding sites, presence of a compatible binding motif within the LTR, and enrichment of genes known to be regulated by the associated TF proximal to the LTR family. Many identified LTRs appear nearby genes involved in immunity, cell cycle, pathways and metastasis-related processes, indicating the possibility of LTR assimilation by cancer cells to promote oncogenesis. Lastly, we investigate 438 paired samples from the TCGA across 11 cancer types to identify LTR-mediated dysregulation of HERVs and cancer-related cellular processes. Our study underscores the remarkable potential of LTRs to act as regulatory elements across diverse cellular pathways and reveals how LTR-driven transcriptional programs—shaped over millions of years—can be repurposed during cancer development.

Cellular Innovation through De Novo Gene Birth Driven by Promiscuous Protein–Protein Interactions

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The traditional view holds that cellular novelty arises mainly from modifications of existing genes. However, recent genomics suggests that functional proteins can also emerge from non-coding regions—a process called de novo gene birth. To explore the mechanisms and prevalence of this phenomenon, we tested a library of 10^5 random protein sequences for their ability to rescue E. coli growth under heat stress. Strikingly, nearly 20% of these sequences significantly enhanced thermal tolerance. Further analyses showed that these peptides improve post-stress viability by modulating the expression of host proteins and/or by protecting heat-stress-related proteins through promiscuous protein–protein interactions. These findings suggest that de novo gene birth may be a more widespread and mechanistically plausible source of evolutionary innovation than previously thought, underscoring the inherent capacity of random polypeptides to functionally integrate with native cellular systems.

The tdk family: an evolutionarily persistent single-gene killer meiotic driver family employing a toxin–antidote strategy

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Killer meiotic drivers (KMDs) are selfish genetic elements that bias their transmission by eliminating meiotic products lacking the driver element in driver+/driver− heterozygotes. Though predicted to arise recurrently, KMDs are often considered evolutionarily ephemeral—going extinct after fixation or host suppression. We recently identified tdk1 in Schizosaccharomyces pombe as a single-gene KMD. Its protein product forms a toxin–antidote pair via structural duality: a toxic conformation forming supramolecular assemblies that induce abnormal chromosome adhesion by interacting with the histone reader Bdf1, and an antidote conformation that neutralizes the toxin by dissolving the toxic supramolecular assemblies. The toxin forms in all meiotic products (spores), whereas the antidote is produced only in carriers upon spore germination, leading to chromosome segregation defects exclusively in noncarriers. We now report two functional homologs (tdk210 and tdk203) from Schizosaccharomyces cryophilus, a fission yeast species that diverged from S. pombe ~100 million years ago. Despite low sequence identity (<30% with Tdk1), all three KMDs disrupt chromosome segregation in noncarriers post-germination. Notably, they are mutually incompatible (showing no cross-resistance), and tdk210 and tdk203 act independently of Bdf1. This demonstrates that a single KMD family can achieve deep evolutionary persistence through repeated functional innovation—generating mutually incompatible variants and rewiring host dependencies—while retaining a conserved killing mode. Our findings challenge the conventional view of KMDs as evolutionarily transient elements and elucidate how KMDs sustain long-term evolutionary success through functional diversification.

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Tracking molecular mechanisms of plant adaptation to climate change with herbaria

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To live across diverse environments, plants have to balance taking up CO2 to grow with the concomitant loss of water through their leaf stomatal pores. Increasing CO2 concentrations, together with climate change induced droughts and increasing temperatures should strongly alter this balance. However, while the genetics of stomata development in Arabidopsis thaliana are well-characterized, little is known about the natural variation of stomata genes across the climatic gradients of the plant's geographic range, let alone across the last centuries of climate change. Using the 1001 A. thaliana genomes resource and genetic variation across a unique set of ~200 historical herbarium specimens dating as far back as 1817, we describe the global natural variation in core stomata genes. By combining published mutant phenotypes for these stomata genes with their genetic variation over time, we develop an experimentally-informed polygenic score for stomatal density to infer phenotype change over 200 years of climate change. Integrating a model organism's historical specimens and a molecularly understood phenotype allows us to understand how this species adapted in the past, at a phenotypic, genetic and ultimately a functional-molecular level. It thus provides a unique opportunity to decipher in detail whether and how plants respond to climate change.

Structural variant load under demographic change: How a small fly can provide big insights

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The democratization of whole-genome sequencing platforms has better informed conservation management strategies by providing high-resolution data on population diversity and structure. However, there is a tension between management strategies that aim to maintain the maximum level of genomic diversity as a means of preserving adaptive potential and the possibility of retaining, or introducing, deleterious alleles in small populations. To date, SNPs have been the genomic marker of choice for estimating key metrics of genomic health, including the prevalence of deleterious alleles (i.e., mutation load). Yet another class of genomic variants, structural variants (SVs), have been shown to impact a higher proportion of the genome and intersect genes and gene regions more often than SNPs. In addition, SVs can alter mutation and recombination rates and are generally more deleterious than SNPs. While a growing body of literature is identifying characteristics of SVs that increase the likelihood of deleteriousness, the interaction of recombination and selection on SV diversity over time under various demographies is largely unexplored in threatened species. We implement a two-pronged approach of evolutionary models and evolve and resequence experiments in the seaweed fly (Coelopa frigida), a globally-populous species with well-described SV diversity, to predict and test the effects of demography on SNP- and SV-load. This highly manipulable model system allows us to assess the impact of SNP- and SV-load on fitness over successive generations and presents an opportunity to identify frameworks for mitigating the consequences of deleterious variants, while maximizing genome-wide diversity in species of conservation concern.

Epistasis between gene expression noise and functional mutations shapes cellular fitness

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Epistasis is the phenomenon in which the phenotypic effect of a mutation depends on the genetic background. Beyond interactions among coding mutations, noncoding mutations—such as those affecting promoter activity—can also contribute to epistatic effects. Notably, the phenotypic consequence of a coding mutation can be deleterious, neutral, or beneficial depending on its expression level, indicating epistasis between regulatory and coding changes. Even within genetically identical populations, the abundance of any given protein varies among individual cells, a phenomenon known as gene expression noise. Such variability can enable rapid responses to fluctuating environments and facilitate phenotypic evolution. We therefore hypothesize that epistasis between expression noise levels and functional mutations can arise within clonal populations. To test this idea, we performed a fitness screen of mutant clones generated by random mutagenesis in budding yeast using a genetic background that allows tunable control of noise levels. Under high-noise conditions, the mutant library exhibited increased phenotypic diversity, suggesting that expression noise could enhance phenotypic heterogeneity. We then identified mutant clones whose fitness differed across noise levels. Intriguingly, one clone displayed a fitness defect that was strongly potentiated by increased noise. Using quantitative trait locus sequencing (QTL-seq), we pinpointed a mutation in RNT1, the gene encoding the sole RNase III in budding yeast, as the causal variant. Taken together, our findings reveal epistasis between gene expression noise and functional mutations and suggest that expression noise can uncover cryptic fitness effects, thereby contributing to phenotypic diversity during evolution.

Rapidly Evolving Epigenetic Controlling Factors of Meiotic Recombination

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Meiotic recombination is essential for gamete formation, with errors leading to miscarriage and infertility. In most vertebrates, recombination is non-random and specified by the rapidly evolving histone methyltransferase PRDM9, which marks chromatin accessibility and defines recombination hotspots. Here, we present a second rapidly evolving epigenetic control system that acts with PRDM9 to regulate meiotic recombination and fertility.

By isolating Prdm9 alleles from hundreds of wild mouse samples worldwide, we identified over 40 novel alleles. We integrated alleles reported in GenBank and characterized more than 250 distinct Prdm9 alleles using phylogenetic reconstruction methods tailored to the Prdm9 coding minisatellite. We observed lineage-specific evolutionary dynamics across mice.

Prdm9 is also a hybrid sterility gene that acts together with the Hstx2 locus. In collaboration with the Forejt laboratory, we resolved the Hstx2 locus and revealed a microRNA-mediated pachytene checkpoint in which copy-number variation modulates fertility and genome-wide recombination rates. Comparative genomics across sterile and fertile mouse strains has now revealed those mature miRNAs that are functionally divergent between the sterility and fertility alleles of Hstx2. Targets were in silico predicted and validated by differential expression levels in testicular cells of sterile and fertile mice.

Finally, we show that Prdm9 and Hstx2 alleles both affect crossover frequency and fine-scale recombination resolution across intersubspecific and intrasubspecific hotspots in fertile mice. We tested three hotspots activated by different Prdm9 alleles, including a human transgene. Together, our results link these two rapidly evolving loci to their roles in recombination, reproductive isolation, and infertility.

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Harnessing genetic rescue: from genomic evidence to management decisions

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Genetic rescue has long been recognized as a means of mitigating inbreeding and loss of adaptive potential in small, fragmented populations. Yet in practice, it is often postponed or avoided because the risks - particularly outbreeding depression - are difficult to assess and have historically been evaluated using indirect proxies rather than direct evidence. This disconnect between evolutionary theory and management practice has fostered a conservative bias that can delay intervention even when populations show clear signs of genetic erosion.

I present a genomics-informed decision framework that reframes genetic rescue as a testable evolutionary hypothesis rather than a precautionary gamble. Building on and extending existing guidelines, the framework integrates genomic estimates of inbreeding, demographic history, gene flow, and signals of local adaptation to explicitly evaluate both the need for genetic rescue and the risk of maladaptive outcomes. A key advance is the inclusion of genomic inbreeding, quantified using runs of homozygosity, as an explicit entry point, ensuring that intervention is focused on populations where genetic processes likely constrain viability.

The framework is illustrated using a fragmented butterfly metapopulation, where recent divergence, historical connectivity, and weak evidence for local adaptation together indicate low risk of outbreeding depression despite substantial genetic structure. Importantly, the framework emphasizes genomic inferences that are feasible and widely applicable across conservation contexts, including non-model systems. More broadly, this work demonstrates how population genomics can replace proxy-based rules with direct evolutionary inference, enabling more confident, timely, and transparent management decisions for vulnerable populations in a rapidly changing world.

Can evolutionary studies on social traits promote 21st-century eugenics?

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A growing number of studies are using genome-wide association studies (GWAS) to investigate genetic correlations with social traits, including educational attainment, income, and socioeconomic class. More recently, several population genetics studies have used these GWAS variants to infer selection on such social traits, while others have used social trait-related polygenic risk scores (PGS) to explain modern-day social hierarchies through natural selection. Here, we review methodological and social dimensions of this body of work. We first discuss technical issues involved, including the limits to controlling for confounding effects, the predominance of indirect effects, the biologically uninterpretable nature of the studied phenotypes, and ignorance of social science models that explain the emergence of social inequalities. We further show examples of how genetic and evolutionary studies on social traits are used to promote essentialist worldviews and appear to serve 21st-century eugenics and racism. We suggest that genetics and evolutionary studies on social traits have strong social impacts and deserve ethical scrutiny.

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Genomic Insights into Biodiversity Decline in Endangered Hallig Beetle, Pseudaplemonus limonii

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The accelerating global decline in biodiversity underscores the urgent need for refined conservation strategies. While traditional approaches emphasize species monitoring and habitat protection, genomic data can reveal early signatures of population decline long before demographic declines are detectable. Despite this potential, most conservation genomic studies have centered on a narrow subset of flagship or model species, limiting our understanding of genetic erosion across the majority of taxa.

The Hallig beetle, Pseudaplemonus limonii is a small weevil in the subfamily Apioninae within the hyperdiverse Curculionidea, a lineage comprising more than 62,000 described species. Despite this extraordinary diversity, only 106 genome assemblies are currently available for Curculionidae, of which just 47 are chromosome-level, and no reference genome has been generated for the genus Pseudaplemonus.

Here, we present a high-quality, chromosome-resolved reference genome for P. limonii and utilise it to investigate genomic consequences of its recent population decline in Germany. We sequenced 20 modern individuals and 20 historical specimens collected from the same population prior to the documented decline, enabling a direct before-and-after comparison. Using these data, we examine multiple genomic indicators of population decline, including mutation load, nucleotide diversity, levels of inbreeding and gene copy variation. By integrating historical and modern genomes, we quantify the extent of genetic erosion and identify genomic signatures of bottlenecks. This study demonstrates how museum genomics combined with high-quality reference genome assemblies can provide powerful insights into biodiversity loss in non-model, endangered insects, offering a framework for genomics-informed conservation across diverse taxa.

Diverse Genomic Routes to the Same Protein: Evolutionary Mechanisms of New Gene Birth and Molecular Convergence

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Novel genes are central to evolutionary innovation, yet the mechanistic diversity of their origins remains incompletely understood. Fish type I antifreeze proteins (AFPI) provide a powerful model: four distantly related lineages independently evolved near-identical, alanine-rich AFPI under strong freezing selection. Here we integrate new chromosome-scale whole-genome assemblies that we generated for winter flounder, grubby sculpin, and Atlantic snailfish with published genomes for cunner and relatives, plus transcriptome sequencing and comparative genomics, to reconstruct and compare AFPI origins. Our cross-lineage analyses reveal rare, extreme protein sequence convergence: all four lineages encode strikingly similar proteins from distinct genomic precursors, yet the underlying routes differ sharply. In flounder AFPI recruited noncoding portions of antiviral gene GIG2; in cunner it arose by gene fission of immune-regulatory GTPase; in sculpin it assembled from fragments of an ER-derived pseudogene. In snailfish AFPI derives from a mosaic of transposable elements (TEs) and noncoding fragments of antiviral gene PARP12, with TEs also promoting regulatory evolution and copy-number expansion. Despite these differences, all four lineages share a theme of partial de novo evolution: most AFPI coding sequence originated from noncoding DNA, whereas regulatory sequences were recruited from fragmented ancestral genes or TEs. This shared pattern motivated a Duplication–Degeneration–Divergence model in which degenerated gene copies and pseudogenes provide modular fragments that can be resurrected as novel, functionally unrelated genes. Part of this work was recently published in Molecular Biology and Evolution; the new snailfish genome extends this framework and illustrates how TEs mediate de novo gene origination.

Leveraging large-scale long-read sequencing data to understand the diversity, drivers and evolution of Lepidoptera cobionts at unprecedented resolution

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https://zenodo.org/records/15359862
Project Psyche is a large-scale genome sequencing project that is creating an unprecedented opportunity to reveal hidden ecological and evolutionary dimensions of microbial partners (“cobionts”) of insects. Here, we screened high-quality PacBio HiFi genome datasets from 1,214 species of butterfly and moths and combined detection of rRNA markers with metagenome assembly methods to identify more than 700 host-cobiont combinations, and produced more than 600 high-quality cobiont genome assemblies. By integrating comprehensive host metadata and host phylogenetic information, we first resolved broad-scale patterns of cobiont presence and diversity, revealing the influence of host relatedness, life-history traits, biogeography, and symbiont mode of transmission. Furthermore, the availability of complete and highly contiguous cobiont genomes allowed us to move beyond cobionts’ presence–absence and co-infection patterns. In particular, we uncovered hidden functional variation, providing insight into some of the ecological strategies of symbionts, and the genomic basis of their intimate interactions with Lepidoptera hosts, such as reproductive parasitism and mutualism. Thus, this study both reveals extensive and previously undescribed microbial diversity and establishes a powerful genomic framework to study insect–microbe symbioses, their ecological roles, and their evolutionary consequences at unprecedented resolution.

Thriving against the odds: bottlenecked invaders show evidence for purging

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Biological invasions threaten global biodiversity and human well-being but also provide opportunities for studying evolution in non-equilibrium systems. These opportunities include investigating the "genetic paradox of invasions" that refers to successful invasive populations originating from low founder numbers. Theory predicts such populations should exhibit reduced genetic diversity and elevated inbreeding, limiting evolutionary potential and often leading to inbreeding depression. Here, we provide evidence for an invader succeeding against these odds, by demonstrating strikingly strong inbreeding and genetic diversity loss in invasive populations of the zebra mussel (Dreissena polymorpha). Using whole-genome resequencing data from over 300 native and invasive mussels, we show that genomes of individuals from thriving invasive populations carry numerous and long runs of homozygosity resulting from severe founder events and subsequent inbreeding during the invasion process. We demonstrate that genetic load (accumulation of deleterious mutations) is correlated with inbreeding levels and invasion history of the populations, in ways not attributable to drift alone. Importantly, we find indications of purging having disproportionately removed highly deleterious mutations from the bottlenecked and inbred invasive populations. Our research thus challenges conventional expectations that strong bottlenecks followed by inbreeding should limit biological invasion success. Our results also suggest that purging may contribute to the success of heavily bottlenecked invaders, by removing (some of) their highly deleterious genetic load exposed to selection by increased inbreeding. Besides providing novel insights into invasion dynamics and success, these findings are broadly relevant for understanding selection in non-equilibrium populations across taxa.

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Mapping JEDI Challenges in the Earth BioGenome Project

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The Earth BioGenome Project (EBP) is a global "network-of-networks" aiming to generate high-quality reference genomes for ~1.8 million named eukaryotes. Achieving this mission requires more than technical capacity; it depends on inclusive governance, equitable partnerships, fair attribution, and meaningful participation across geographies, institutions, and knowledge systems. In this talk, we present EBP's Justice, Equity, Diversity, and Inclusion (JEDI) Committee's efforts to date across its mandate in advisory, educational, and advocacy roles. We begin presenting the perspective of a forthcoming manuscript developed in response to feedback from the EBP community. Because the EBP is decentralized, JEDI issues are expected to manifest differently across regions and affiliated projects; meaningful action therefore requires first understanding how these challenges arise within biodiversity genomics across the globe. The manuscript maps ten cross-cutting themes—power, funding, capacity development, knowledge transfer, network expansion, epistemologies, community engagement, attribution, outreach, and compliance—and highlights the challenges they bring to participation, decision-making, recognition, and benefit-sharing in practice. Rather than proposing solutions, this work aims to build a common language and shared awareness that can support context-appropriate approaches across affiliated initiatives. We'll also summarize activities undertaken to date, including workshops, training and outreach, and contributions to EBP governance to embed JEDI across the project's structures. Recognizing the scale of the EBP and the persistence of global inequalities, we conclude by inviting symposium participants to engage in dialogue on practical strategies for advancing JEDI in biodiversity genomics, and to identify approaches that are effective, transferable, and responsive to the field's most pressing challenges.

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Pangenomes Illuminate Genetic Diversity in Sheep and Their Wild Relatives

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Pangenomes represented as variation graphs are increasingly important genomic resources for characterizing the full spectrum of genetic diversity within and across species. By capturing single-nucleotide variants (SNVs), structural variants (SVs), and copy-number variants (CNVs), pangenomes provide a powerful framework for linking genomic variation to phenotypic diversity. The genus Ovis exhibits substantial biodiversity and phenotypic variation that has accumulated since its divergence from goats approximately 5 million years ago. Here, we leverage a pangenome constructed from 25 sheep genomes including 22 domestic breeds and three wild relatives to investigate genetic drivers underlying trait variation across the Ovis genus. We compare pangenomes generated using two variation-graph construction approaches: Pangenome Graph Builder (PGGB) and Minigraph-Cactus (MC). Using these variation graphs, we identify structural variants associated with known biological and phenotypic variation among sheep breeds. Graph-based pangenome approaches offer powerful opportunities for investigating SVs within species from an evolutionary perspective.

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Genome characterization of rainbow trout-associated Midichloria-like organism reveals a novel, potentially pathogenic bacterial lineage in a vertebrate host

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The family “Candidatus Midichloriaceae” remains the least characterised lineage within the Rickettsiales, and its diversity, biology, and host range are still poorly understood. Members of this intracellular group typically associate with protists and invertebrates, and species of Midichloria are especially notable for their ability to invade arthropod mitochondria. Because Rickettsiales lineages have been linked to the ancestral origin of mitochondria, Midichloriaceae provides an important model for investigating intracellular evolution and symbiotic interactions.

In 2008, a previously unknown Rickettsia-like bacterium was detected in skin lesions of rainbow trout with red mark syndrome (also called strawberry disease). This Midichloria-like organism (MLO), closely related to Midichloria mitochondrii, represents the first documented member of this bacterial family in a vertebrate host, suggesting a remarkable expansion of host range.

Here, we present the complete 1.08 Mb genome of the MLO, assembled as a single circular contig. Phylogenomic analyses reveal that MLO forms a deeply divergent sister lineage to Candidatus Midichloria, supporting its status as a novel genus within the family. The genome shows a limited metabolic repertoire, underscoring its obligate intracellular lifestyle. Furthermore, the presence of numerous unique genes absent from related taxa highlights its distinct evolutionary trajectory and provides new opportunities to investigate potential host shifts into vertebrates and mechanisms shaping host–mitochondrial interactions.

The deadly past of Yersinia enterocolitica: insights from paleogenomics

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Yersinia enterocolitica is one of the pathogenic bacteria within the Yersinia genus, alongside Yersinia pseudotuberculosis and Yersinia pestis. In humans, Y. enterocolitica primarily causes yersiniosis, an enteric infection characterized by fever, abdominal pain, diarrhea, and vomiting. In some cases, infection progresses to septicemia, which in modern populations is largely restricted to strains belonging to “virulent” biotypes (1B, 2, 3, and 4). In contrast, biotype 1A, the only group lacking the virulence plasmid pYV, is considered “non-virulent” in humans. Using a dataset of 56 ancient and 249 modern genomes, we show that the relationship between biotype and disease severity has shifted over time. All ancient Y. enterocolitica genomes were recovered from teeth, consistent with septicemia cases, yet all genetically seemed to belong to biotype 1A and lack of the virulence plasmid pYV. Biotype 1A thus appears to have been the dominant lineage associated with invasive infection in the past, potentially explaining its high diversity today. By comparing ancient and modern genomes from biotype 1A, we identify multiple loci associated with virulence that were present or intact in ancient strains but are absent or pseudogenized in modern ones. These patterns indicate a long-term evolutionary trajectory toward attenuated virulence in biotype 1A, rather than solely recent acquisition of pathogenicity in other biotypes. Our results highlight the importance of ancient pathogen genomes for reconstructing past disease severity, and demonstrate how paleogenomics can reveal shifts in pathogen virulence relevant to palaeoepidemiology and host–pathogen coevolution.

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The population-level mutation dynamics of SARS-CoV-2 spike under immune selection

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Recent advances in genomics, accelerated by the COVID-19 pandemic, have enabled evolutionary analyses at unprecedented scale. In particular, the public availability of more than 15 million high-quality SARS-CoV-2 genomes provides a unique opportunity to explore how host-mediated immune selection has shaped viral evolution across time.

We investigate the mutation dynamics of SARS-CoV-2 evolving under immune-driven host selection. Drawing from ~27,500 non-synonymous mutations on the spike protein detected between 2020 and 2025, we developed an analytical framework that combines large-scale viral genomics with structural biology and immunological annotations. We further use machine learning to assess the relative contributions of phenotypic and biophysical features to mutation “success” using allele-frequency trajectories as a proxy for fitness. Our lineage-agnostic approach applies a sliding temporal window to pinpoint mutation frequencies expected to impact B- and T-cell immunogenicity, whilst directly quantifying the biophysical trade-offs shaping mutation success.

For B-cell epitope sites, mutations rising in frequency increasingly occur at immunodominant regions of spike, consistent with antigenic drift. We observe a non-monotonic time-dependent pattern, strongly pronounced during the emergence of new variants. However, many mutations fail to persist, reflecting the biophysical trade-offs constraining viable adaptive pathways. In contrast, time-resolved mutation mapping onto T-cell epitope sites shows apparent structure but no sustained enrichment beyond random expectations, indicating that virus evolution is unlikely to be driven by selective pressure exerted by T-cell immunity.

Our results highlight how phenotypic and biophysical properties that shape viral evolution can be quantified, raising the possibility of forecasting mutation trajectories to anticipate immune escape.

Parvovirus B19 from early modern warships suggests genotype 2 continuity in Europe, bridging a millennium-long gap

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Early modern warships were crowded, highly structured communities that facilitated pathogen transmission and provide a time-bounded setting to contrast multiple introductions with onboard amplification. We performed shotgun sequencing of calcified tissues from 31 sailors from the Mary Rose (n = 19) and Kronan (n = 12) and screened for viruses. Human parvovirus B19 (B19V), which causes fifth disease (slapped-cheek syndrome) and can lead to severe anaemia and foetal complications, was detected in 21 individuals (14/19 and 7/12). We reconstructed two complete B19V genomes and one partial genome and recovered low-coverage fragments from eight additional individuals, with authenticity supported by post-mortem damage, characteristic ssDNA coverage patterns and read-level corroboration. All were assigned to genotype 2, a lineage no longer detected in acute infections where genotype 1 predominates today. Phylogenetic analyses place the three genomes within genotype 2 and show the early modern sequences branching basal to twentieth-century genotype 2 diversity. Together with early medieval European genomes (~1000 CE) and twentieth-century clinical material, these sequences bridge a near-millennium gap in the European record and are consistent with potential genotype 2 continuity over that interval. Notably, within-ship genetic diversity across individuals is inconsistent with a single-source onboard outbreak and instead supports multiple introductions and long-term tissue persistence, aligning with predominantly childhood exposure and decades-long persistence of B19V DNA in bone. Our results show that submerged shipwreck assemblages can preserve authentic viral DNA and can be used to extend time-stamped pathogen genomes in ways that inform hypotheses about past circulation and transmission context.

Scientist as a citizen-subject in a collapsing habitat

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While the Global North attempts to mitigate the "polycrisis" through technocratic reforms, such as "greening" laboratories or tweaking Open Access models, the Global South faces an asymmetrical reality. For researchers in Turkey and similar geographies, the primary crisis is not solely the affordability of Article Processing Charges (APCs), but the erosion of science's public legitimacy and scientific freedom. I argue that internal academic adaptation is ineffectual when the societal "habitat" is collapsing.

Using the resilience of the Ecology and Evolutionary Biology Society of Turkey (EkoEvo) as a brief case study, I illustrate how building autonomous networks is a survival mechanism. However, our experience reveals a critical limit: societal welfare cannot be achieved solely by transforming the academy. A healthy scientific community cannot exist within a decaying socio-political ecosystem. Consequently, this presentation proposes a framework of "Total Struggle." I call the SMBE community to recognise that solidarity is not defined only by financial aid or collaborative projects. Real solutions require us to redefine the role of the scientist, seeing them not merely as producers of data, but as "citizen-subjects" who are actively engaged in the struggle for societal emancipation and economic justice. In order to effectively address the polycrisis, we must dismantle the walls of the ivory tower and acknowledge that the fight for evolutionary truth is inherently linked to the broader fight for an equitable society.

Profiling mutation rates and characteristics of somatic structural variants in the aging brain using long read sequencing

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Somatic mutation drives cellular evolution across the lifetimes of individuals. Recent research has found that different species and tissues show differences in the rate and signatures of somatic single nucleotide variants that accumulate through life. However, somatic structural variants (SVs) have remained almost entirely unexplored in healthy aging tissues despite their known roles in aging-associated processes due to technical challenges. We developed methods to identify somatic structural variants in single molecules using long-read PacBio sequencing data. Simulations of the most common SV type (deletions) found a high true positive rate (45-71%) and low false positive rate (~5%). We then applied these methods to PacBio data from mouse hippocampus and sperm. We found a lower mutation rate for somatic SVs in sperm compared to hippocampus samples, as expected, as well as differences in the types of SVs. We also found enrichment of deletion breakpoints overlapping expressed genes in each tissue. The rate of L1 retrotransposon insertions derived from the sperm data was consistent with previous publications in mouse, validating our ability to detect insertions. In the hippocampus, we found on average 20 large deletions (>1 Mbp) per sample, corroborating findings from human neurons using single cell whole genome sequencing. Finally, we applied these methods to brain samples from young and old mice and characterized somatic SV accumulation with age in different brain regions. These results highlight our ability to accurately characterize somatic SVs and will shed light on the mutational processes affecting structural variant formation in different tissues throughout aging.

Investigating cell type-specific gene expression in Salpingoeca rosetta

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Developmental gene regulation is a fundamental biological process which is essential for cell differentiation. In animals, once specialized, most cells cannot revert to a more potent state. Meanwhile, in choanoflagellates, the sister group of animals, cells can be temporally differentiated and can adopt cell identities while retaining the capacity to form other cell types as part of their, often complex, life cycles. The model species Salpingoeca rosetta presents multiple cell types representing distinct stages in its life cycle including multicellular rosettes, sessile thecate cells, and solitary slow swimming cells. Thecate cells are the only diploid stage, and they show highly distinct gene expression profiles compared to their haploid counterparts. The underlying basis of these differences and how this compares to the mechanisms deployed during animal cell differentiation is unknown. We aim to investigate this by comparing gene expression and regulation in slow swimmers and thecate cells by sequencing a de novo genome using Nanopore, and profiling histone post-translational modifications with ChIP-seq. Finally, we dissect how chromatin changes may underlie the observed transcriptional differences by mapping nucleosome occupancy using MNAse-seq. Preliminary results indicate a difference in MNAse digestion among thecate and slow swimming cells. Cell type specific genes are marked by H3K27me3 with cases of H3K4me1/K27me3 bivalency. Our study will provide an in-depth view of cell type-specific gene expression in S. rosetta and lead to a better understanding of temporal differentiation in choanoflagellates and its evolutionary links to animal development.

StrataBionn: a neural network supervised classification method for microbial communities

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The accurate classification of microbial communities is essential for clinical diagnostics and ecological monitoring; however, the high dimensionality and inherent sparsity of microbiome data often limit the efficacy of traditional linear models. Here, we present a supervised artificial neural network (ANN) classifier specifically designed for the robust categorization of microbial profiles.
We evaluated the performance of this method using two distinct datasets: vaginal and oral microbial communities. When compared to traditional nearest centroid classification algorithms, our ANN-based approach demonstrated a significant performance gain, with an increase of 11.0% to 13.3% across all evaluated metrics, including accuracy, recall, precision, and F1-score. We also provide a measure of uncertainty, an empirical estimate of the probability of assignment to communities to facilitate any post-assignment filters.
Beyond predictive power, we address the "black box" challenge often associated with deep learning by implementing a feature attribution framework. We implemented a perturbation algorithm and visualization tool to identify key species that disproportionally contributes to changes in performance in the assignment to communities. This allows users to identify the specific taxonomic or functional features that drive the classification, providing biological insights and increasing trust in the model's outputs. We show that our tool provides increased performance and also offers interpretability of the results, which are important features that will allow researchers to translate complex microbial community differences into a better understanding of the species delimitations of communities.

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Detecting local adaptation within chromosomal inversions

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Chromosomal inversions are structural mutations that can facilitate local adaptation by suppressing recombination between heterokaryotypes, thereby protecting co-adapted gene complexes. Despite growing empirical evidence linking inversion polymorphisms with local adaptation, e.g. latitudinal clines in Drosophila melanogaster, methods for identifying targets of selection within inversions remain challenging. Coalescent theory has demonstrated that local adaptation within inversions yields distinct signatures in statistics such as FST. However, in practice, these signals are often obscured by genomic noise and uncertainty, making it unclear under which specific conditions traditional outlier scans retain power.

To address this, we developed a simulation-based framework to characterize signatures of local adaptation using various population genetic summary statistics. We implemented this in an automated Snakemake pipeline that integrates simulations, data processing, and downstream analysis. Through extensive power analyses of outlier scans, we identify the "sweet spots" for detection, specifically focusing on the interplay between migration and selection (m/s) and varying genomic architectures of local adaptation. Additionally, outlier scans of empirical data from the inversion In(3R)Payne in D. melanogaster show promising results.

Building on these findings, we are extending this framework to include machine learning (ML) and deep learning (DL) architectures. The ML method utilizes summary statistics-based classifiers with local-capture features across genomic windows, whereas the DL approach employs neural networks for image-based pattern recognition, effectively treating raw genotype matrices as images. The architectures are trained using simulated data and will be tested on empirical data. This multi-tiered approach provides a comprehensive and scalable workflow for detecting local adaptation within inversions.

Evolution of the inflammasome pathway in bats: a comparative genomics perspective

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Amongst mammals, bats are singularly capable of flight and equipped with an altered response to cellular damage and viruses. How these cellular stress responses have evolved alongside adaptation to flight is of great interest in understanding bat biology. A key pathway involved in sensing molecular signals derived from both pathogens and cellular damage is the inflammasome pathway, which induces cell death and inflammation upon activation. Previous studies have shown that key components of the inflammasome pathway are modified in bats, however a systematic evolutionary analysis of all genes in the pathway is currently lacking. Using the Tool to infer Orthologs from Genome Alignments (TOGA), we examined patterns of gene losses, expansions and positive selection in the inflammasome pathway (n=39 genes) across 339 mammals (103 bats; 236 non-bats). We find that overall, sensory components of the inflammasome pathway are prone to clade-specific losses in mammals. We uphold previous observations of the complete loss of the PYHIN gene family in bats, including inflammasomes AIM2 and IFI16, involved in sensing host and pathogenic DNA. However, reconstructing the PYHIN locus using orthologous fragments across different bats, revealed that ancestral chiropterans likely contained an AIM2-like and IFI16-like gene that was subsequently lost. Bats have also expanded caspases of the non-canonical inflammasome pathway, involved in sensing lipopolysaccharides. Regarding positive selection, a Z-DNA binding protein (ZBP1) showed adaptive signatures in many bat species. Overall, this study paints a picture of the various changes that potentially underlie response to pathogens and cellular damage in chiropterans.

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Metagenome-derived population genomics of a vertically transmitted endosymbiont during ecological speciation of its insect host

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The ecology and evolution of bacterial symbionts and their hosts are highly interdependent. This is clear from many examples of codivergence across host and symbiont phylogenies. Yet, little is known about the evolutionary dynamics of symbionts during the earliest stages of host divergence and speciation. Over the past 0.5-1M years, the specialist fly Tephritis conura colonized a novel thistle plant, initiating ecological speciation between different host plant lineages. This provides a natural system in which to test whether this has also led to divergence in their unculturable, vertically transmitted bacterial symbiont, Candidatus Stammerula tephritidis (Stammerula). Using microbial sequences mined from whole genome resequencing samples of Tephritis flies, we assembled the first metagenome-assembled genome (MAG) for Stammerula to a single 1.48 MB contig (99.99% complete). Its small size, AT bias, and lack of flagellar genes reflect adaptation to life inside the fly's midgut crypts. Functional annotation revealed that Stammerula can synthesize nine of the ten essential amino acids for insects, suggesting a nutrient-provisioning role. We then compared Stammerula population structure across host lineages and geographic regions. Population genomic analysis revealed Stammerula are broadly structured by fly lineage. Importantly, we found geographic distance was not correlated with population differentiation. Stammerula in ecologically divergent flies in sympatry can show stronger differentiation than those in allopatry. Genomic regions with strong signatures of both divergence and selection included fast-evolving toxin-antitoxin modules. Together, these results suggest symbiont evolution can track ecological and evolutionary divergence of hosts from its earliest stages.

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Rapid chromosome evolution in parthenogenetic Panagrolaimus nematodes

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The conservation or disruption of chromosome organization in animal species is becoming a central point of evolutionary analyses. Structural conservation is generally favored over long evolutionary time, yet short-term disruptions have been observed in some phyla. Genomic architecture may be reshaped through chromosomal rearrangements and, in drastic cases, polyploidization through whole-genome duplication or hybridization.

Some polyploidization events in animals have been associated with the transition to parthenogenesis, through which offspring is produced without outcrossing. Strict parthenogenesis is expected to release constraints on chromosomal structure due to its association with the loss of recombination.

The nematodes Panagrolaimus include mostly sexually reproducing species, and several exclusively parthenogenetic strains originating from a single event of transition to asexuality. A second separate origin was identified for the parthenogenetic strain Panagrolaimus kolymaensis, revived from the Siberian permafrost. Both transitions are associated with distinct triploidization events. Panagrolaimus species have also demonstrated a resistance to desiccation and freezing, which may be expected to disrupt chromosome structure by inducing DNA breaks and repairs.

We generated high-quality assemblies for Panagrolaimus species and close relatives, including phased triploid assemblies for parthenogenetic species, to investigate genome evolution under parthenogenesis, polyploidy and cryptobiosis. We found extensive intra- and interchromosomal rearrangements and several events of blunt chromosome fusion, which are haplotype exclusive. These extensive structural rearrangements highlight the release of chromosomal constraints, favoring chromosomal plasticity and promoting genetic innovation.

Investigating the genomics of reindeer (Rangifer tarandus) domestication

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Reindeer (Rangifer tarandus) are cold-adapted ruminants with a circumpolar distribution. Reindeer husbandry is performed by several different peoples across Eurasia. Herded reindeer are often considered as semi-domesticated or at the early stage of domestication because they overlap in distribution and morphologically closely resemble wild reindeer. There is also only recent archaeological evidence of a switch from using reindeer mainly as working animals to pastoral management, with the oldest milking grounds in Scandinavia dated to 1350 CE. While previous research using nuclear and mitochondrial data suggests that reindeer were domesticated at least twice, the timing, geographic origin, and number of the domestications remain debated. To investigate these questions we analyzed whole-genome sequencing data from over 400 reindeer from wild and human-managed herds, spanning their entire circumpolar distribution and diversity. We found stronger geographic population structure in human-managed herds compared to wild herds and no significant differences in heterozygosity between wild mainland Eurasian and human-managed herds as well as population structure separating wild and human-managed herds. A time-calibrated phylogenetic analysis of mitochondrial genomes revealed several clades containing mainly individuals from human-managed herds. These “domestic” clades show geographic patterns similar to that of the nuclear genome. Through the inclusion of ancient radiocarbon-dated samples, we found that one domestic clade which is widespread in Russia and China is considerably older (TMRCA ~16,000 years ago) than e.g. those common in Scandinavia (TMRCA ~6,000 years ago). This suggests that reindeer management may have begun earlier in some regions than others.

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Nonlinearity in Complex Trait Genomics: Limits of Linear GWAS and Interpretable Deep Learning for Locus Discovery

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Conventional genome-wide association studies (GWAS) typically rely on additivity and linearity assumptions. These assumptions can be problematic for polygenic traits shaped by complex evolutionary forces, which can give rise to genetic architectures with multiple interacting components. In this series of studies, we first derive analytically how unmodeled genotype–genotype interactions can bias GWAS test statistics. Using phenotype simulations based on Estonian Biobank genotypes, we validate the mathematical model and show that conventional linear models can yield biased test statistics and false-positive associations, especially in large-scale GWAS.

Motivated by these limitations, we present an artificial neural network (ANN)–based alternative to linear GWAS to model genotype–phenotype associations without linearity assumptions. We train ANNs to predict complex traits from genotype data and introduce a model-agnostic framework to compute feature importance scores and identify potentially associated loci (PAL). Across simulations spanning multiple parameter settings, we show that PAL can be detected with good precision when stringent selection criteria are used. Applying this framework to the schizophrenia cohort in the Estonian Biobank, we identify multiple loci that overlap with previously reported loci for schizophrenia and bipolar disorder. We further perform enrichment analyses which demonstrate that genes mapped to PAL predominantly highlight terms related to brain morphology and function.

With advancements in model optimization and uncertainty quantification, ANN-based frameworks have the potential to enhance GWAS by improving locus discovery under non-additive genetic architectures and by serving as initial screening tools for downstream functional studies.

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Characterizing the DNA methylation landscape in O. sativa ssp indica

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Epigenetic modifications in the form of cytosine methylation have been increasingly recognized as a contributor to phenotypic diversity and organismal adaptation. These changes are heritable, making this source of variation a complement to DNA variation for improving agronomic traits and developing climate-ready crops. Despite the fact that Indica rice varieties make up 80% of cultivated rice worldwide, methylome diversity among landraces is still poorly explored. Existing studies investigating methylome variation in rice generally have limited sample sizes and focus on other rice subspecies.

In this ongoing study, I aim to address this knowledge gap by performing whole-genome methylome sequencing to characterize cytosine methylation variation in Indica rice using 285 landraces whose origins span a wide latitudinal range across Southeast Asia, capturing both genetic variation and climatic diversity. I then examine how population history has shaped the epigenome of indica rice by testing whether genetic clusters differ in their methylation profiles.

Beyond describing the DNA methylation profile in Indica rice, this work reveals how epigenetic variation is structured among populations. By linking population history to differentially methylated regions, these results clarify the extent to which DNA methylation patterns are associated with genetic variation and identify methylation differences that persist beyond DNA variation.

Future work will incorporate transcriptomic and phenotypic data collected from a recently completed field experiment to investigate the functional consequences of methylation variation. Overall, these findings provide a more comprehensive framework for incorporating epigenetic information into crop improvement programs.

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Genomic analysis reveals local adaptation and vulnerability to climate change of the African orphan crop finger millet (Eleusine coracana)

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A neglected but promising crop in arid and semi-arid regions, finger millet is valued for its nutritional composition and climate-resilience, exhibiting improved biotic and abiotic stress tolerance compared to major cereals. These properties have earned finger millet the reputation of a climate-smart "super food" with strategic importance in the fight against food and nutrition insecurity - especially in regions where climate change negatively impacts agricultural production of other essential staples. Despite this great potential, genomic resources of finger millet remain scarce and the genetic basis of its climate adaptation has not been investigated to date. We aim to fill this gap by providing a whole-genome reference panel of more than 200 finger millet accessions sampled across its cultivation range in Africa and Asia. Based on genome-wide patterns of diversity and genome-environment associations, we identify signatures of local adaptation and their environmental drivers. Using predicted values of future environmental conditions that are relevant to the crop-cycle, we map the evolutionary consequences of climate change for adaptations that evolved over millennia, and identify areas where reduced fitness in the future environment may occur as a result. Finally, we leverage the full range of genetic diversity present in this reference panel to identify candidates for assisted migration into (and out of) areas that are vulnerable to climate change. This could serve to mitigate potential yield losses in the short-term, and help to safeguard the underutilised adaptive potential of this orphan crop for future generations.

Comparing archaic and modern human genomes using deleteriousness predictions from a DNA language model

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For more than 200,000 years, archaic and modern humans inhabited different regions of the world, evolving in unique ways that led to the emergence of distinct biological traits. The genetic basis of these traits can be studied using the genomes of these humans. However, most of our knowledge about the phenotypic consequences of genetic variants is derived from studies of present-day human variation, which limits and biases comparisons between modern and archaic humans towards modern human biology.

In this study, we aim to identify biological differences between modern and archaic humans based on differences in deleteriousness using variant effect predictions from a DNA language model (GPN-MSA), trained without accounting for present-day human genetic variation. Leveraging the predictions, we found that genome-wide levels of deleteriousness of derived variants differed between modern and archaic human genomes, being more deleterious in archaic humans, and the difference among them was partly linked to the proportion of homozygosity and age. Regions with large differences in deleteriousness showed an enrichment for keratin filaments. Such regions also overlapped genomic segments devoid of archaic introgression in modern humans, including genes such as FOXP2, IMMP2L and PRR20. Furthermore, when comparing archaic introgressed haplotypes to their non-introgressed counterparts among present-day humans, we found that introgressed DNA has a higher level of deleteriousness, consistent with the general pattern between archaic and modern humans. Overall, our study highlights the potential of large-scale neural network models as another promising source of information for studying human evolutionary history.

Landscape barriers shape genetic connectivity in the Golden langur (Trachypithecus geei)

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The Golden langur (Trachypithecus geei) is one of the most range-restricted colobine monkeys, confined to the region between Sunkosh and Manas rivers in Bhutan and adjoining Assam, India. Rapid land-use change and infrastructure development increasingly threaten population connectivity, yet the spatial scale and axes of genetic subdivision and subspecies status remain poorly resolved for informing management. Here, we evaluate population genetic structure in Golden langur using mitochondrial hypervariable region-I (D-loop) and 8 polymorphic microsatellite loci, testing patterns of connectivity along North–South and East–West geographic axes. Mitochondrial phylogenetic analyses revealed extensive sharing of haplotypes between northern and southern populations, indicating long term maternal connectivity and the absence of a strong historical phylogeographic break. While nuclear marker analyses—including Bayesian clustering (STRUCTURE), principal component analysis (PCA), analysis of molecular variance (AMOVA), and neighbor joining (NJ) trees—consistently detected moderate genetic subdivision between east–west populations (FST ≈ 0.09), whereas north–south differentiation was weak (FST ≈ 0.04). The discordance between mitochondrial and nuclear patterns indicates restricted but ongoing gene flow. These results highlight that East–West landscape features impose measurable constraints on connectivity, whereas North–South populations remain more permeable to gene flow. Our findings provide an evolutionary framework for prioritizing habitat corridors, maintaining functional connectivity and informing transboundary management of this endangered primate in a rapidly changing landscape.

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3,500 years of sheeppox virus evolution inferred from archaeological and codicological genomes.

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Sheeppox virus (SPPV) is a major pathogen of small ruminants, with descriptions of the disease dating back to Roman antiquity. We report the recovery of ancient SPPV genomes spanning the Bronze Age to the pre-modern period across the Eurasian steppes and Western Europe (n = 24). Our dataset includes multiple genomes obtained from medieval parchment manuscripts, highlighting animal-skin documents as an under-recognized source for reconstructing ancient livestock pathogen genomes. Notably, SPPV sequences recovered from parchment derive from a range of different host species. Phylogenomic analyses reveal that medieval SPPV strains were widespread and diverse during the Middle Ages, forming a now-extinct sister clade. Using this expanded temporal framework, we refine the evolutionary history of the Capripoxvirus genus and estimate that major lineages diverged ~5,000 years BP, with SPPV representing the earliest split from the lineage leading to goatpox and lumpy skin disease viruses.

These results also highlight potential convergent gene-inactivation events between sheeppox and goatpox viruses.

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Genomic diversity across 200 plant species of variable Red List status

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Protecting the genetic diversity of threatened species arose as a major conservation priority in recent years. In vertebrates, IUCN Red List status scales reliably with metrics of genetic diversity. However, given the vast differences in life history between plants and animals, it is unclear if this relationship holds for the plant kingdom. This study investigates the degree of contemporary genetic diversity loss in plants through a meta-analysis of 200 species with publicly available genomes and resequencing data and an evaluation on the IUCN Red List. We re-called several measures of diversity (nucleotide diversity, heterozygosity, frequency of runs of homozygosity, and historical effective population size) in species from their original published data and a standardized bioinformatic workflow. We then combined this with data on 15 functional traits—including life form, lifespan, and reproductive mode— for each species to investigate how threat status affects diversity and what species traits potentially attenuate or exaggerate diversity loss. Preliminary results indicate that the mating system explains the most variation in genetic diversity across plant species. These findings suggest that plant extinction risk assessments based on genetic diversity must integrate life-history traits to accurately contextualize genetic health.

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The westward expansion of Asian rice

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Asian rice (Oryza sativa) was domesticated around 8,000 years ago in the Lower Yangtze valley in southeastern China. A series of recent studies have leveraged whole genome sequencing data to elucidate the routes of dispersal of rice across Asia following domestication. The westward spread of Asian rice to Europe, Africa, and the Americas has not been investigated to the same extent. While there is historical and archaeological evidence of rice cultivation or presence in Africa and Europe centuries before the Columbian exchange, it is unclear whether the genetic ancestry of rice cultivated in these regions today traces that far back or were reshaped by colonial trade networks. In particular, the histories of heritage varieties like arborio from Italy and bomba from Spain famously used to make risotto and paella, respectively, and Carolina Gold from the United States are of key cultural interest. In this study, we analyze newly resequenced and previously published European, African, and North and South American rice landraces or varieties alongside Asian rice landraces to identify their proximal and distant geographical origins, reconstruct their routes of spread, and estimate the timing of major divergence and dispersal events. In the process, we shed light on the complex origins of heritage varieties, with evident connections to colonialism, globalization, and the transatlantic slave trade.

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Natural variation in sex chromosome drive enables the discovery of a neo-X meiotic drive gene family

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During gametogenesis, chromosomes segregate equally, ensuring that gametes retain only a single copy of each chromosome. However, selfish genetic elements such as meiotic drive genes frequently 'cheat' equal segregation to propagate their own transmission to the gametes. When meiotic drivers occur on sex chromosomes in males, they cause unequal transmission of X and Y chromosomes, resulting in a skewed sex ratio among offspring—a phenomenon known as sex chromosome drive. Only a few meiotic drivers have been identified at the gene level so far, and none have had their molecular mechanisms fully elucidated. Here, we study sex chromosome drive in hybrids between D. albomicans and D. nasuta—two relatively young Drosophila species in the immigrans group. Building on the prior quantitative trait loci (QTL) map of meiotic drive regions on the neo-X chromosome in D. albomicans, we integrated single-molecule sequencing and testis transcriptomics from multiple D. albomicans strains that exhibit near-complete sex chromosome drive to rescue of drive (50:50 male-to-female ratio) to uncover putative meiotic drive genes within the QTL windows. Our comparative transcriptomic analyses of testes from the drive and non-drive strains identified a recently expanded zinc-finger domain-containing gene family linked to the drive phenotype in D. albomicans. Currently, we are seeking to validate our candidate driver in additional drive and non-drive strains and to elucidate the mechanisms by which the D. albomicans sex-chromosome driver causes sex-ratio distortion and/or hybrid sterility phenotypes.

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The frontier of genome SFS-based demographic inference

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Since the development of the Kingman coalescent in the late 20th century, the site frequency spectrum (SFS) has become a widely used summary statistic in population genetics to infer past demographic events. Over the past decades, numerous tools have been developed for this purpose. However, most rely on mathematical approximations, stochastic algorithms, or a combination of both, which can introduce biases and errors in demographic inference. To meet the theoretical limits inherent to the SFS, we developed Blockbuster, a new method that leverages advanced mathematical tools combined with exhaustive search. It is fully deterministic and designed to minimize bias when reconstructing changes in effective population size over time, even in reasonably complex demographic scenarios. Additionally, we expanded upon previous work to explore the statistical power, especially in recent times that could be of particular interest for conservation, to detect demographic changes under panmixia, depending on parameters such as sample size, change intensity, and present-day effective size. Finally, we illustrate how violations of key assumptions (e.g., structure or multiple mergers) affect inference-

Repeated losses of self-fertility shaped heterozygosity and polyploidy in yeast evolution

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Evolutionary transitions in mating strategy have profound consequences for genetic variation and adaptation. In the yeast Saccharomyces cerevisiae, mating-type switching is a central feature of the life cycle that enables haploid cells to be self-fertile and mate with their own mitotic descendants (homothallism). Yet heterothallic isolates that have lost this ability are found across diverse niches, indicating that this trait is polymorphic. Here, we experimentally characterized loss of mating-type switching in a representative panel of strains. Analysis of 117 telomere-to-telomere genome assemblies revealed multiple independent loss-of-function mutations in the Ho endonuclease gene which is essential for switching. We estimated that at least 13 independent transitions from homothallism to heterothallism have occurred in the species history. Analysis of the HO genotype of 2,910 strains shows that at least 27% are heterothallic. We found that heterothallism is strongly associated with polyploidy and elevated genome-wide heterozygosity, although the strength of these associations varies between populations. Heterothallic isolates are most prevalent in domesticated and clinical clades, consistent with an origin linked to human-associated environments. However, they are also found, though less frequently, in natural niches. Signatures of recombination in HO sequences suggest that outcrossing contributed to the ecological and geographical distribution of the trait. Our findings reveal that mating-type switching has undergone repeated losses in Saccharomyces cerevisiae evolution, with major consequences for genome architecture and ecological diversification.

From Drift Debt to Inbreeding Depression: Genomic Consequences of Population Decline in Ruffed Lemurs

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Recently bottlenecked populations may retain historical genetic diversity but continue to lose variation and fitness through genetic drift. This drift debt may in part explain why lemurs are among the most endangered taxa on earth, yet their genetic diversity is often high. To test this hypothesis, we sequenced the genomes of two Critically Endangered species, red ruffed lemurs (Varecia rubra; n=75) and black-and-white ruffed lemurs (V. variegata; n=12), and generated a chromosome-level reference genome. Compared to samples collected >50 years ago, modern red ruffed lemurs have similar levels of genetic diversity and inbreeding, but linkage disequilibrium-based effective population size (Ne) trajectories reflect the recent and severe declines in census size and habitat, pointing to drift debt. Halting habitat loss is paramount, but even if populations stabilize at their current Ne, we expect 10–20% loss of genetic diversity and elevated inbreeding over 5–10 decades. The negative correlation between inbreeding coefficients and fitness in hundreds of zoo-born individuals suggests wild lemurs may have 36% fewer offspring and 16% higher mortality in 50 years. Genetic management may help circumvent inbreeding depression. Substructure and evidence of natural introgression indicate that gene flow between populations or even species could help relieve inbreeding in the future.

ARG-based inference of regional maize demographic histories

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Domesticated plants and people share tightly entwined relationships: without their human partners, crops fail to survive and reproduce, and without their staple crops, agricultural societies cannot support rapid human population growth. Given these tight interactions, we hypothesize that crop demographic histories should mirror the histories of associated human populations. We test this in maize by inferring regional demographic histories and comparing them with archaeological proxies of human population size in the Yucatán Peninsula. Previous demographic inference approaches lacked power during the period of agricultural intensification and human population growth in this region. However, recent advances in the inference and analysis of the ancestral recombination graph (ARG) substantially improve resolution within this period. We therefore apply ARG-based demographic inference approaches to maize from the archaeologically well-documented Yucatán Peninsula, an area both historically and presently a significant part of the Maya region. Using simulations in msprime and SLiM, we validated the ARG-based framework under relatively complex demographic and selective scenarios. Given an accurately inferred ARG, we find that background selection and ancient population structure consistent with maize's known history do not confound inference of population expansion or contraction. Analysis on the Yucatán maize remains under active development, but we predict two key shifts: (i) a population expansion ~3,000-4,000 generations ago associated with archaeological evidence of a local transition to a maize-dominant diet, and (ii) a sharp decline beginning ~500 generations ago following European colonization and the violent disruption of Indigenous agricultural systems.

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Persistence and Resilience: Tracking the Genomes of North American Brown Bears

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The brown bear (Ursus arctos) has a Holarctic distribution; however, it has experienced severe range contractions and fragmentation over the past century and a half, primarily due to human persecution and habitat loss. The complex history of brown bears in North America is not yet fully resolved. To address this, we sequenced 268 brown bear genomes, spanning all populations in the contiguous US and most of their contemporary range in Alaska and Canada. Our results show continent-wide population declines, signatures of recent and severe inbreeding in some isolated populations, but minimal genetic load. All populations exhibited a marked and rapid decline beginning approximately 250 years ago. However, we see limited accumulation of deleterious and loss-of-function alleles following population decline in North American brown bears. The results also reveal evidence of selection on genes associated with hibernation and dietary phenotypes. We conclude with discussions potential implications for the species' future persistence.

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Whole-Genome Population Genomics Reveals Lineage Structure and Adaptive Potential of Philaenus spumarius, the Principal Vector of Xylella fastidiosa in Europe

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Philaenus spumarius (L.), the meadow spittlebug, is the principal European vector of Xylella fastidiosa. This xylem-feeding insect has a broad host range, ecological plasticity, and mobility, making it an efficient vector across diverse landscapes. Yet, major gaps remain in understanding its genetic diversity, migration patterns, and local adaptation, limiting effective control of X. fastidiosa outbreaks. To address these gaps, we worked with a global network of researchers and citizen scientists to assemble a geographically and ecologically diverse collection of P. spumarius samples. We generated a chromosome-level genome assembly for P. spumarius and high-quality assemblies for four related spittlebug species, providing a robust genomic framework for evolutionary and epidemiological studies. Resequencing 430 P. spumarius individuals from across the globe uncovered boreal, temperate, and semi-arid lineages shaped by geography and climate. The lineages vary in reproductive isolation and in the degree of mitonuclear divergence. Iberian populations grouped with an individual identified as P. tesselatus contributing to regional genetic complexity. Genomic scans identified loci under selection in Apulian populations, including signatures in sulfotransferase (SULT) genes potentially linked to behavioural plasticity, host plant specialisation, or insecticide resistance in olive-growing regions. Migration analyses indicated limited long-distance dispersal but strong local connectivity, consistent with the rapid regional spread of X. fastidiosa. Together, these findings reveal the lineage structure and adaptive potential of P. spumarius, the key vector of X. fastidiosa in Europe. They underscore the importance of targeted surveillance of locally adapted populations and provide genomic tools for monitoring vector dynamics and mitigating emerging disease risks.

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Insertion of an invading retrovirus regulates a novel color trait in swordtail fish

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For over a century, evolutionary biologists have been motivated to understand the mechanisms through which organisms adapt to their environments. Coloration and pigmentation are remarkably variable within and between species and can serve as an important window into the mechanisms of adaptation. We mapped the genetic basis of a newly described iridescence trait in swordtail fish to a single locus. Individuals with this trait appear to sparkle as they move through the water. We find that the trait is driven by the recent endogenization of a retrovirus that inserted near the gene alkal2a. This insertion is associated with changes in the chromatin landscape, upregulation of alkal2a, and accumulation of iridescent cells that adhere to the scales. Rather than causing diseases, our results demonstrate that invading endogenous retroviruses can also regulate novel trait variation in the host. Moreover, we find that this coloration trait may act as an important signal in interactions between fish and their predators in the natural environment. Strikingly, another closely related species from this region in Mexico has evolved a phenotypically similar iridescence trait through distinct genetic and developmental mechanisms. We hypothesize that comparison of this trait across species may yield exciting insights into the genetic mechanisms underlying the evolution of novel traits.

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Population boom or bust? Kraken the population connectivity and demographic history of Octopus vulgaris

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Making the most of genomic tools to understand and predict species responses to global change is increasingly important, particularly for exploited marine species. Octopus vulgaris is an ecologically and economically important species that has recently shown a marked increase in abundance in the northeast Atlantic. However, the mechanisms underlying this increase and the long-term stability of these populations remain poorly understood. Moreover, although structural variants are increasingly recognised as key contributors to ecotypes, local adaptation, and cryptic population structure, they are still under-represented in eco-evolutionary studies. Here, we analyse genomic variation in 380 O. vulgaris individuals sampled across the United Kingdom, France, Spain, Portugal, and Senegal using low-coverage whole-genome sequencing. Our analyses shed light on population structure across the northeast Atlantic and investigate genomic patterns consistent with recent demographic changes and local adaptation. We also explore structural variation in the genomes to uncover its potential role in shaping population differentiation across environmental gradients. Together, these results provide new insights into the demographic history of O. vulgaris and the distribution of its genetic variation, including structural variation, providing a comprehensive population genomic study of an exploited marine species under environmental change.

Public microbial single-cell RNA sequencing data reveal opposing transcriptional relationships at population and single-cell scales

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Public repositories contain a rapidly expanding and remarkably underexplored body of microbial single-cell RNA sequencing data. While these datasets were often generated for narrow experimental goals, they capture rich transcriptional variation that has rarely been analyzed beyond standard clustering or annotation approaches. Consequently, their potential for uncovering fundamental principles of microbial physiology remains largely untapped. Here, we reanalyzed public single-cell transcriptomes from yeast and bacteria and found that canonical population-level principles of microbial growth and gene regulation do not extend to individual cells. To enable robust interpretation, we developed analysis strategies that account for microbe-specific transcriptome structure, including extreme rRNA dominance, which can distort conventional single-cell analyses. Across datasets, we uncovered striking divergences between population-level and single-cell behavior. While population averages reproduce the well-established positive coupling between growth-associated gene transcription, ribosomal RNA abundance, and growth rates, these relationships collapse at single-cell resolution. Ribosome levels vary widely among cells within the same population, population growth rate explains little single-cell variance, and growth-associated gene expression is surprisingly and consistently anticorrelated with rRNA within samples. Similar population and single-cell mismatches emerge stress-associated programs and transposable element expression, revealing further persistent physiological substructure even within exponentially growing cultures. Together, these results show that publicly available microbial single-cell datasets contain far more biological information than is captured by standard population-level analyses. By revisiting these data with organism and single-cell-aware approaches, we demonstrate how data reuse can yield new insights into microbial growth regulation and explore the limits of population-level principles, all without generating new experiments.

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Quantifying DNA Methylation Consistency and Specificity Across Genomes

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Epigenetic modifications play essential roles in regulating gene expression, maintaining genome stability, and determining cell identity. Although mammalian methylation maps have been generated, these studies reveal that methylation is not randomly distributed across the genome but forms distinct hypermethylated and hypomethylated regions. Whether these regions exhibit consistent methylation enrichment across samples within a species, how methylation consistency and specificity are distributed genome-wide, and how such patterns can be quantitatively assessed remain poorly understood. Here, we establish a quantitative framework to characterize methylation consistency and specificity across individuals in cattle and sheep. We introduce a Consistent Methylation Index (CMI) to quantify methylation level stability across samples, and a Methylation Specificity Index (MSI) constructed using Tau, Hoyer sparsity, and Shannon entropy metrics to describe sample-specific methylation variation. By integrating multi-tissue and multi-individual WGBS datasets, we generated quantitative genome-wide landscapes of DNA methylation consistency and specificity. Our analyses revealed that: (1) Methylation levels (MLs) vary substantially among samples, with marked differences among tissues; (2) Autosomes exhibit higher MLs than the X chromosome in both cattle and sheep; (3) Genome-wide site-level MLs display skewed distributions, with enrichment around ~ 0.8 in cattle and ~ 0.65 in sheep; (4) Most sites show low consistency (MCI ≈ 0), indicating high inter-sample variability, yet a subset of regions exhibit consistency (MCI ≈ 0.8) with nearly uniform high MLs across samples. This approach identifies both evolutionarily stable methylation regions and dynamically regulated sample-specific sites, offering insight into how epigenetic conservation and regulatory plasticity influence genome regulation.

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Single-cell analysis of prefrontal cortex differences in selectively bred tame and aggressive foxes (Vulpes vulpes)

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Selection of foxes for divergent behavioral phenotypes—tame and aggressive—resulted in increased gray matter volume in the prefrontal cortex (PFC). While these shared structural changes likely reflect the PFC's fundamental role in the higher-order decision-making required for both approach and avoidance behaviors, the cellular and molecular mechanisms underlying this expansion may differ between the two populations. Using single nucleus RNA-seq (snRNA-seq) of 6 tame and 6 aggressive foxes we developed the fox PFC cell census including 11 clusters of excitatory neurons, five clusters of interneurons, astrocytes, oligodendrocytes, oligodendrocyte precursor cells, microglia, and endothelial cells. By integrating the snRNA-seq clusters with spatial transcriptomics data, we determined laminar distribution of the neuronal clusters in the fox cortex. Cell-type abundance analysis revealed a significantly higher proportion of layer 5 inhibitory neurons in tame foxes. Differential expression (DE) analysis identified the greatest number of DE genes within excitatory neurons of the superficial layers 2/3. In tame foxes, upregulated DE genes were significantly enriched for terms related to the glutamatergic synapse and postsynaptic membrane. Conversely, upregulated DE genes in aggressive foxes were enriched for terms related to translation, mitochondrial function, and neurodegenerative disorders. These findings suggest a more refined fine-tuning of gene expression in the PFC of tame foxes, contrasting with an overall higher activity of the translational machinery and likely higher metabolic demand in aggressive foxes. These cell-type-specific PFC differences provide insight into the potential mechanistic basis for the regulation of social behaviors in foxes and other mammals.

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Genomic time-series of a butterfly biocontrol agent reveal selection under extreme demographic constraint

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Detecting selection in small, bottlenecked populations is notoriously difficult, as strong genetic drift and demography are often assumed to overwhelm signatures of adaptation. Furthermore, many applied systems such as invasive or endangered populations are effectively unreplicated (n = 1), leaving few alternatives for studying selection under extreme demographic constraint in the wild. Biocontrols used to suppress invasive species provide powerful natural experiments in this context, imposing severe founding bottlenecks, abrupt environmental change, enforced isolation, and rapid population expansion on known timescales.

We present a whole-genome time series from the butterfly Heliconius erato cyrbia, introduced to the Cook Islands in 2016 as a biocontrol agent against an invasive passionflower. The population was founded by a handful of individuals and experienced several generations at very low census size before establishment. We sequenced ~150 individuals spanning the founding population and two post-establishment timepoints (2019 and 2021), together with ~100 genomes from the native Ecuadorian range.

Using this inherently unreplicated system, we tackle three aims. First, we quantify how effective selection can be following an extreme bottleneck characterised by intense drift. Second, we search for signatures of selection in an agnostic framework, combining forward simulations that incorporate recombination-rate variation with haplotype-based analyses to distinguish selection from drift. Third, we test for selection in genes underlying traits that have changed significantly following introduction, including colour patterns and biosynthetic pathways involved in chemical defence and toxicity.

Together, this work demonstrates how selection, drift, and trait evolution can be studied in systems traditionally considered intractable.

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Tracing the spread of Beak and Feather Disease Virus over the past two centuries

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Epizootic diseases have gained increasing attention in recent years, particularly those maintained in avian reservoirs that threaten species critical for ecosystem services, food security, and biodiversity conservation. Among these, Beak and Feather Disease Virus (BFDV), a rapidly evolving circovirus and major pathogen of parrots and other birds, causes severe feather and beak deformities, immunosuppression, and persistent infections. Its ability to transmit through direct contact and contaminated materials facilitates transmission across both wild and traded bird populations, including species of conservation concern.

Major questions remain regarding the historical prevalence of BFDV and the extent to which the trade of birds has shaped its dissemination. We apply a whole-genome sequencing and metagenomic mining framework to recover over 30 previously unrecognised historical and contemporary BFDV infections. This includes genomes from 1937 and 1837 Australia, recovered at 214- and 114-fold coverage, respectively. Using genome-wide assembly approaches, we reconstruct complete BFDV genomes, including those recovered from museum specimens over 100 years in age and predating the first clinical description of psittacine beak and feather disease syndrome.

Through time-resolved phylogenetic analyses, we infer the temporal and geographic spread of BFDV and establish the timing of major outbreaks. Finally, we quantify the contribution of the pet and wildlife trade to shaping within-host viral diversity by integrating phylogenetic data with international trade records to predict patterns of recovered BFDV diversity across avian hosts.

Together, our results demonstrate the value of cross-disciplinary data integration for identifying the drivers and predictors of epidemic behaviour in a globally significant wildlife pathogen.

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The application of ancestral recombination graphs to understand the temporal dynamics of hybridization

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The genome-wide inference of ancestral recombination graphs (ARGs) has become increasingly tractable over recent years. The ready application of ARGs, also to non-model organisms, holds substantial promise for the field of population genomics due to the rich evolutionary signal held within the structure. One major advantage of this approach is the ability to apply analyses not only to genomic windows, but also to time windows, as the genealogies encode the temporal history of variation. In this way, we may better understand how genomic signatures vary when looking backwards in time. Here, we apply ARG-based methods to understand the temporal dynamics of hybridization and divergence. We inferred the ARG from 378 individuals across the Oenanthe hispanica species complex, a group of passerines composed of five lineages that hybridize in multiple regions across their ranges. Using a combination of empirical and simulation-based analyses, we address two main aims. Firstly, we uncover the evolutionary history of convergent coloration phenotypes within the complex. Comparing haplotypes containing variants associated with plumage coloration, we use ARG-based estimates of the time to the most recent common ancestor (TMRCA) to establish in which species a white throat and white mantle phenotype evolved, and that the variation subsequently spread to another species through introgression. Further, we investigate how reproductive isolation has established across the genome over time within a hybrid zone, thus improving our understanding of the formation and maintenance of species boundaries. With these varied analyses, we highlight the exciting potential ARGs hold for population and speciation genomics.

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Cooperative interactions between measles viruses facilitate rapid dissemination throughout the brain

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Measles virus (MeV) usually infects respiratory and immune cells, but intra-host evolution can enable viral brain spread, leading to fatal encephalitis. This neuron-to-neuron transmission requires mutations that destabilize the viral trimeric fusion protein. While single mutations can allow the virus to spread independently, clinical isolates can harbor cooperative populations. These groups are made up of some genotypes that produce stable proteins and others with highly destabilizing truncation mutations–both non-viable alone but their subunits can pair to form functional hybrid trimers. Given the availability of mutations that enable spread self sufficiently, why do cooperative collectives emerge? To investigate this phenomenon, we developed a computational model of MeV neuronal replication and spread, and show that these cooperative mutations provide a transient "heterozygote advantage". Because de novo mutants initially arise in cells alongside stable wildtype genomes, truncations can immediately form functional hybrids that facilitate faster initial spread than a new self-sufficient mutation. However, this strategy is vulnerable to stochastic bottlenecks during cell-to-cell transmission that can separate the two interdependent genotypes. We show that MeV transmitting on a network structure parameterized with human neuronal connectivity data can nevertheless spread robustly as cooperating genomes because such networks contain redundant pathways that buffer the population against local drift. This work provides new insight into viral adaptation to a new host environment, and reveals how transmission dynamics can impact viral heritability in a case where viruses blur the line between collective and individual fitness.

Efficient Bayesian Phylogenetics under the Infinite Sites Model

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Bayesian phylogenetic inference from molecular sequences can provide key insights into the evolutionary history of populations. Existing tools, however, often scale poorly with sample size. We present inPhynite, a highly-efficient Bayesian phylogenetics algorithm for genomic datasets compatible with the infinite sites mutation model. A key advantage of this model is that likelihood calculation, which typically incurs a substantial computational cost, becomes trivial. We show that under the infinite sites assumption, it is possible to sample a coarse space of mutations and coalescences from which we may recover complete phylogenetic trees. We design an efficient Markov chain for this space together with effective population size trajectories, modeled as piecewise constant functions. Based on real and synthetic data, our method significantly outperforms competing methods, offering a speedup of over 225 times in statistical efficiency on large datasets without incurring any loss in accuracy. Finally, we demonstrate how inPhynite can help us understand the evolutionary history and past effective population sizes of human populations based on mitochondrial DNA.

Scaling and Representation Learning for Deep Ancestral Sequence Reconstruction

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Though currently few deep sequence models explicitly represent evolution in a principled manner, deep learning methods are increasingly entering phylogenetics, primarily through variational inference, latent representations, and neural sequence models. These approaches aim to alleviate the computational bottlenecks associated with MCMC methods and to enable wider ranges of models and observations. In [1], we introduced Draupnir, the first deep generative model for ancestral sequence reconstruction. It goes beyond conventional substitution models by modeling evolution in a latent space using a tree-structured Ornstein–Uhlenbeck (OU) process. These latent variables are mapped to observations (protein sequences) via neural decoders. Latent representations of entire sequences relax the assumption of site-independent evolution and enable representing epistasis. We perform stochastic variational inference, which optimizes the evidence lower bound via stochastic gradient ascent, replacing MCMC-based Bayesian inference with approximate but scalable optimization. Draupnir achieves state-of-the-art ASR accuracy, captures coevolutionary structure, and is computationally efficient. We plan to use Draupnir to explore relationships in diverse families of carbohydrate-binding proteins, with novel functions [2]. As we advance development of the model to achieve this, we present progress, including the integration of ESM protein language models into the encoder, mini-batch training that scales to larger data sets, and an analysis of the influence of the OU priors.

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Turtles reveal novel insights into PRDM9's role in recombination rate landscape evolution

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Functional PRDM9 drives rapid recombination evolution across vertebrates, while its absence, as shown in yeast, birds and dogs, slows evolution. This reduced turnover is due to 'default' hotspots near gene promoters, which are more stable over time. Recent work in snakes challenged this dichotomous framework that intact PRDM9 recruits hotspots away from promoters. This duality is also prevalent across mammals, but functional PRDM9 still directs the majority of hotspots. Here, we constructed a novel LD-based fine-scale recombination map in the diamond-backed terrapin. Similar to snakes, we uncovered more balanced hotspot usage between PRDM9 and default mechanisms in turtles, with default hotspots more common on microchromosomes and PRDM9 hotspots more common on macrochromosomes. Our results suggest this balanced hotspot usage is shared across reptiles, having evolved at least ~250-300 mya. We complement our recombination analysis with a PRDM9 survey targeting reptiles, specifically squamates and testudines, and identify at least 5 novel losses. Our findings increase the number of independent losses across vertebrates by 50%, and suggest these clades are particularly prone to loss, including several quite recent. When combined with documented PRDM9 loss in Archosauria (birds, crocodiles) this suggests a possible connection between PRDM9 loss and its role in suppressing default hotspots. Finally, expanding genome coverage in underrepresented, species-rich clades, such as reptiles, enabled this work and promises further evolutionary insights. Future work on these and other clades could yield novel insights on the function of PRDM9, as well as its role in fine-tuning the evolutionary rate of the recombination landscape.

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Ecology-mediated demographic instability shapes genetic diversity in a cichlid adaptive radiation

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Historical demographic changes leave lasting signatures in genomes and are central to understanding why genetic diversity varies so widely among species. Under neutral theory, larger and demographically stable populations are expected to maintain higher genetic diversity, yet this relationship is often inconsistent in natural systems subject to environmental instability. Here we investigate how long-term demographic fluctuations have shaped present-day genetic diversity across the adaptive radiation of cichlid fishes from African Lake Tanganyika, one of the most species-rich freshwater assemblages worldwide. Using large-scale data integration of genomic data from 620 wild individuals representing 40 species and a comprehensive set of ecological and life-history traits, we reconstructed coalescent-based population size changes over the last million years. We applied a novel innovative approach establishing historical demographic baselines and link these histories to contemporary genetic diversity. We show that species experienced shared population declines during major lake-level fluctuations, but differed in the magnitude and stability of their effective population sizes. Contrary to expectations, species with greater historical population size fluctuations often exhibit higher genetic diversity. This pattern is associated with ecological traits, particularly habitat depth and trophic ecology, with shallow-water littoral benthic species showing greater demographic instability and higher present-day genetic diversity. Habitat choice likely mediated historical demographic responses, as repeated lake-level–driven habitat contractions promoted transient panmixia and admixture among shoreline populations, leaving lasting genomic signatures of elevated diversity. Together, our results highlight how demographic instability shapes present-day genetic diversity, offering insights into molecular evolutionary processes relevant to biodiversity monitoring under ongoing environmental change.

Salmonids reveal principles of regulatory evolution following autotetraploidization

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Whole-genome duplication can accelerate evolution by creating redundant genes and cis-regulatory elements, yet the principles shaping regulatory divergence after genome doubling remain poorly understood. Salmonids experienced a relatively recent autotetraploidization and are still undergoing rediploidization, providing a powerful vertebrate system to study how gene regulation evolves following genome duplication. Using large-scale functional genomics datasets in two salmonids, Atlantic salmon and rainbow trout, spanning embryogenesis and adult tissues, we combine RNA-seq with chromatin accessibility (ATAC-seq) and histone-mark profiling (ChIP-seq) to map active promoters and enhancers and to quantify their evolutionary fates across duplicated genomic regions. We integrate comparative whole-genome alignments to measure divergence in gene expression and regulatory element activity, explicitly accounting for differences in rediploidization timing.

We find that regulatory divergence is strongly context dependent, with the strongest constraint during late embryogenesis and in brain, and comparatively relaxed constraint in liver and gonads. Enhancers show faster evolutionary turnover than promoters, and changes in enhancer sequence and activity are closely associated with expression divergence between ohnologs. Finally, transposable element insertions disproportionately contribute to lineage- and tissue-specific enhancer innovation, while being depleted from duplicated enhancers active in constrained regulatory contexts. Together, these results identify general principles of regulatory evolution following autotetraploidization and provide a comparative multi-omics framework for understanding how cis-regulatory landscapes evolve after genome duplication.

Comparative Genomics of Syngnathiform Fishes

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Syngnathiform fishes, including seahorses, pipefishes, and their relatives, are an incredibly diverse and evolutionarily intriguing clade. They show a remarkable variety of morphological and life-history traits, such as male pregnancy, elongated bodies, and dermal body armor, offering a unique vertebrate model for the evolution of reproductive and morphological novelty. In addition to their phenotypic diversity, Syngnathiformes are distributed globally and inhabit a broad range of ecological niches, spanning gradients in temperature, salinity, depth, and habitat types. To investigate the genomic basis of this ecological breadth and trait diversity, we newly generated a densely sampled dataset consisting of short-read draft genome assemblies for more than 200 species. For all these species, we characterized genomic features such as genome size, repeat content, gene content, evolutionary rates, GC content, and codon usage. We find large differences in genome size, varying by a factor of six among species. By integrating this in a phylogenetic context and reconstructing evolutionary relationships across all sampled species, we identify multiple lineages that appear to have undergone independent genome expansions, largely driven by differences in the transposable element content. Additionally, this dataset allows for comparative analyses that link genomic variation to key ecological and phenotypic traits. For example, we identify losses of specific genes, including associations between opsin gene loss and species depth distribution. Overall, our findings provide a large-scale comparative genomic framework for understanding how vertebrate genomes evolve during major ecological and phenotypic transitions.

Structural variants and their contribution to successful and unsuccessful colonizations

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In the current context of rapid environmental change and increasing anthropogenic impacts, understanding the evolutionary mechanisms underlying the uneven distribution of biodiversity is crucial for predicting species redistribution. While some populations struggle to survive or adapt, others persist or expand beyond their native ranges. Among the genetic factors potentially influencing these contrasting outcomes, structural variations (SVs) may play a key role in shaping population fitness. Here, we investigated the effects of SVs on colonization outcomes in the marine gastropod Littorina saxatilis, a species that provides a natural experiment of repeated colonization events, including both historical and recent, successful and failed range expansions. Using high-coverage (50×) whole-genomes from 149 individuals sampled across the species distribution range, we identified SVs from paired-end short reads using a robust and widely adopted bioinformatic pipeline which includes a manual curation step. We then compared SV abundance and allele-frequency distribution in populations that underwent successful and unsuccessful colonization events to assess the potential role of chromosomal rearrangements in the colonization outcome. Finally, we used SVs to estimate genetic load quantifying deletions (DELs) in coding sequences, as potentially deleterious mutations that can affect gene expression and functioning. Overall, our results highlight the complex role of SVs during population range shift dynamics. These findings improve our understanding of the colonization process and the evolutionary dynamics underlying range shifts, shedding light on the genomic mechanisms distinguishing populations that persist from those that fail under rapid environmental change.

Metagenomic Characterization of Canids from the Pre-Contact (3,475–360 yBP) Patagonian Coastal Region of Argentina

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Dogs have been closely associated with human societies in the Americas since their early occupation (~10,000–10,200 years ago), and archaeological evidence from pre-contact South America suggests that canids held important economic and symbolic roles. To better understand human–canid interactions through commensal and pathogen exchange, we generated shotgun sequencing data from dentine and/or bone of 47 pre-contact canid individuals (3,475–360 yBP) from the Patagonian coastal region of Argentina. The dataset included Pampas fox (Lycalopex gymnocercus, n = 9), Andean fox (Lycalopex culpaeus, n = 5), grey fox (Lycalopex griseus, n = 2), domestic dogs (Canis lupus familiaris, n = 8), and undetermined canids (n = 23). We analyzed the metagenomic fraction using Kraken2 to identify commensal bacteria and potential pathogens. In two individuals—one Pampas fox and one Andean fox—we reconstructed two ancient Actinomyces capricornis genomes (7X and 1.8X coverage), previously reported in healthy goat–antelope oral cavities. In the same Pampas fox, we recovered one ancient Corynebacterium freiburgense genome (16.3X), previously isolated from a dog-associated wound in a human. Additionally, in an undetermined canid, we recovered two low-coverage ancient genomes, Olsenella sp. oral taxon 807 (~1X) and Actinomyces sp. oral taxon 414 (~0.2X), both linked to periodontal disease and previously recovered from ancient human remains. Further high-depth genome reconstruction of these taxa, together with genomic comparative analyses, will illuminate long-term microbial exchange between humans and canids and the ecological contexts that facilitated shared disease histories. These insights rely on collaboration with local communities in the Argentine Patagonia.

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Measuring selection on regulatory networks combining population transcriptomics and experimental evolution

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Understanding how plants adapt to drought is critical to predicting species vulnerability under climate change and optimising management practices. Extensive research has uncovered the molecular genetic mechanisms of many key genes for drought adaptation. However, our understanding of how natural selection operates on individual gene expression and interacting regulatory networks remains limited. In this work, we measured selective forces acting on co-expression regulatory networks, focusing on transcription factors (TFs), during environmental adaptation in Arabidopsis thaliana. First, we performed population transcriptomic and genomic analyses to characterize the patterns of diversity in regulatory networks and drought-related TFs. We identified a set of TFs with signatures of genomic selection that are central in highly conserved co-expression modules. Second, using long-term evolution experiments in outdoor common gardens that started from the same founder population (GrENE-net.org), we inferred selection on gene expression by associating transcriptome data from founder accessions with their relative abundance changes across environments with contrasting precipitation. To validate these, we aim to replicate these trends using a barcoded evolution experiment with TF knockout lines, simulating drought in growth chambers. This work presents a novel approach to studying environmentally driven selection on plant regulatory networks to better understand rapid environmental adaptation.

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Ancestral introgression and the origin of a unique asexual vertebrate, the Amazon molly

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Despite close to a century of research concerned with the non-recombining gynogenetic Amazon molly, a classic model system for investigating the origins and consequences of asexuality in vertebrates, details regarding the origin of the lineage remain unclear. Specifically, the transition between sexual reproduction and gynogenesis has thus far been impossible to replicate in lab crosses of the widely accepted progenitors of this hybrid species. Building off the hypothesis that the transition to and success as a hybrid asexual lineage is facilitated through the combination of specific genotypes, we hypothesize that in the Amazon molly, some of these genotypes may have themselves been the result of introgression prior to the hybridization event associated with reproductive mode transition. We re-analyze resequenced genomes from across the range of the Amazon molly and each parental species. Assessing hybrid genotypes at sites informative of parental ancestry, we find evidence of loss of heterozygosity tracts which are shared across all hybrid Amazon genomes. These same loss of heterozygosity tracts are supported within reconstructions of the ancestral Amazon molly haplotypes, with demographic modelling of the species complex also suggesting gene flow between the parental species prior to the focal hybridization event associated with reproductive mode transition. We interpret these signals as support for the singular progenitors of modern Amazon mollies themselves having histories of introgression within their genealogies, and suggest that admixed status of progenitor individuals may have played a key role in facilitating the formation of this hybrid gynogenetic lineage.

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Modeling repeats allows k-mer-based, alignment-free methods to calculate population genomic distances

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Understanding ecological change requires robust and ideally inexpensive methods for monitoring species population dynamics. Given the continually reducing costs of sequencing, one promising approach is to sequence genomes at low coverage and use these so-called genome skims to compute population genetic measures of diversity. Assembly-free and alignment-free methods relying on sequence signatures such as k-mers can compute distances between genomes from reads covering those genomes. A widely used and efficient approach is to compute the intersection size of k-mer sets (e.g., Mash), which can be translated to distance estimates. The Skmer method has extended this approach to low-coverage genome skims. However, these methods largely ignore the repetitive nature of many genomes; many k-mers can appear multiple times within genomes, even for large k. This omission can hamper computing lower genomic distances at high resolution, which is what we need to enable population genetic analyses. Here, we develop a method, ReSkmer, which models the impact of repeats on k-mer set intersection. ReSkmer can compute the distance between two genome skims, providing high accuracy despite high levels of repetition, substantial sequencing error, and small genomic distances. We show that the modeling of repeats increases the accuracy of distances and nucleotide diversity estimates, especially for highly repetitive genomes and at low population genetic level distances.

From Sequence to Expression Across Evolution: Promise and Limits of AI Genome Models

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Deep sequence-to-function models are rapidly transforming our ability to predict regulatory phenotypes directly from genome sequence. With the parallel emergence of highly predictive foundation models and high-quality, contiguous vertebrate genomes, a central question comes into focus: beyond coding sequence, can genome-wide regulatory output -gene expression- be broadly inferred across mammalian and vertebrate lineages to enable comparative evolutionary studies?
We address this question by evaluating AlphaGenome in an end-to-end pipeline across five additional vertebrates (rhesus macaque, rabbit, rat, opossum, and chicken), spanning substantial evolutionary distances. For each species, rich gene expression compendia across diverse tissues and developmental stages enable context-aware evaluation across ~20,000 protein-coding genes, directly probing both phylogenetic generalization and tissue specificity.
AlphaGenome recovers broad expression landscapes across taxa, achieving robust correlations even in distant lineages, with the lowest performance observed in chicken brain (Pearson ≈ 0.6 averaged across developmental stages). Analysis across six tissues (brain, heart, kidney, liver, ovary, and testis) shows that performance is driven primarily by global expression structure, while tissue-specific regulatory effects are captured more weakly.
Together, these results highlight both the promise and shortcomings of AI-driven genome interpretation. While sequence models can be adapted to non-model organisms to recover coarse expression patterns, they remain limited in capturing context-specific regulation. Our findings motivate a shift from accuracy benchmarks toward evolutionary stress tests that aim to disentangle model limitations from genuine regulatory divergence, clarifying which failures reflect incomplete learning and which arise from lineage-specific regulatory evolution.

Neo-sex chromosome evolution and reproductive isolation in hybridizing gazelle lineages

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The Grant's gazelle complex in eastern Africa harbours rare autosome-sex chromosome translocations that have generated neo-sex chromosomes. We have sequenced 33 whole genomes from two principal lineages; Peter's gazelle and Grant's gazelle as well as a hybrid population, and performed population genetic analyses to understand how these neo-sex chromosomes influence variation within and between lineages. Using a novel method we find that two regions on the neo-sex chromosomes, one ≈51 megabase (Mb) segment derived from ancestral chromosome 16 and another ≈12.5 Mb segment from ancestral chromosome 5, have stopped recombining and show relaxation of purifying selection in their neo-Y-linked homologs, both hallmarks of sex chromosome degeneration. The hybrid population carries slightly more genomic ancestry from Peter's gazelle than Grant's gazelle, with admixture being both ancient and recent. Parental ancestry is unevenly distributed across the genome, with extensive "deserts" devoid of Grant's gazelle ancestry. These non-recombining regions may constitute major barriers to gene flow: hybrid individuals from Mkomazi are fixed for Peter's gazelle alleles in the neo-Y linked homologs in both regions, and nearly fixed for Peter's gazelle in one of the corresponding neo-X regions. These results suggest that neo-sex chromosomes are helping to reinforce genetic barriers between these nascent species, providing an example of their role in an ongoing mammalian speciation process.
In addition, ongoing comparative analyses of similar chromosomal rearrangements in the tribe of Tragelaphines, could also help showcase the role of the neo-sex chromosomes on a broader scale between the different species of Tragelaphines which we have sampled.

1398

What do bats and belugas have in common? Comparative genomics reveals convergent anti-deafness adaptations in echolocating Cetacea and Chiroptera

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Echolocation has evolved independently in bats (Chiroptera: Yangochiroptera + Rhinolophoidea) and toothed whales (Odontoceti). While echolocation is an indispensable adaptation for navigation and foraging in these taxa, constant exposure to intense noise paired with cellular senescence are known to cause the death of cochlear sensory hair cells (HCs) and subsequent hearing loss in mammals. Selection to maintain functional hearing by delaying cellular senescence into old age in echolocating mammals is therefore likely to be strong, but evidence for convergence in senescence-associated molecular pathways among these taxa remains limited. We conducted a comparative genomics study across 101 highly contiguous mammal genomes to test for convergence in positively selected genes and functional pathways among echolocating bats and toothed whales. Using an orthologous gene set several times larger than previously studied, we found positive selection in genes not previously investigated in these clades whose functions include spatial reasoning and cognition, cochlear cell survival and repair, and tumor suppression. We also detected positive selection in all three echolocating lineages for genes essential for the structural integrity of cochlear HC stereocilia bundles, whose breakage directly leads to hearing loss in mammals. Finally, we found evidence of convergent selection in senescence-associated functional pathways, including immune and DNA damage pattern recognition, mitochondrial homeostasis, and cellular response to hypoxia and cytotoxic reactive oxygen species. Our study aligns with previous findings supporting parallel evolution in hearing-associated genes among distantly related echolocating mammals and expands these findings to include convergence in other cellular processes relevant to maintaining crucial sensory phenotypes.

Heritability of germline mutagenesis in 40 large three- and four-generation pedigrees

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Germline mutations are the basis for genetic disease and underlie all heritable phenotypic variation on which evolution can act. Estimating the mutation rate, or the expected number of de novo mutations (DNMs) per site, genome, and generation, is therefore critical for modeling disease burden and selection. In the human germline, few studies have identified specific genetic loci that commonly affect mutation rate or measured its heritability.

Here, we present the first phase of the Gametes Through Generations (GTG) project, comprised of new WGS of >1000 individuals from 40 CEPH/Utah pedigrees. With a median of eight (generation three) and four (generation four) children, we are able to measure germline mutations in hundreds of individuals, eliminate false positives, and assign mutations to a parent-of-origin. With large family sizes, we observe substantially greater power to detect nonzero heritability than with trios, and can estimate repeatability. Repeatability provides an upper bound on heritability and has never been calculated for mutation rates. We observe low repeatability of 0.15 and 0.51 for maternal and paternal mutation rates, respectively. Thus, detecting nonzero maternal mutation-rate heritability may be impossible in trio- or family studies.

Accordingly, initial results show low-to-zero heritability for both maternal and paternal mutation rates. While preliminary, these findings indicate that GTG provides novel resolution critical for accurately estimating the heritability of germline mutagenesis and, as we will present, related genomic traits. The sequencing of these pedigrees has broad implications for both molecular evolution and genomic medicine, helping quantify an individual's unique risk for mutational burden.

1404

Genome association studies of range-wide introduction of Douglas fir in Europe

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Douglas fir (Pseudotsuga menziesii) is a coniferous tree species native to western North America. It can grow up to 100 m tall and live for 1000 years, while it has substantial economic importance due to rapid growth and high-quality timber. The species was first introduced to Europe in the nineteenth century and has since been progressively planted, becoming one of the most common non-native tree species in several central European forests. A large-scale European common garden trial of Douglas fir was established in Denmark in the ‘70s. The common garden comprises trees originating from across the species’ natural geographic range, providing a unique opportunity to investigate growth performance and adaptive capacity under the Northern European climate conditions. By applying quantitative genetic approaches together with an Axiom single-nucleotide polymorphism (SNP) genotyping array, we seek to investigate the species' performance in the Danish forests and identify any genetic variants associated with environmental adaptation. Furthermore, the use of genome-wide genetic markers allows for detailed analyses of population structure throughout the native range and supports the identification and verification of the geographic origin of the Douglas fir that has been planted in Denmark. The outcomes of this project are highly valuable for improving our understanding of the genetics basis and survival potential of Douglas fir in a changing climate in Europe, as well as potentially improving tree breeding of one of the most ecologically and economically important tree species on the continent.

1407

Zooming into Host–Microbiome Evolution via Micro-Scale Spatial Metagenomics

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Understanding microbial contributions to host biology and evolution is central to the hologenomic framework, yet most metagenomic studies rely on bulk sampling that averages across spatial heterogeneity and masks local ecological and selective contexts. To address this limitation, we developed Micro-Scale Spatial Metagenomics (MSSM), a methodology that reconstructs host-associated microbial communities directly from intact gut tissue at micron-scale resolution. MSSM combines laser microdissection of cryosections, ultra-low-input shotgun metagenomics, and genome-resolved bioinformatics to characterise communities from microsamples as small as ~500 µm², corresponding to ~100 bacterial cells.

Using the chicken gut as a model system, MSSM revealed fine-scale spatial heterogeneity in community composition and functional potential, pointing to spatially structured microbial assemblages and localised segregation of metabolic capacities. Additionally, MSSM recovered de novo assembled bacterial genomes absent from the conventional macro-scale dataset. At the strain level, MSSM uncovered coexisting strain lineages with distinct spatial distributions and host-specific occurrence patterns. At the SNP level, microdiversity analyses showed that clonal populations cluster at spatial scales below ~200 µm.

We implemented MSSM alongside conventional metagenomics to investigate gut-associated microbiomes across controlled host perturbations, including dietary shifts, microbial supplementation, infection, and vaccination, in poultry and swine. Using large collections of spatially resolved microsamples, we discuss methodological insights, analytical constraints, and emerging spatial patterns that are not accessible through bulk sampling. By resolving microbial communities at the spatial scales at which ecological interactions and population structuring occur, MSSM expands the hologenomic toolkit and enables spatially explicit analyses of microbial evolution, niche partitioning, and host-associated interactions.

1411

Evidence for asynchronous rediploidisation following the 1R whole genome duplication in vertebrates

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Vertebrate genomes have been shaped by multiple rounds of whole genome duplications (WGDs). The first round (1R) happened before gnathostomes and cyclostomes diverged, with both subsequently experiencing independent WGDs (2R). WGDs, providing much raw genetic material, have been implicated in the evolution of vertebrate innovations.

Early WGDs have not been well-studied in the context of rediploidisation, the under-appreciated process of polyploid genomes returning to diploidy. Rediploidisation can occur asynchronously over millions of years. Only after re-establishment of diploid inheritance can gene duplicates (ohnologs) diverge in sequence and function. Rediploidisation extending past cyclostome-gnathostome divergence would therefore facilitate lineage-specific ohnolog establishment following 1R, and emergence of gnathostome- and cyclostome-specific novelties.

Utilising publicly-available genomes, including recently-released hagfish genomes crucial for our analyses, we investigate if 1R ohnologs rediploidised before or after gnathostome-cyclostome divergence (pre-speciation or post-speciation).

Our in-depth Hox analysis, including identification of previously missing/mislabelled cyclostome Hox genes, reveals both simple and compositionally-aware phylogenetic models support post-speciation Hox cluster rediploidisation. Genome-wide, we incorporate macro-synteny with topology information to label trees featuring extensive gene loss, substantially increasing our dataset size compared to previous work. We recover both pre-speciation and post-speciation ohnolog sets. These ohnologs cluster by rediploidisation timing when mapped onto modern genomes, furthering confidence in our classifications, with rediploidisation thought to occur segmentally.

Our findings indicate some genomic regions rediploidised early following 1R, with others remaining tetraploid until after cyclostome-gnathostome divergence. Functional analysis of pre-speciation and post-speciation ohnologs may shed further light on the impact of asynchronous rediploidisation on vertebrate, including human, evolution.

Disentangling the relationships between microbial taxa and metabolic outputs in a seaweed holobiont

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In molecular evolutionary biology, genotype-phenotype maps are common tools for understanding the associative relationships between genetic variation and phenotypic variation. Combined with mechanistic assays, these maps can elucidate the causal contribution of specific genes or mutations to specific phenotypic outcomes. Previous work has recognized the strength of this approach for understanding the contribution of microbial biodiversity to ecosystem function. However, for many ecologically important holobiont systems, we still lack empirical knowledge of the ecological and evolutionary mechanisms that give rise to observed associative relationships.
In this work, we used field-based metabolomic data to generate an associative map between bacterial community composition and the metabolic outputs of the bull kelp Nereocystis luetkeana. We applied antibiotics to kelp in situ and analyzed the resulting metabolic profiles in comparison to untreated controls to broadly address the question ‘how do kelp-associated bacteria affect host metabolic response?’ We then identified specific metabolic features associated with disturbance of the microbiome and will test the effect of these compounds on the growth of diverse kelp-associated bacteria in the lab. Eco-evolutionary theory predicts many possible metabolic interactions between microbial community members and kelp hosts. We investigate three hypotheses: 1) Compounds detected in environmental samples are toxic to kelp-associated bacteria. 2) Compounds detected in environmental samples are carbon sources for kelp-associated bacteria. 3) Compounds detected in environmental samples are protective against oxidative stress for kelp-associated bacteria. The results of this work will address different mechanistic hypotheses about the nature of host-microbe metabolic interactions in an understudied seaweed system.

Completing the Tree of Life with High-throughput Phylogenetics

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Understanding evolutionary relationships among species is central to evolutionary biology and functional genomics. Despite abundant sequence data, species representation in existing molecular tree aggregation databases remains limited because sequence curation for molecular phylogenetics is labor-intensive. Some efforts to achieve species completeness in large phylogenies have used data-free imputation approaches, which cannot recover true topological relationships or divergence times and may mislead macroevolutionary analyses. We introduce an end-to-end automated platform for high-throughput phylogenetics and divergence time estimation. Using this platform, we performed de novo tree inference to produce three new ultra-large, time-calibrated phylogenies of Vertebrates (>50,000 species), the insect order Diptera (>18,500 species), and the plant clade Monocots (>26,000 species). These yield increases of over 50% in species representation for each group compared with the entire aggregated time-calibrated molecular phylogenetics literature in the Timetree of Life 5 database. We validate the accuracy of our trees by comparing them with gold-standard phylogenomics studies. We also show that greater species completeness improves macroevolutionary metrics compared with preexisting trees and enhances genotype-phenotype predictive modeling of the convergent acquisition of C4 photosynthesis in monocots. Our freely available cross-platform software not only automatically generates a phylogeny for a user-specified target taxonomic group but also provides marker alignments that will be useful to researchers who wish to perform manual curation. Generation of de novo phylogenies across the tree of life is now feasible and can be continuously updated to incorporate the latest data.

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Detecting balancing selection using ancestral recombination graphs

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Balancing selection maintains polymorphism within populations and, by definition, contributes to genetic variance in fitness. Identifying its genomic targets is therefore central to understanding the genetic basis of evolutionarily relevant phenotypic variation. Genome-wide scans can detect balancing selection through its signature of excess polymorphism at linked sites; however, existing methods are generally conservative and likely miss many biologically relevant targets. Here, we show that leveraging ancestral recombination graphs (ARGs) substantially improves power to detect balancing selection relative to current state-of-the-art approaches. We evaluate several ARG-based summary statistics, some of which have higher power than existing methods for the scenarios we simulated. Applying this framework to ARGs inferred from human genomic data identified candidates with properties that strongly suggest that they are true targets of balancing selection, rather than the consequence of complex demographic processes. We identify well known-targets of balancing selection as well as novel candidate targets. More broadly, our results demonstrate that ARG-based approaches provide a powerful framework for detecting balancing selection, with great promise for non-model species, where traditional methods (largely developed with a focus on humans) may be especially underpowered.

Gene losses promoted skeletal innovation and cancer resistance in turtles

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Stem-turtles were the ultimate “hopeful monsters”. They reconfigured the tetrapod skeleton giving rise to their unique body plan with one of the most iconic vertebrate novelties: the turtle shell. In addition, turtles adapted to low oxygen environments and evolved extreme longevity with exceptional cancer resistance. However, progress toward understanding the molecular basis of these traits has been limited by the lack of reference genomes for one of the two extant turtle clades, the side-necked turtles (Pleurodira).
In this study, we generated seven high-quality reference genomes for side-necked turtles to comprehensively investigate stem-turtle genome evolution.
We discover several gene losses associated with evolutionary innovations in stem-turtles including skeletal transformation, hypoxia tolerance and cancer resistance. Notably, mutations in two of the twelve genes lost in stem-turtles cause dwarfism with short, stout body shapes in mammals, resembling the body shape transformation in stem-turtles. Loss of NMRAL1 further decoupled increased oxidative stress exposure from stress-induced error-prone DNA repair. Beyond gene losses, we detect signatures of positive selection on genes across successive functional stages from early damage prevention and accurate DNA repair (e.g., ATMIN, SETX) to decisive cell elimination mediated by the p53-inducible CDIP1. These genomic changes are consistent with slow growth, reduced mutation accumulation, and enhanced cancer resistance in turtles. Overall, our results highlight gene loss as an important driver of phenotypic innovation and identify key genomic mechanisms underlying turtle skeletal evolution and cancer resistance.

Genome reorganisation in Ithomiini butterflies

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Chromosome-level structural variation, such as fusions, fissions, inversions, and translocations, can directly influence gene flow by disrupting meiosis and reducing hybrid fitness. In addition, changes in linkage disequilibrium between loci can indirectly promote reproductive isolation and speciation by altering the efficacy of selection and preserving coadapted gene complexes. Lepidoptera (butterflies and moths) generally have a conserved karyotype, with a modal haploid chromosome number of 31. However, there are some lineages that exhibit extensive chromosomal rearrangements. Among these, the Ithomiini tribe displays exceptional karyotypic diversity, with haploid chromosome numbers ranging from n = 5 to n = 120 (Brown et al. 2004). Ithomiini is a taxonomically rich group that has been extensively studied for its roles in mimicry rings, chemical ecology, and tropical biodiversity. Its rapid radiation, including recent explosive diversification in several genera, makes it a good system for investigating links between structural genome evolution and speciation. Here, we characterise genome architecture and quantify chromosomal rearrangements across 150 genomes spanning the Ithomiini phylogeny. We identify substantial variation in genome size driven by differences in transposable element content, as well as an association between genome size and chromosome number. Rates of chromosomal fusion and fission vary dramatically across the phylogeny and through time, with distinct patterns among subclades. We further explore potential mechanisms underlying these rearrangements, including repeat accumulation, gene gains and losses, small-scale structural variation, and potential environmental factors, such as plant derived genotoxins.

Tracing the Genomic History of Spotted Owls and Their Relatives

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Spotted owls (Strix occidentalis) comprise three subspecies that inhabit mountain forests in western North America. Over the past one hundred years, spotted owls have experienced extensive habitat loss, particularly in the Pacific Northwest, where they have become a symbol for the preservation of old-growth forest ecosystems. These threats have presumably intensified with the recent expansion of barred owls (their sister species) into spotted owl territories. To investigate the ancient and recent demographic history of spotted owls and their close relatives, we obtained and analyzed over 350 owl genomes from across the species' range, including 14 mexican spotted owls, a subspecies for which genomic data has been virtually non-existent. We found substantial population structure across subspecies, particularly between Northern/California spotted owls and Mexican spotted owls, which diverged around a hundred thousand years ago. Using SFS- and genealogy-based methods, we found signs of admixture between Northern and California, but no evidence for admixture between California and Mexican spotted owls. We sampled several spotted-barred owl hybrids across the West Coast, most of which are genetically F1s or backcrosses, pointing to a strong reproductive barrier after the first generations. We also looked for evidence of ancient admixture between the Mexican spotted owls and barred owls, as they may have coexisted longer than previously assumed. Our study provides insights into the recent and ancient demography of a flagship species that has been threatened by anthropogenic change, with important implications for ongoing conservation debates.

A Tale of Skink Sex Chromosome Evolution

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Sex chromosomes typically originate from a pair of autosomes after one member acquires a sex-determining locus across which recombination becomes suppressed with its partner. Following the onset of recombination suppression, the sex-specific chromosome—here the Y—loses gene function and undergoes structural and sequence degeneration, resulting in a gene poor, repeat rich, small chromosome that recombines with the X in a small pseudoautosomal region (PAR). Here we present near chromosome level genome assemblies for four genera of skinks. Surprisingly, each genus has a unique trajectory of sex chromosome evolution. The genus Bassiana is the only one that has what would be considered the traditional trajectory of sex chromosome evolution described above. The genus Pseudemoia has a small PAR, but in contrast to Bassiana has not wasted away. In the genus Lampropholis, there is no evidence of sex chromosomes, suggesting that the Y has been lost and there is a new genetic or environmental sex determining system. Finally, the genus Tiliqua has a large PAR and small X/Y specific regions. In these regions there is direct evidence of inversions on the Y that supressed recombination with the X. These skinks offer rare insight into different evolutionary trajectories that shape sex chromosomes.

RepeatOBserver: Tandem repeat visualisation and putative centromere detection in 2000 genomes from across the tree of life

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Tandem repeats play an important role in centromere structure, subtelomeric regions, DNA methylation, recombination and the regulation of gene activity. Although chromosome-scale genome assemblies are increasingly available for a wide range of non-model species, there is still little information on species specific repetitive elements and rarely experimentally verified centromere locations. The ability to predict putative centromeres and detect imperfect repeats from just the genome sequence alone can help us better annotate these genomes.

RepeatOBserver is a new bioinformatics tool for visualizing chromosome-scale repeat patterns and identifying putative centromere locations and sizes in chromosome-scale genome assemblies (https://github.com/celphin/RepeatOBserverV1). RepeatOBserver detects a broad spectrum of repeats ranging from 3 to 20,000 bp in length, without requiring prior knowledge of repeat sequences or parameter optimization. In addition to centromere prediction, the tool enables visualization of potential inversion boundaries, retrotransposon clusters, and gene copy number variation.

By analyzing 107 chromosomes with known centromere positions, we observe that centromeres consistently occur in regions exhibiting the lowest diversity of repeat types. Using this information, we apply a genomic Shannon diversity index to predict centromere locations in an additional 2,000 chromosome-scale genome assemblies. We will discuss patterns observed in putative centromeres across 2,000 genomes spanning the tree of life, as well as other genomic features that can be revealed using RepeatOBserver.

Heterosis vs. adaptation: genomic insights from a 25-year mixed-source plant translocation program

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Mixed-source translocation can reduce immediate extinction risk in endangered populations, but their long-term consequences remain debated. Arenaria grandiflora L. (Caryophyllaceae) experienced a drastic decline in the Fontainebleau Forest (Ile-de-France) in the late 20th century, likely due to inbreeding depression. To save it from extinction, local and non-local (Chinon) plants were multiplied in vitro and introduced in three unoccupied sites in Fontainebleau in 1999. Yearly monitoring of plant's fitness coupled with analyses based on microsatellites revealed better fitness of admixed individuals. To gain more insights into the genetic consequences of the translocation, we whole genome sequenced a time series consisting of : i) individuals from the reintroduced populations (2007 and 2023) ii) part of the original clones; iii) samples from the 19th century from Fontainebleau (16 individuals) and Chinon (14 individuals) stored in the MNHN herbarium. Reintroduced populations exhibited increased genome-wide diversity and reduced inbreeding (shorter runs of homozygosity) relative to pre-translocation populations. Extant individuals showed wide variation in ancestry proportions, with non-local ancestry increasing more than expected under neutrality between 2007 and 2023, consistent with previous microsatellite-based results. To disentangle the roles of heterosis and local adaptation, we are estimating the variation in mutation load within the temporal series and searching for genomic signatures of the potential advantage of non-local alleles. Finally, we are conducting forward-in-time simulations using SLiM to predict the future evolutionary trajectory of the reintroduced populations and inform conservation management. This study provides a rare opportunity to assess the real-time genomic consequences of a mixed-source translocation program.

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Exploring Time-Nonreversibility in Deep Phylogenetics with ABySS

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Modern genomic sequencing technologies mean we now have more resources than ever to decipher the tree of life using phylogenetic inference methods. However, an abundance of data cannot always compete with systematic biases such as long branch attraction, where mutational saturation causes distant lineages to be incorrectly inferred as closely related. Phylogenetic inference traditionally involves the use of a time-reversible substitution model, favoured for their simplicity and small parameter-space. But as the field grows to tackle more ancient and saturated lineages, we must investigate under-explored approaches to modelling substitution processes, in the hopes of more realistic and effective inference.

ABySS (Advanced Bayesian Site and Substitution) is a new software package with a generalised time-nonreversible substitution model for use in a Bayesian framework (BEAST 2) with any type of data. I will discuss how simulation studies show the benefits of time-nonreversible models for root placement accuracy even with saturated data, and the potential cost of time-reversibility assumptions on inference. I will also discuss the model's performance in empirical contexts, and how much time-nonreversibility may be found in deep phylogenies.

Heavy-tailed dispersal and its impact on local adaptation: Revisiting the British peppered moth

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Local adaptation arises when selection varies across space, and gene flow is limited. The melanism cline of the British peppered moth (Biston betularia) is a canonical example, yet it sparked controversy: classical migration–selection models could not fit the Liverpool–Wales transect using selection coefficients from mark–release–recapture (MRR) studies (Bishop 1974), and fits were often rescued by invoking inflated dispersal and non-visual selection advantage (Cook 1980; Mani 1980); this fueled doubts about the classical interpretation (Coyne 1998; Hooper 2002). We argue the mismatch reflects a modeling limitation—assuming Gaussian dispersal—rather than a failure of the selection narrative. We derive a general approximation for migration–selection clines under broad classes of symmetric dispersal distributions, including leptokurtic/heavy-tailed distributions, and under arbitrary spatial selection gradients. We develop a maximum-likelihood framework that tests for heavy-tailed dispersal and jointly estimates the tail-decay exponent and a local dispersal scale parameter from spatial allele-frequency clines. Crucially, the framework is general and applies to many empirical clines directly. We connect the approximation to previous theoretical work done on the topic of clines, including existence conditions in Slatkin (1973) and Nagylaki (1975), and recover the Gaussian diffusive limit as a special case. Applied to the historical transect, our method fits the moth data using the MRR-measured selection coefficients, inferring realistic local dispersal and a tail-decay exponent indicative of heavy-tailed dispersal, consistent with wind-borne larval ballooning in Biston betularia (Liebert and Brakefield 1987). Our work provides evidence for a genetic signature of heavy-tailed dispersal that is likely important for many systems experiencing local adaptation.

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Evolutionary Signatures of Host–Pathogen Interactions Revealed by Polygenic Adaptation in Ancient Genomes

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Pathogens have been among the most persistent and powerful selective forces shaping human evolution, influencing immune diversity, physiology, and population-level responses to disease. Yet the genomic mechanisms by which host populations adapt to pathogen pressure, particularly through polygenic traits, remain incompletely understood. Here, we use ancient DNA (aDNA) data to investigate how past epidemics have reshaped human susceptibility and resistance to infectious diseases across millennia. Using GWAS results for over 1,000 immune- and infection-related traits, we calculated polygenic risk scores (PRS) for more than 3,000 publicly available ancient human genomes from Eurasia spanning prehistory to the historical era. This framework allowed us to track changes in immune-related polygenic traits through time. We test the hypothesis that major shifts in pathogen landscapes imposed selective pressure on standing genetic variation, leaving detectable signatures at the polygenic level in ancient genomes. We identify statistically significant shifts in PRS distributions associated with three major epidemiological transitions: the Antonine Plague, the Justinian Plague, and historical (putative) measles outbreaks. The implicated biological pathways extend beyond canonical immune genes and include lipid metabolism, megakaryocyte development, and hormonal signaling, highlighting the systemic nature of host defense and the infection response. Together, our results demonstrate how integrating aDNA data with polygenic frameworks can reveal evolutionary interactions between hosts and pathogens, providing insights into immune diversity and resilience in changing ecological and epidemiological contexts. We discuss these findings in light of methodological limitations, including the portability of PRS across time and populations.

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Quantifying the Genome-Wide Effect of Polygenic Selection over a Single Generation

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Genomic variation is shaped by neutral and selective evolutionary forces such as genetic drift and selection. While their relative contribution is actively debated, how short-term evolutionary change plays out remains relatively unaddressed. Most genetic evidence of short-term selection has been based on the identification of major allele frequency (AF) changes at few loci with large selective advantage. Yet most traits are polygenic, where short-term selection response is shaped by thousands of loci with small AF changes that are difficult to distinguish from drift. Here, we quantify the genome-wide effect of polygenic selection over one generation using the signal mediated by the random association [linkage disequilibrium (LD)] of loci with a large set of selected loci across the genome. We rely on the idea that loci in stronger LD with selected loci show greater variance in AF change than expected under drift. We derive expressions relating variation in LD among loci to the variance in AF change due to linked selection and drift, and leverage a mathematical framework that quantifies their relative contribution to a single generation of AF change. To demonstrate our approach, we decompose the genome-wide variance in AF change in the UK Biobank using AF changes predicted from the fitness proxy of the number of children, showing that there is a small percentage of AF change due to linked selection even within a generation. This framework would allow to investigate the short-term, genome-wide effects of polygenic selection across a wide range of species.

Identifying the presence of Yersinia pestis in Medieval Turkey during the Second Plague Pandemic

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Yersinia pestis, the causative bacterium of the Plague, killed ~30-50% of Europe's population during the Black Death (1348-1353), the initial epidemic wave of the second Plague pandemic (1346-1840). This devastating disease persisted in cyclical outbreaks across Afro-Eurasia for 500 years, and its descendants established global reservoirs, which continue to cause outbreaks today. Genomic studies of ancient Y. pestis recovered from archaeological remains have attempted to trace the bacterium's origins, locate reservoirs, and understand these patterns of persistence and reintroduction. One significant region currently lacking genomic evidence of Y. pestis is the Ottoman Empire. Situated between Asia and Europe, Eurocentric narratives continuously paint the Ottoman Empire as an importer of Plague into Europe. Here, we screen 289 human and animal remains from across Medieval and Early Modern Turkey for evidence of Y. pestis and its reservoirs. We recover two ancient Y. pestis genomes from early outbreaks of the pandemic at the historically significant site of Nicaea, providing the first genomic evidence of ancient Y. pestis in the region. We then grapple with the complications of weaving together genomic and historical narratives to identify specific epidemic waves. As well as test the impact of stringent and standard mapping criteria on variant calling and subsequent phylogenetic positioning. We then place the samples on an updated second pandemic phylogeny and interpret the significance of their placement with respect to understanding the trans-continental dynamics of Plague spread during the second Plague pandemic.

Comparative analysis of KAP1 binding reveals species-specific KRAB-ZNF regulatory landscapes in primates

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Phenotypic differences between species often arise from complex gene regulatory interactions. KRAB zinc finger (KRAB-ZNF) proteins play a central role in shaping this diversity. They are rapidly evolving transcription factors that silence transposable elements (TEs) and regulate gene expression. KAP1 is considered a universal cofactor of KRAB-ZNFs; consequently, KAP1 binding marks sites of KRAB-ZNF activity. Despite their evolutionary importance, a systematic cross-species analysis of KRAB-ZNF targets is still lacking.

Here, we address this gap by analyzing KAP1 binding sites identified by ChIP-seq in B-lymphoblastoid cell lines from humans, chimpanzees, and orangutans, with three biological replicates per species. We identified thousands of KAP1-binding sites per species, the majority overlapping TEs, predominantly in intronic and intergenic regions. Gene ontology analysis revealed that genes proximal to KAP1 peaks in chimpanzees and orangutans were enriched for neuronal development functions and were more frequently downregulated compared to humans. Comparative analyses showed that most KAP1-bound regions are species-specific and exhibit low sequence conservation. Locus-specific quantification of TE expression in the same cell lines demonstrated that KAP1-bound loci are generally repressed and rarely transcribed. By integrating motif occurrence, expression data, and peak overlap, we linked differentially expressed KRAB-ZNFs to putative target genes and constructed a candidate regulatory network. Together, our results suggest that species-specific KRAB-ZNF targeting contributes to differential TE regulation and neuronal gene expression across primates, potentially influencing lineage-specific aspects of brain development.

A pangenomic approach to evaluate fate of ancesteral and novel structural variants in a homopoloid hybrid sparrow.

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The importance of hybridization as a factor driving evolutionary novelty and speciation is increasingly recognized. Despite its significance, understanding the processes underlying sorting of genetic variation and the formation of novel genetic variation within hybrid taxa remains a major challenge. The Italian sparrow (Passer italiae) serves as an intriguing model for investigating these processes, as it is a young hybrid species between House sparrow and Spanish sparrow. It exhibits significant genomic mosaicism across its distribution in Italy and Mediterranean islands, with parental ancestry proportions ranging from 25% to 75% depending on population. Current reference-based methods often fail to capture complex genomic variation in hybrid systems. To address this, we assembled individual genomes from both parental species as well as three isolated hybrid populations (Crete, Corsica, and Sicily). We then used these individual assemblies to construct a pangenome to capture the full extent of genetic diversity within and among populations of Italian sparrows. This pangenomic approach gives us an unbiased view of the distribution of ancestral, derived, and novel genetic variation within and among the species, but will also enable us to identify the genetic basis of transgressive gene expression and other phenotypes in the hybrid populations. In this study, we use this pangenomic framework to track the evolutionary fate of structural variants (SVs) inherited from the two parental lineages. We assess how parental as well as novel SVs are sorted in hybrid populations with varying ancestry proportions and investigate whether they are retained or purged.

Fine-scale mapping of meiotic recombination in Saccharomyces cerevisiae unveils shifts in genetic exchanges driven by DNA heterologies

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Meiotic recombination is a driver of genetic diversity, yet its fine-scale mapping remains technically challenging and is limited by marker density and availability of gametes. HapDS is a deep sequencing approach that reconstructs haplotypes from hundreds of thousands of short chromatid fragments while preserving their molecular identities. This large number of haplotypes (~300 base pairs long) enables the detection of rare recombinants and the accurate estimation of very low recombination frequencies. Using HapDS in Saccharomyces cerevisiae we mapped genetic exchanges at four or 16 different genomic regions each spanning 1.5 kilobases in a hybrid cross (SK1BY) and in a SK1 strain with multiple informative sites introduced by recombineering. We observed clear differences in recombination between sexual and asexual divisions and mapped recombination with resolution primarily determined by marker density rather than sequencing depth, albeit the short haplotype length precluded the distinction between crossovers and non-crossovers. Further, recombination activity closely matched programmed DNA double-strand break (DSB) sites at kilobase resolution. However, at the base-pair level, HapDS revealed sharp recombination peaks adjacent to gaps coinciding with DNA palindromes, hairpins, or large sequence heterologies. We hypothesize that these DNA sequence features are important modifiers of genetic exchanges influenced by alternative DSB repair in place at secondary DNA structures, which could also be a hub for de novo mutations.

Coalescent-Based Introgression Inference: Theory, Biases, and Solutions

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The evolution of species has traditionally been viewed as a bifurcating process; however, studies over the past 16 years have revealed that introgression is a pervasive force shaping genetic variation across the Tree of Life. Introgression is typically inferred from genomic data using statistics that quantify discordance between marginal genealogies and an assumed species tree, often using site patterns or genetic distances.

Here, we use coalescent theory to derive the expected branch lengths for all six site patterns and the expected pairwise coalescence times under a single-pulse model with variable population sizes. These results allow us to analytically study the expectations of previously proposed introgression statistics, including those proposed by verbal arguments and simulations. We show that all existing statistics are inherently biased by unavoidable contributions from incomplete lineage sorting (ILS) and therefore cannot provide unbiased estimates of the introgression proportion. Motivated by this, we introduce two new statistics. First, $D^\star$ is the only statistic that is fully agnostic to ILS, providing a robust test for the presence of introgression. Second, $f^\star$ dynamically corrects bias in estimating the introgression proportion by approximating a demographic nuisance parameter, enabling more accurate inferences without prior demographic knowledge.

We benchmark existing and new statistics for detecting and quantifying introgression at genome-wide and local scales using empirical human- and canine-like demographic models that incorporate heterogeneity in recombination and mutation rates. We find that $D^\star$ consistently outperforms existing approaches for detecting introgression, while $f^\star$ substantially improves estimation of introgression proportions, especially when demographic bias is severe.

Multi-Omics Characterization of the Hibernation Phenotype in Ground Squirrels

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Hibernation is a complex physiological state that enables mammals to survive prolonged periods with minimal metabolic activity. A critical aspect of this strategy is the dynamic control of body temperature. Small-bodied hibernators within the squirrel family (Sciuridae) exemplify extreme thermoregulatory strategies by cycling between near-freezing body temperatures and euthermia during energetically demanding interbout arousals. Central to this process is brown adipose tissue (BAT), which plays a crucial role in non-shivering thermogenesis via mitochondrial biogenesis and respiratory chain uncoupling.

To uncover the genomic bases underlying hibernation adaptations, in combination with previously available genomes, we generated high-quality, chromosome-scale genomes for four Marmotini species, including three hibernators from the genera Ictidomys, Marmota, and Callospermophilus, alongside one non-hibernating relative (Ammospermophilus leucurus). Our results revealed distinct signatures of positive selection in genes linked to metabolism, tumor suppression, and blood coagulation within hibernating species. Gene family expansions were notably enriched in lipid metabolism pathways, with additional gene copies showing high expression in BAT, likely supporting thermogenic processes. Adaptation through gene loss appears to have played a minor role in these evolutionary changes.

Transcriptomic profiling further revealed conserved seasonal gene expression programs associated with BAT remodeling during active and hibernating states, contrasting with a blunted thermogenic gene expression response to cold in A. leucurus, which instead compensates through skeletal muscle shivering thermogenesis but shows limited capacity for muscle remodeling necessary for prolonged cold tolerance.

Collectively, this work highlights how genomic changes and transcriptional coordination drive the multifaceted adaptations that enable hibernation in ground squirrels.

Ecology and evolution of the mammalian oral microbiome elucidated using museum specimen metagenomics

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Despite growing interest, the microbiomes of wild animals, remain poorly characterized, especially for body sites beyond the gut, and largely due to the challenges of sampling in the wild. Here, we use dental calculus preserved on museum specimens to investigate the ecological and evolutionary drivers of the oral microbiome across 32 ecologically and phylogenetically diverse mammal species, constituting, to our knowledge, the most diverse dataset of animal oral microbiomes to date. We show that host diet and digestive physiology shape both the composition and function of the oral microbiome, consistent with patterns reported for the gut. However, in contrast to the gut, where herbivores harbour the most diverse microbiomes, oral microbiome diversity is highest in carnivores and omnivores, which are enriched in taxa and functions associated with protein and lipid degradation. Host phylogeny only weakly affects microbiome composition across broad mammalian diversity, but its importance increases within narrower host clades. At the same time, we identify several microbial taxa showing signatures of host co-diversification, many of which are rumen-associated and exhibit host-specific metabolism. Together, these findings show that the oral microbiome follows eco-evolutionary dynamics that are related to, but distinct from, those governing the gut microbiome, and demonstrate the relevance of this mostly overlooked microbial community for studies of wild animals.

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Inference of high-dimensional fitness landscapes with site-specific contributions to epistatic interactions

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Although fitness landscapes were long treated primarily as theoretical objects, recent advances in genetic engineering and high-throughput phenotyping now allow us to make millions of fitness measurements from high-dimensional empirical fitness landscapes. Here, we introduce two new families of highly expressive Gaussian process models for Bayesian inference of fitness landscapes from this type of data. These models work by defining a prior distribution over all possible fitness landscapes, where the hyper-parameters of the prior are interpretable in terms of classical quantities from the fitness landscape literature, and the resulting landscapes include epistatic interactions of all orders. The first family of models is parametrized by the tendency of individual mutations to participate in epistatic interactions, allowing us to identify key mutations that broadly interact with many others. The second family of models is parametrized by the tendency of specific pairs of mutations to be involved in epistatic interactions, allowing us to identify not only highly interactive mutations but also the particular combinations of mutations with which they interact. Moreover, this additional flexibility naturally accommodates interactions with the environment by treating different environmental conditions as additional loci with environment-specific parameters. These models achieved high predictive performance, and allowed us to identify both known and novel features and genetic interactions across a wide range of datasets, including protein sequences, regulatory elements and genome-wide SNPs. Overall, this work provides a general and scalable framework for modeling empirical fitness landscapes and for deciphering how genetic interactions and environmental context shape phenotypic variation in natural systems.

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A Statistical Framework for Mutation Model Inference of Tandem Repeat Variants via the Ancestral Recombination Graph

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Short tandem repeats (STRs), or microsatellites, are repetitive sequences that make up approximately 3% of the human genome. More than 10,000 STR variants are known to influence gene expression and account for 10–15% of its heritability. Modern long-read sequencing technologies now enable us to determine STR genotypes with higher accuracy and investigate their role in complex traits. However, understanding the evolutionary and mutational behavior of STRs is essential to characterize their impact on different phenotypes. To this end, inferring the mutation model that governs STR variation is critical. This task is particularly complicated by the fact that the mutational dynamics vary substantially across loci. To solve this problem we created Tandem Repeat Ancestral recombination graph Mutational Analysis (TRAMA), a tool that infers the mutational process of each STR locus individually. For each STR, TRAMA uses information from the local Ancestral Recombination Graph (ARG), which encodes the complete local genealogical history of the samples. TRAMA uses a novel maximum-likelihood approach conditioning on the local ARG information to infer the most probable STR mutation model and its parameters per locus from observed variation in a set of samples. We demonstrate the method's accuracy through extensive simulations showing that it can infer the known mutational model acting on each loci along with the parameters that explain its evolutionary history across a wide range of scenarios. We further apply TRAMA to data from the Human Pangenome Reference Consortium - Phase 2. This work offers a path toward modeling STR mutational processes more accurately.

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Comparing population genomic variation across ploidy levels

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Present-day population genomic projects routinely deal with multi-species datasets, aiming to compare variation in organisms with different evolutionary histories. An impactful complication to analyzing such data is polyploidy: in autopolyploids, multiple allele calls per site have to be considered, and in allopolyploids, subgenomic attribution of alleles has to be preserved. Here, we present a workflow for accurate calculation of diversity and divergence statistics in polyploid and mixed-ploidy data using the ubiquitous Variant Call Format (VCF) files.

First, we have built a simple and flexible tool piawka that calculates population statistics in arbitrary sample sets in VCF files and handles missing data and polyploid variant calls correctly. It can be extended with further population statistics using simple module files. Built with large multi-species datasets in mind, piawka extracts information from typically overlooked cases like multiallelic sites that are biallelic in a given subset of samples.

Second, we suggest a way to compare genomic variation between diploids and allopolyploids through liftover of subgenomic coordinates onto the diploid assembly. Since polyploid systems present a corner case for whole-genome aligners, we developed a simplified liftover workflow based on alignments of orthogroups, implemented in the tool ulitka.

We showcase our developments with thousand-genomes-scale auto- and allopolyploid datasets: we used piawka to summarize diversity and divergence across diploid and tetraploid populations of wild perennial Arabidopsis species, and combining ulitka and piawka allowed us to study natural selection and introgression in Potamogeton, the largest aquatic plant genus on Earth with numerous diploid and allopolyploid species.

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Macro-evolutionary perspectives on a large chromosomal rearrangement underlying alternative life-histories in seaweed flies

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Discrete alternative phenotypes, such as morphotypes and ecotypes, are often underpinned by complex genomic architectures termed supergenes. How supergenes evolve over long evolutionary timescales remains an open question. They often occur in highly plastic regions and involve large-scale structural rearrangements, including successive inversions or translocations. At the evolutionary level, they can involve parallel evolution, introgression, and trans-species balancing selection. This highlights the importance of studying supergene evolution in multi-species systems with large geographical distributions.

In the seaweed fly Coelopa frigida, a 25-Mb supergene formed by nested chromosomal inversions is associated with polymorphism in several life-history traits. Indeed, males harbouring one arrangement have a larger size, longer development time, and higher reproductive success than males with the other arrangement. Interestingly, similar male size polymorphisms were qualitatively reported in other Coelopidae species across the globe, suggesting that this chromosomal rearrangement may be shared across species boundaries.

To address this hypothesis, we quantified development time in five Coelopa species, and size in 13 Coelopidae species, using machine learning-assisted high-throughput phenotyping. This supported the presence of phenotypic polymorphism comparable to C. frigida in some coelopid species – but not all. Then, for 17 species, we implemented a species vs. gene tree approach with a combination of short- and long-read data to investigate the supergene's phylogenetic origin and evolution. Using genome assemblies, we also studied inter-species synteny to retrace the structural dynamics in this genomic region. Our results provide valuable information on multi-species evolution of phenotypic polymorphism and structural rearrangements associated with an adaptive supergene.

Engineering Hope: How Genetic Rescue Biotechnologies are Reshaping Wildlife Conservation

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In 2020, Revive & Restore achieved something never accomplished before in conservation: we cloned an endangered black-footed ferret from cells cryopreserved 30 years earlier, restoring genetic diversity previously lost to the living population. This breakthrough represents just one application of what we call “the Genetic Rescue Toolkit” - an integrated platform of genomics, cell culture and reprogramming, reproductive technologies, and bioengineering that can enhance existing conservation measures and, particularly through gene editing, create entirely new opportunities to save species.

Since our founding in 2012, Revive & Restore has been developing this toolkit to address some of conservation's most intractable challenges, including helping species adapt to disease and climate change. Although many of these biotechnology applications are still in early research phases, they are no longer science fiction. We're now working with partners to ensure these options become available for some of the world's most endangered and biotechnologically challenging groups - amphibians, birds, and coral reefs. Looking forward, our work spans from the ambitious goal of passenger pigeon de-extinction to our most recently launched programs: expanding capabilities in stem cell reprogramming and democratizing conservation genomics through AI tools tailored for genomicists and conservation practitioners via our GAIA collaboration with partners at Rockefeller and Cornell Universities.

With strategic investments in conservation biotechnology today, it will be possible to save any species and ecosystem, no matter the severity of human-induced threats. In this talk, I'll share the key technologies underlying the Genetic Rescue Toolkit and highlight the pioneering projects demonstrating their real-world applications.

Germline mutation rate variation and its consequences for speciation in a cichlid adaptive radiation

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De novo mutations are the ultimate source of genetic diversity and can strongly influence evolutionary dynamics and biodiversity. Although germline mutation rates vary by an order of magnitude among vertebrates, their consequences for genetic diversity and speciation have been challenging to study. African cichlid fishes offer an exceptional system to address this challenge: extraordinary phenotypic and genomic diversity, with species richness and genetic diversity unevenly distributed across their adaptive radiation. Here, we leverage parent-offspring sequencing data from 21 families representing 19 Lake Tanganyika cichlid species to estimate germline mutation rates across a wide range of species abundance. We find substantial mutation rate variation among closely related species spanning a 14-fold range with a mean rate of 3.0×10^{-9} mutations per site per generation. We also detect shared mutations among siblings, evidence for mutation clustering, and shifts in the mutation spectrum. Mutation rates show a positive association with genetic diversity, suggesting that mutation rate heterogeneity may contribute to patterns of biodiversity. However, mutation rate variation alone does not fully account for the observed diversity as life-history traits, ecological factors, and long-term population size likely play major roles. Together, our results demonstrate that mutation rate variation shapes biodiversity patterns in adaptive radiations and should be incorporated into population genetic and speciation models.

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Gene-by-gene evolution of dosage compensation in a neo-XY sex chromosome system

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In eukaryotes with separate sexes, sex determination often involves heteromorphic sex chromosomes which have diverged as a consequence of recombination suppression. In species with very old heteromorphic sex chromosomes, dosage compensation adjusts for the fact that sex chromosomes occur as a single copy in the heterogametic sex. However, how dosage compensation evolve remains largely unknown because species with young sex chromosomes characterised by recent recombination suppression remain understudied. We discovered such young neo-sex chromosomes in the ant cricket Myrmecophilus myrmecophilus, which displays a neo-XY system. This system likely evolved approximately 7 million years ago from an XX/XO system through an X-autosome fusion. Comparative genomics has revealed the existence of three evolutionary strata on the X, with varying degrees of Y chromosome degeneration. While the first stratum corresponds to the X chromosome before fusion and has no homolog on the Y, the second and third strata have lost only a fraction of the Y-linked genes (~40% and ~25%, respectively). Using transcriptomics, we describe the ongoing evolution of dosage compensation in Myrmecophilus myrmecophilus, and show that it occurs on a gene-by-gene basis with respect to the degree of Y-linked gene degradation and expression.

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Genome plasticity through a large chromosomal inversion structures phenotypic and regulatory responses to environmental variation

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Structural variation represents a powerful, and often underexplored, source of genome plasticity with the potential to reorganize genomic architecture and shape how organisms respond to environmental variation. Among such variants, large chromosomal inversions can act by suppressing recombination and coupling linked genes and regulatory elements, facilitating both phenotypic and regulatory responses to selection. However, it remains unclear how these inversions shape phenotypic and regulatory differences across environments. Here, we investigate the evolutionary consequences of a large chromosomal inversion on chromosome Omy5 in Rainbow trout (Oncorhynchus mykiss) using a long-term common-garden experiment. This inversion, harboring approximately 1200 protein-coding genes, has been associated with alternative life-histories strategies, metabolism and circadian regulation, making it a strong candidate to explain both phenotypic and regulatory responses to environmental variation. Over two years, we followed 12 full-sib families reared under control and food-restricted conditions to test how inversion genotypes shape phenotypic expression and genotype-by-environment interactions (G×E) in fitness-related traits. We find that inversion genotypes, particularly individuals carrying the double inversion, show pronounced G×E effects, including consistent divergence in migration-related traits and reduced growth, under resource limitation. By integrating long-term phenotyping with transcriptomic profiling, preliminary RNA-seq results reveal important regulatory differences between inversion genotypes, with dozens of differentially expressed genes within the inverted genomic region itself. Together, our findings highlight how genome plasticity arising from structural rearrangements can generate environmentally dependent phenotypes by integrating genomic architecture and regulatory variation, with implications for species adaptive potencial and resiliance under climate change.

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From Specimen to Sequence: International Researcher Perspectives on Indigenous Data Sovereignty in Biodiversity Genomics

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Global biodiversity genomics initiatives are rapidly expanding large-scale sequencing and open data infrastructures to support evolutionary research, conservation, and comparative genomics. These efforts rely on extensive specimen collection and cross-institutional data sharing, often involving samples obtained from Indigenous territories. This raises questions about consent, governance, benefit-sharing, and Indigenous Data Sovereignty (IDSov), which affirms Global Indigenous Peoples' rights to control the collection, use, and stewardship of data derived from their lands and resources. Despite increasing discussions of IDSov, little empirical work has examined how biodiversity and evolutionary genomics researchers interpret and apply these principles in practice.

We conducted an anonymized, international online survey (24 close-ended questions) to assess researcher perspectives and decision-making across the genomics data lifecycle. The survey captured subdiscipline, career stage, institution type, and country of research, and randomly assigned respondents to one of three hypothetical vignettes focused on (1) specimen collection, (2) genome sequencing and data generation, or (3) reuse of publicly available sequence data. Vignette-based questions evaluated how respondents approach governance, permissions, and data-sharing decisions under realistic research conditions.

Preliminary results suggest that governance considerations are unevenly applied across project stages, with greatest attention at specimen collection but substantially less during downstream sequencing and secondary data reuse. Responses also highlight geographic and institutional asymmetries between sites of specimen collection and genomic analysis, and limited institutional guidance on IDSov-aligned data governance.

We discuss implications for evolutionary genomics workflows and data reuse practices, and opportunities to integrate IDSov-informed governance through collaboration with Indigenous scholars and community partners.

1491

The genomic architecture of rapid local adaptation under extreme demographic perturbations in native and invasive cichlid fish populations

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Cichlid fishes are a famous model in evolutionary research due to their rapid adaptive radiations. However, they are also important to humans as food source and pet fish. Both has led to rapid human-induced demographic and adaptive challenges. Here we analyse whole-genome sequencing data of large population samples of (1) Malawi cichlids under recent strong fisheries pressure that has led to extreme phenotypic and demographic responses and (2) man-made hybrid cichlids that rapidly expanded into a completely novel environment – ancient lake Matano on Sulawesi.

We apply existing and novel inference methods to reconstruct recent demographic histories and detect signatures of recent adaptation. Specifically, patterns of linkage-disequilibrium and identity by descent (IBD) prove highly informative in reconstructing very recent demography in a Bayesian inference framework.

In heavily fished Malawi cichlids, a combination of divergence-based and within-population, haplotype-based selection scans reveals recent allele frequency shifts consistent with widespread polygenic adaptation, including evidence for a role of structural genetic variants and gene flow in adaptation. Connecting selection evidence with genome annotation, differential expression and experimental data allows us to identify candidate genes for human-induced evolution of life history traits in response to fishing pressure.

Highly invasive hybrid-cichlids in Sulawesi show intriguing patterns of variation in hybrid ancestry. However, recent timeframes and strong drift during species expansion presents a severe challenge the inference of local adaptation, raising questions about limits to statistical inference.

Early Interferon Pathways as Targets of Selection in an Anthropogenic Yellow Fever - Primate System

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RNA viruses are among the strongest and most pervasive drivers of mammalian evolution, and Brazilian outbreaks of yellow fever virus (YFV) have revealed an extreme evolutionary paradox: marmosets (Callithrix) frequently survive infection while acting as efficient viral amplifiers, sustaining viral transmission that threatens humans and other primates. Both the pathogen and many of its contemporary primate hosts in southeastern Brazil are products of human activity. YFV was introduced into the Americas through trans-Atlantic human movement, and invasive marmoset species—C. jacchus and C. penicillata—have been widely translocated into southeastern Brazil via the pet trade, establishing large, bottlenecked populations with little input of new genetic variation. We leverage this fully anthropogenic system to test whether natural selection on innate antiviral pathways can nonetheless be detected. We analyze whole-genome data from >80 individuals spanning four Callithrix species, including introduced C. jacchus/C. penicillata and native taxa (C. geoffroyi and the critically endangered C. aurita), all of which may now experience recurrent, human-driven YFV exposure. We identify convergent signatures of putative positive selection across multiple tiers of early innate antiviral pathways. Candidate loci play roles in pattern recognition (TLRs), interferon signaling (TRIMs), and interferon-stimulated antiviral RNA metabolism (IFIT1, PDE12). These patterns point to pathway-level evolution of early antiviral response dynamics in timing and magnitude of interferon activation, suggesting a host tolerance-based strategy that limits immunopathology while permitting viral replication and amplification. This work establishes a foundation for functional studies linking host genetic variation to early antiviral responses in an “impossible” primate system.

1498

Leveraging Herbarium Collections to access Natural Genetic Variation

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Easy exploration of the natural genetic diversity can enh comparative and population genetics approaches for understanding the function and evolution of adaptive traits. We showcase our study based on whole genome sequencing of the entire herbarium collection of Siberian Arabidopsis lyrata. A. lyrata is highly variable outcrossing relative of Arabidopsis thaliana with multiple origins of autotetraploidy and multiple independent transitions to self-compatibility. Screening the genomes from the herbarium, we found autotetraploid A. lyrata lineages in Northern Urals and Central Siberia in addition to known Central European lineages. We showed that the establishment of Siberian tetraploids is mediated by introgression of adaptive alleles of meiotic genes from European tetraploid A. lyrata and Arabidopsis arenosa, despite large geographical distance. We combined the whole genome sequencing data of A. lyrata from several extensive studies, including ours, to cover the whole range of geographical distribution across Eurasia and North America reaching close to 1k samples. We provide interactive ways of genomic data exploration: a searchable genome browser with A. lyrata and A. arenosa alignments to their respective reference genomes, cross-linked by orthologous gene names, geographical distribution of samples, and their assignments to population structure clusters. As an example of use-case of this resource, available at arabidopsislyrata.org, we explored genome-wide associations with climate variables and latitude within one of the diploid A. lyrata lineages showing polygenic adaptation along day-length gradient in East Siberia.

1500

Expanding the Mammalverse of Genomes

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The Mammalverse is comprised of the ecologies and genomes of the approximately 6,800 extant and recently extinct mammal species. Improvements in sequencing technologies and assembly techniques have led to a dramatic rise in the availability and quality of mammal genomes in recent years. However, the gaps in genomic sampling of taxa in different geographies and ecologies are poorly characterized. Aligning NCBI data to the Mammal Diversity Database taxonomy, we find that only ~10% of mammals have had their genomes sequenced to date, many of which are low quality (two-thirds with scaffold N50 < 1 Mb). We also find biases regarding which mammals have genome data available, including sparse sampling of rodents, shrews, and bats globally. We review the current landscape of the Mammalverse of Genomes, including how disparity in genome availability and quality constrains our ability to study patterns of trait evolution, genome organisation, and repetitive sequence diversification. We also highlight the need for associating genome assemblies with preserved voucher specimens to future-proof these data to ongoing taxonomic changes. Each new assembly provides crucial insights into the evolution and diversity of mammals and their genomes across the last 180 million years, so planning with a view of the Mammalverse is well warranted.

1501

Cumulative epistatic changes in fitness effects drove contingency and entrenchment in the billion-year evolution of Hsp90

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Epistatic interactions can change the accessibility of a mutation within a protein by modifying its fitness effects as substitutions occur at other sites. However, no studies have directly evaluated historical changes in fitness effects with sufficient resolution to elucidate their temporal dynamics and genetic mechanisms. Here we experimentally track fluctuations in the fitness effect of every substitution that occurred along a billion-year-old evolutionary trajectory of the essential chaperone Hsp90 from a deep eukaryotic ancestor to modern Saccharomyces cerevisiae. We prepared mutant libraries containing every historical ancestral and derived amino acid states and used a high-precision bulk-competition assay to measure their selection coefficients when introduced into all 27 reconstructed ancestral backgrounds along this trajectory. Most changes in fitness effects were small between consecutive ancestors, but their cumulative change across multiple intervals was sufficient to change accessibility of many historical states at various points along the trajectory. Many substitutions were contingent on the long-term accumulation of multiple permissive substitutions; once these contingently permitted substitutions occurred, they immediately entrenched all their permissive modifiers, restricting their access back to the ancestral residue. Moreover, some permissive substitutions were contingent on prior permissive changes of their own, and some nonspecifically changed the accessibility of many target substitutions in a correlated fashion. Our findings show that the historical changes that occurred during Hsp90 evolution depended not just on their most temporally proximal epistatic modifiers but on a long chain of mutually contingent events that began in the long-distant past.

1502

The trans-Pacific voyage that shaped the pattern of genetic variation and enrichment of functional alleles in Native Hawaiians

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The evolutionary history can impact the genetic architecture of traits and diseases of a population. Native Hawaiians (NH) provide a notable example, having experienced serial bottlenecks and recent admixture. Using whole-genome sequencing (WGS) data from 1,065 NH individuals, we modeled their ancestry as a recent four-way admixture and defined Polynesian (PNS)-like ancestry as the dominant pre-colonial component on the Hawaiian Islands. We conducted three lines of investigation linking this demographic history to patterns of genetic variation and disease risk. First, identity-by-descent analyses accounting for admixture in NH revealed a stronger bottleneck in the PNS-like ancestry than in other ancestries, with an estimated effective size as low as ~600 individuals, possibly reflecting the combined bottleneck effects of recent colonization and multiple trans-Pacific voyages. Second, using a genealogy-based method, we detected fine-scale substructure within the PNS-like ancestry, consistent with long-term geographical isolation and correlates with Austronesian ancestries predating the founding of the NH population. Third, we observed enrichment of predicted functional alleles shaped by this history. We identified ~5 million alleles that are rare (<0.5%) in other populations but common (>5%) in NH. Driven by PNS-like ancestry, NH individuals carry 15–27% fewer rare and 4–19% more common functionally important alleles than individuals from other continental ancestries (p = 5e-3). Among the functional alleles most enriched in NH (>20% higher frequency), 132 are associated, in either direction, with risk of various diseases. Together, these findings underscore the importance of demographic context for interpreting genetic variation and disease risk in Native Hawaiians.

1504

Gene expression and disease susceptibility of the genetically depauperate Channel Island fox (Urocyon littoralis)

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Although conservation of endangered species is often focused on the time-sensitive aspect of increasing population numbers to avoid extinction, it is important to examine the unintended side effects if such efforts are successful. The Channel Island fox (Urocyon littoralis) is a species that approached near extinction in the early 2000s, with population declines up to 90% in four of its six island-specific subspecies. Remarkably, through interventions including captive breeding, numbers have increased substantially, with all time highs in recent years. However, the species' health and longevity remains at risk from genetic complications associated with long-term small population size as well as recent bottlenecks. One of the biggest health concerns is high levels of ear mite infections documented in three island subspecies. Specifically, inflammation from mites has been associated with development of ear tumors in Catalina Island foxes, but not in other similarly mite-infected subspecies. This is especially noteworthy because the original Catalina population decline was also driven by disease, specifically canine distemper virus. Our research explores underlying genetic factors contributing to the unique disease susceptibility of Catalina foxes through RNA-sequencing of foxes on all six islands in varying health and infection conditions. Preliminary Weighted Gene Co-Expression Network Analysis (WGCNA) shows individuals with early tumor indicators clustering distinctly from those with only mite infection, with key differentiation in genes associated with inflammation response and cancer development. Additional analysis is underway, seeking to further explore these pathways and identify specific immune differences contributing to tumor and disease development in Catalina foxes.

1520

Is sex-biased expression an evolutionary advantage – or a liability?

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Sexual dimorphism poses a fundamental evolutionary puzzle: why do largely shared genomes generate sex-specific phenotypes? Sex-specific selective pressures are often thought to drive sex-biased gene expression. These differences in gene expression between the sexes are the key to sexual dimorphism in physiology, morphology and behaviour. Under these assumptions, sex-biased expression may reflect the resolution of sexual conflict. Theory predicts that sex-bias can arise as a response to sex-specific selection. However, empirical studies show inconsistent patterns.
The extent to which different evolutionary forces influence sex-bias is, therefore, not fully understood. Here, we investigate the relative contributions of neutral and selective forces towards the evolution of sex-bias across metazoans. Swifter and more effective adaptation occurs in species with larger effective population sizes (Ne). These species experience a smaller variance in allele frequencies across generations, i.e. lower rates of genetic drift. Alternatively, alleles might fix more promptly in smaller populations with lower Ne.
We applied a similar reasoning to the evolution of sex-biased expression and analysed RNA sequencing datasets of females and males for over 100 metazoan species spanning a broad range of Ne values. Our results show no detectable relationship between longevity – a proxy for Ne – and average sex-bias. These patterns are consistent with the majority of sex-biased expression being effectively neutral rather than adaptive. We also investigate πS (synonymous site diversity) and recombination rates as proxies for Ne. Overall, our findings suggest that the adaptive significance of sex-biased expression may be overestimated.

1523

On Inferring the Virulence of Ancient Pathogens, Especially Prehistoric Plague

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While palaeogenomics has substantially revised understanding of ancient pathogens, as a data source in itself, it provides little insight into the actual virulence of presumed pathogens (especially as studies focus deeper into the evolutionary past). Prehistoric plague (Yersinia pestis) has been particularly controversial in this regard. Recurrent outbreaks across an extended familial pedigree in Neolithic southern Sweden and from France are posited to be linked to the Late Neolithic demographic decline. Virulence in the former case was disputed on the interpretation that the absence of the gene ymt in these early plague strains would have precluded flea-borne transmission, and instead caused food-borne enteritis, similar to the profile of Y. pseudotuberculosis. The discovery of apparently fatal outbreaks of plague amongst prehistoric hunter-gatherers at Lake Baikal expands on the availability of other lines of evidence to interpret virulence based on lethality, particularly through demography, though this in itself does not provide a causal explanation. Assessments of gene content based on pangenome analysis show unique configurations of genes and ORFs linked to virulence from which, alongside well-characterised genes, we undertake to infer probable host immunological interactions. In particular, the question of whether pathogens such as Y. pestis underwent attenuation of virulence in prehistoric contexts (where no documentation for pandemic-like scenarios in humans or animal hosts exists) particularly significant. This talk will focus on utilising distinct data types to inform models of virulence in prehistoric pathogens, a vital objective as the field aspires to move towards palaeogenomic epidemiology.

1531

Novel examples of natural selection in ethnically and culturally diverse sub-Saharan Africans

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Sub-Saharan Africa is the birthplace of modern humans and contains the greatest levels of human genetic diversity, some of which may have been shaped by genetic adaptations to the diverse environmental and cultural selective pressures across the region. This includes genetic adaptations relating to diet, climate and pathogen exposure, which may influence disease risk today. Still, many studies of human adaptation remain unrepresentative of the extensive ethnic, linguistic, and cultural diversity of sub-Saharan Africa.

Using a new dataset of over 6,000 newly sequenced, high-quality whole-genomes from individuals across Western, Central, Eastern, and Southern Africa, representing all major language groups, subsistence strategies and a range of environments, we infer novel instances of local genetic adaptation across sub-Saharan Africa. By combining complimentary statistical and genealogical methods, we identify signatures of positive adaptation for traits including height, adiposity, kidney function, immunity and carbohydrate and lipid metabolism.

We also discuss the potential of hair structure as an adaptive trait, given the striking signatures of recent adaptation relating to hair differentiation and development shared between Western Niger-Congo and Southern Khoe-San populations. In the >400 Khoe-San individuals, we identify additional signatures of positive selection for skin and hair-associated traits, suggesting that selection on skin and hair phenotypes may have shaped the genetic variation of one the earliest diverging branches of Homo sapiens.

Finally, using multiple genealogical reconstruction methods, we identify unusually elevated TMRCA in regions of the genome associated with immunity and sensory perception, consistent with long-term balancing selection acting on these traits in modern humans.

1537

Rare variation in malaria parasites biases population-genetic inference

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Understanding how pathogens evolve is fundamental to disease control and is a basic question in evolutionary biology, yet pathogens with complex life cycles violate assumptions of classic evolutionary models. Genetic analyses of the malaria parasite \textit{Plasmodium falciparum} have shown multiple surprising patterns. For example, empirical analyses produce effective population size estimates that vary by orders of magnitude depending on the method and an excess of genes with elevated nonsynonymous variation (measured as π_N/π_S). Here, reanalyzing genomic data from 18 worldwide populations from the MalariaGEN repository and PlasmoDB, I show that these observations directly follow from distributions of genetic variation enriched for rare variants. Multiple potential mechanisms may increase the proportion of rare variants, including host expansions, lifecycle dynamics, population structure, or selection. The observed genealogies are more consistent with a multiple-merger coalescent than a Kingman coalescent, causing common summary statistics to be biased in predictable directions. In particular, the abundance of rare variants interacts with the mathematical properties of ratio statistics to systematically inflate gene-level π_N/π_S estimates even in the absence of selection. Notably, filtering this rare variation reveals previously masked candidates for selection, including well-characterized antigens such as merozoite surface proteins. This framework provides a foundation for interpreting genomic data in pathogens with high variance in reproductive success.

1544

A Blast from the Past: ‘Living Fossil’ Fish Genomes Bridge Gene Regulation Across Long Evolutionary Distances

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Identifying orthologous cis-regulatory elements (CREs) across distant vertebrate lineages remains challenging. Many CREs are undetectable across taxa due to sequence divergence beyond recognition, CRE turnover, and the emergence of lineage-specific regulatory elements. This disconnect is especially pronounced in widely used model systems like rodents and teleost fishes, which exhibit rapid molecular sequence evolution.

Teleosts, including key biomedical models like zebrafish, are often used to study vertebrate genome function and regulation. However, a lineage-specific teleost genome duplication (TGD) drastically reshaped their genome structure and regulatory networks. Their accelerated sequence evolution, likely driven by the TGD, has obscured many ancestral CREs, complicating efforts to trace the evolution of gene regulation across vertebrates.

In contrast, holostean fishes – gars and bowfins – retain some of the slowest-evolving vertebrate genomes. These “living fossils” provide a unique window into early vertebrate evolution. Their unduplicated genomes, conserved development, and archaic morphologies offer critical insights into deep homologies that have been masked by rapid evolution in derived teleost and tetrapod lineages.

Leveraging haplotype-resolved genome assemblies from multiple holostean species, we use comparative genomics, single-cell transcriptomics, and epigenomic profiling in holosteans to reveal ancestral CREs and recover hidden gene regulatory landscapes across bony vertebrates. The evolutionary stability of holostean genomes enables the identification of conserved vertebrate CREs that would otherwise remain hidden for fast-evolving taxa.

Our work underscores the immense value of including slow-evolving lineages across the Tree of Life to reconstruct the deep history of gene regulation and uncover the genome regulatory logic that shapes vertebrate biodiversity.

1545

Investigating gene regulatory underpinnings of human-great ape divergence: insights from new models

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Gene regulatory mutations play an important role in species divergence, but questions remain about which gene networks, cell types, and developmental timepoints tend to be targeted by such mutations. We bring to this inquiry a new model system for investigating species divergence within our own genus: tetraploid composite cell lines formed by fusing human and great ape iPSCs. Inspired by prior work on hybrid organisms, this model system can be used to disentangle cis- acting regulatory mutations from differences in the trans- regulatory environment by exposing two species' genomes to the same genetic background. Using single-cell sequencing with new computational tools for pooled cell culture data analysis, we analyze data from 233 composite cell lines representing 114 unique combinations of 21 hominid cell lines from 4 species. We uncover new evidence for co-inherited sets of compensatory mutations contributing to species divergence, including alterations to mitochondrial gene regulatory networks possibly contributing to human/chimpanzee hybrid incompatibility.

1546

Mobile chromosomes as drivers of clonal pathogen evolution

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Crop disease pandemics are frequently driven by genetically uniform, asexually reproducing plant pathogen lineages. Despite limited genetic diversity and the absence of sexual recombination, these clonal populations repeatedly adapt to new hosts, environments, and control measures, raising fundamental questions about the origins of their evolutionary potential.

Here, we demonstrate that horizontal chromosome transfer provides a mechanism for rapid genetic innovation in pandemic clonal lineages of the blast fungus Magnaporthe oryzae. Through comparative genomic analyses of field-collected isolates, we identify horizontally transferred accessory mini-chromosomes shared between pathogen populations infecting cultivated cereals and wild grasses. Furthermore, population-scale phylogenetic analyses reveal that horizontal mini-chromosome transfer is a recurrent evolutionary process actively shaping pathogen genomes across diverse agricultural and natural ecosystems.

Initial functional characterization indicates that horizontally acquired chromosomes influence both virulence phenotypes and reproductive modes, directly linking chromosome transfer to key adaptive traits in pathogen biology. Together, these findings establish horizontal chromosome transfer as a driver of rapid adaptation in clonal pathogen lineages, with direct implications for predicting pathogen evolution and developing strategies for sustainable crop protection in an era of rapidly evolving agricultural threats.

1547

Developing open tools and datasets to uncover the role of whole genome duplications in early vertebrate evolution

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Whole genome duplications (WGDs) profoundly shaped early vertebrate evolution, most famously the 2 rounds (2R) that occurred at the base of the lineage. We now know that the first event (dubbed 1R) is shared by all vertebrate genomes and was shortly followed by two independent events in jawed and jawless vertebrates. The set of paralogs retained from these events—'ohnologs'—have had lasting impacts on genome structure and function, including disease-gene enrichment. Despite this, we still lack a gold standard ohnologs database. Here, we have harnessed ancestral genome reconstructions, together with phylogenetic and synteny information, to produce a robust ohnolog dataset available at ohnologs.com. For the first time, we have been able to resolve the 1R versus 2R origins of a large number of cases, as well as including previously hard-to-detect ohnologs. We find that 1R-retained ohnologs are involved in cellular transport, while those retained after both 1R and 2R are biased towards signalling functions, especially neuronal signalling. These findings suggest that after an initial adaptation to the cellular burden of polyploidy, WGD expanded the opportunities for intercellular communication. Furthermore, using our dataset, we uncover that rediploidisation, or return to diploidy, was both asynchronous and temporally protracted after 1R, suggesting that some loci began to diverge in sequence and function millions of years after duplication. Rather than a single 'big bang', 1R may have provided vertebrate genomes with a steady stream of innovation. In the spirit of open science, our tools and datasets are publicly available, documented, and accessible for future work.

1549

Pleistocene wolves genome revealed new insight on migration and hybridization in North American canids

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Species boundaries are extremely porous in the genus Canis and interspecific gene flow appears to be ubiquitous across its phylogeny. This is particularly evident in North America where the morphological and ecological variation of wolf-like canids is represented by a group of distinct lineages which are known to hybridize extensively. Although the exact origins of these lineages and the timeframes of these admixture events is yet unclear.

Migration and population replacement driven by the climatic fluctuations in the Late Pleistocene further complicate the picture while habitat depletion and persecution by humans in the last few hundred years have dramatically altered their present range and census, making it impossible to reconstruct the evolutionary history of these lineages from modern genomes alone.

In this study, we sequenced the genomes of pre-LGM canid specimens (23,000 to 43,000 cal yrs BP) from Natural Trap Cave in Wyoming, USA, at the southern end of the Pleistocene ice-free corridor. We analysed these sequences along with publicly available modern, historical, and ancient genomes.

These data confirm that hybridization had taken place between canid taxa in the contiguous USA prior to the Last Glacial Maximum. Our results expand our understanding of the known diversity and distribution of the group of Late Pleistocene American Canis providing new insights into the complex history of migration and gene flow that shaped the ancestry of modern North American canid populations.

1550

Diversity and integration of endosymbiotic associations in microbial eukaryotes

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Endosymbiosis, the phenomenon in which one organism lives within another, underlies some of the most profound evolutionary transitions in the history of life, including the origin of mitochondria and plastids. Despite its fundamental importance, the mechanisms governing endosymbiotic integration remain poorly understood. Progress in this area depends on identifying contemporary endosymbiotic associations that represent different stages of integration.

Microbial eukaryotes (protist), which comprise much of eukaryotic diversity, frequently engage in endosymbiotic relationships with prokaryotes and other unicellular eukaryotes, often altering host metabolism and enabling exploitation of new ecological niches. However, systematic assessments of the prevalence and distribution of these associations across protist lineages and environments remain limited.

Here, we combine screening of natural environments with single-cell genomics to identify intermediate stages of endosymbiotic integration and novel systems for their study. We survey diverse protist communities and apply comparative genomic analyses to host–endosymbiont systems across multiple phylogenetic scales, encompassing closely related hosts as well as broad cross-lineage distributions of endosymbionts. Our analyses suggest that endosymbiosis is prevalent among microbial eukaryotes. We recover known endosymbionts from environmental samples, document host-range expansions, and identify novel associations. The recovered diversity reveals contrasting evolutionary trajectories among endosymbiont lineages, raising questions about the dynamics of integration. In parallel, we are establishing model systems to study endosymbiosis, including the euglenid Rapaza viridis, constituting a putative intermediate stage in plastid emergence. Together, these findings demonstrate the value of integrating environmental surveys and comparative genomics to elucidate endosymbiotic integration and major evolutionary transitions in eukaryotes.

1553

Tuning meiosis in different habitats: lessons from Arabidopsis arenosa

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Meiotic crossover recombination exchanges genetic information between homologous chromosomes and is essential for meiotic stability and evolution. Crossover number and location influence chromosome segregation accuracy, which is critical for individual fertility. At the population level, crossovers promote genetic diversity and adaptive potential in challenging environments. Although tightly regulated and broadly conserved, crossover rates vary across taxonomic levels and environmental conditions, but the evolutionary significance and molecular mechanisms of this variation remain largely unknown.

We investigated temperature-induced crossover rate variation in two genetic lineages of Arabidopsis arenosa from thermally distinct habitats. Crossover response curves across 14-34°C differed between populations, with the gradient of responses reflecting their geography. Cytological analysis revealed that the population from the warmer habitat exhibits more distally positioned crossovers, which correlated with reduced chromosome missegregation at high temperatures. Complementary fertility assays following heat treatment provided additional insight into the relationship between crossover recombination, meiotic stability, and fitness.

Furthermore, we used a genome-scan approach to identify genetic variation and candidate genes that may be governing the observed differences in recombination plasticity and meiotic stability between these two lineages of A. arenosa. This combination of approaches provides a unique opportunity to address the adaptive value of preferential crossover positioning, contributing to the debate about the nature of selection that shapes the variation in crossover patterning. We are continuing to investigate mechanisms by which environmental challenges may affect crossover distribution and meiotic stability, and how meiotic processes evolve as organisms adapt to different habitats.

A telomere atlas to study vertebrate chromosome evolution

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Annotation of telomeres and interstitial telomeric sequences (ITSs) can support many applications, ranging from assessing the quality of genome assemblies to studying chromosome stability, aging, and genome rearrangements. We built Teloscope, a fast telomere annotation tool for assembly and genome graphs. Teloscope produces per-contig and assembly summary statistics, and classifies chromosomes based on telomeres and gap presence. We applied it to 581 vertebrate assemblies from the Vertebrate Genomes Project (VGP) Phase I to generate arm-resolved calls of terminal telomeres and ITSs at single-nucleotide resolution. Among 15,401 assembled chromosomes, we identified 9,531 terminal telomeres. Telomere completeness and assembled telomere lengths differed systematically by sequencing technology, with higher values in PacBio HiFi than in PacBio CLR-based assemblies. We found that the telomere completeness is highest in primates, which have a higher number of Telomere-to-Telomere (T2T) and near-T2T assemblies, and lowest in large-genome clades such as amphibians. Assembled telomere lengths varied among clades. For instance, sharks and turtles exhibit the longest lengths among vertebrates, while birds show the shortest lengths among tetrapods. We also identified candidate ITSs, which were classified into 162,051 short and 7,087 long ITSs using a 1kbp threshold. Overall, ITSs were asymmetrically distributed across vertebrate clades. In conclusion, Teloscope enables comprehensive telomere annotation across genome assemblies, supports assembly QC, and easily scales to thousands of genomes. The VGP-wide exploration assesses variable telomere completeness across taxa and quantifies clade-specific length distributions, allowing downstream comparative and trait association analyses.

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Different mutation rates, shared architecture: SNPs and SVs across the Neurospora crassa interactome

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Protein-protein interaction (PPI) networks capture the functional organization of the proteome, yet how network topology relates to the distribution of genetic variation remains poorly understood. SNPs and structural variants (SVs) arise at dramatically different rates — SNPs are abundant but individually small-scale while SVs are rare but large-effect. How these distinct mutational processes jointly shape variation from genome to PPI networks is unexplored. Here, using data from wild strains of the fungal species Neurospora crassa, we ask whether mutations cluster within PPI network modules and how patterns differ between SNPs and SVs.

Network topology strongly predicts mutational constraint for SNPs: hub proteins carry fewer non-synonymous variants per kilobase, consistent with stronger purifying selection on central network components. Several communities were enriched for rare variants, while one peripheral module accumulated both rare and common variants, suggesting relaxed constraint or rapid functional divergence.
SVs, though less frequent, also affect protein-coding sequences and show distributional patterns informative of chromatin-level genome organization. Despite their lower mutation rate, SVs exhibit distinct clustering relative to PPI topology. By combining both variant types, we reveal how mutational processes operating at different rates converge on the same functional architecture. Integrating genome organization with PPI network topology, we show that network position predicts where mutations accumulate (periphery) versus where they are removed by selection (hubs), providing a framework for identifying distinct selective regimes in natural populations.

1574

An Evolutionary Multi-Omic Framework to Assess the Evidence for Adaptive Regulatory Evolution Across Diverse Molecular Traits

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Local adaptation may lead to elevated population differentiation not only in DNA sequences and organismal phenotypes, but also in intermediate molecular traits. However, multi-omic data remains under-utilized in evolutionary biology, and most studies do not analyze such data in an evolutionary framework. A few studies have compared quantitative trait differentiation (QST) to levels of genetic differentiation (FST), to find outlier regulatory traits that may have been shaped by local adaptation. However, environmental or experimental variation can lead such studies to be under-powered.

Here, we introduce REDQuanTA (Replication-Enhanced Detection of Quantitative Traits under Adaptation), an experimental design and analysis framework that leverages replicated trait measurements from the same genotypes, along with an Approximate Bayesian Computation approach, to separate extrinsic from genetic variance. Using simulations, we show that this methodology improves power to detect QST outlier traits at reasonable experimental scales.

We empirically apply this framework to a large new multi-omic data set from the brains of Drosophila melanogaster populations adapted to (ancestral) warmer or (derived) cooler natural environments, motivated by prior population genomic evidence for an important role of nervous system genes in local adaptation. We analyze tens of thousands of molecular traits, including from chromatin accessibility (ATAC-seq), coding and non-coding RNA abundance, alternative splicing, RNA editing, protein abundance, and post-translational modifications. We thus identify numerous -omic traits that may have contributed to environmental adaptation, and for the first time, we are able to ask which levels of gene regulation show the clearest evidence for adaptive evolution.

1581

Genomic Landscapes of Oceania and Island Southeast Asia: Insights from 92 populations

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Oceania and Island Southeast Asia have a rich, yet understudied, human genomic landscape. Here, we describe the first region-wide analysis of samples from population groups spanning Oceania and its broad perimeter. In total, we generate and analyze genome-wide data from 92 different populations, 58 separate islands, and 30 countries, covering one-third of the planet. Leveraging this diverse dataset, we resolve genetic connections among islands, providing a detailed view of regional population structure. Identity-by-descent (IBD) analyses identify Samoa and Tuvalu as the most likely source island groups for the settlement of the Polynesian Outliers (Polynesian communities outside the Polynesian geographic region), consistent with west-to-east back migration from Western Polynesia. We also find evidence that Polynesian Outliers harbor high proportions of Micronesian-like ancestry. Furthermore, we use ancestry-specific analyses to deconvolve different layers of history in both the basal Papuan component and in Lapita-related East Asian-like ancestry in Oceanian populations. Notably, our findings are most consistent with continuity of Lapita-related Austronesian ancestry into Polynesia and are less compatible with models in which the primary Austronesian-related ancestry in present-day Polynesians derives from a distinct, later-branching source. Together, these findings refine models of oceanic settlement and admixture and establish a comprehensive reference that will enable subsequent work on genetic, historical, and health-related diversity while advancing global efforts to ensure broad and equitable representation in human genomics.

1582

Population history and migration in sub-Saharan African Drosophila melanogaster

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Demographic inference in species with functionally dense genomes is challenging because pervasive selection distorts variation in ways that can mimic or obscure demographic signals. Here, we infer the demographic history of three sub-Saharan African Drosophila melanogaster populations using data previously made available on NCBI's Sequence Read Archive by previous studies, including flies sampled from remote regions proposed to lie within the ancestral range of the species. We combine high-quality genome annotations with conservation information to parameterize theoretical expectations for background selection that explicitly incorporate the distribution of fitness effects of new mutations in coding and conserved non-coding regions, and use these expectations to identify and retain sites least affected by selection for downstream inference. Using these putatively neutral sites, we estimate the best-supported three-population topology and obtain parameter estimates that include asymmetric, bidirectional migration rates among populations, consistent with previously reported unique mating behaviors in flies from West Africa that confer reproductive isolation with flies from other D. melanogaster populations. These findings refine our understanding of D. melanogaster's ancestral dynamics while highlighting the challenges of inferring complex demographic history in functionally dense genomes highly influenced by selection.

1588

Identifying phenotype- and tissue-associated regulatory elements across species using public genomic and transcriptomic data

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Environmental adaptation in eukaryotes frequently involves changes influencing gene expression, some of which persist across phylogenetic timescales. Combining information about the evolution of gene expression and the evolution of non-coding sequences across species can thus be a way to identify both adaptive gene expression changes and their underlying cis-regulatory changes. We here explore signatures of adaptive gene expression changes in response to repeated dietary shifts in mammals, making use of large publicly available datasets of RNA sequencing from the metabolically relevant tissue liver, as well as high-quality whole genome sequences from the Vertebrate Genomes Project (VGP). We apply a consistent processing and filtering pipeline to public RNA-seq data from liver for 200 mammals, and we use phylogenetic generalized linear models to test for an association between normalized expression level and diet. We then examine data from high-quality genome alignments to identify candidate cis-regulatory elements underlying diet-associated changes in gene expression. Using sub-alignments from the VGP mammalian Cactus alignment, we identify regions within 1 Mb of diet-associated differentially expressed genes whose rates of molecular evolution are predicted by diet or by normalized liver gene expression level. Our results allow us to identify candidate cis-regulatory elements underlying repeated dietary adaptation via influencing expression specifically in liver, as well as to examine the potential cis-regulatory landscape surrounding diet-associated genes for elements that may act through other tissues. As large-scale genomic and transcriptomic data become available for more species, such approaches may yield broader insights into adaptive gene regulatory evolution.

1591

Pangenome analyses for understanding adaptation to ash dieback disease in European ash populations

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European ash (Fraxinus excelsior) populations are severely threatened by ash dieback (ADB), a fungal disease currently decimating ash forests with major ecological and economic consequences.
Although there is evidence that populations are already adapting to the disease via highly polygenic selection on standing genetic variation, it is still unclear if this process will be fast enough to rescue populations and if a few variants with partially higher phenotypic effect are going undetected.
While SNPs have been widely investigated, Structural Variants (SVs) have potentially larger phenotypic effects, can be generated quickly under stress (e.g. via transposition or recombination), and are only recently becoming detectable at large-scale with the increasing accessibility of long reads and pangenome approaches.
To investigate the role of SVs in adaptation to ADB, we phenotyped and sequenced three UK populations of European ash, generating whole genome short-read data for ~950 trees and long HiFi-reads for ~280, for which we had assigned parent-child relationships between a pre-epidemic (adult) and a post-epidemic onset (juvenile) cohort.
We assembled genomes and called SVs in the ~280 long-read sequenced samples, detecting extensive variation and resolving a likely Sex Determining Region. We used the detected SVs to construct a pangenome and genotyped them in all ~950 samples using short-reads.
We present the results of both SNP-based and SV-based Genome-Wide Association for ADB susceptibility - providing new insights into adaptive genetic variation in these natural populations - and highlight some of the challenges and opportunities of pangenome analyses involving hundreds of assembled genomes.

Deep-Time Demographic Inference in the Americas Using Site Frequency Spectrum–Based Modeling

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Reconstructing deep-time demographic history in the Americas presents unique methodological challenges. As the last continent populated by humans, American populations experienced rapid dispersals and strong bottlenecks, which violate assumptions underlying many demographic inference methods. We used site frequency spectrum–based demographic modeling with Moments on a collection of high-coverage modern genomes, both published and unpublished, to investigate population dynamics across South America from the late Pleistocene to the Holocene.

We reconstruct the emergence of the three major continental genetic clusters, Amazonian, Andean, and Southern Cone populations, as a near-simultaneous trifurcation around ~15,000 years ago. This rapid differentiation, which likely occurred after populations crossed the Panama Isthmus, is consistent with a fast southward dispersal followed by early regional structuring. Subsequent demographic trajectories diverged among regions, with heterogeneous effective population sizes and asymmetric gene flow shaping long-term histories.

Contrary to simplified models that assume American populations are uniformly small and isolated, some South American populations exhibit relatively large long-term effective population sizes, highlighting substantial demographic diversity across the continent. Importantly, we observe persistent connectivity between Amazonian and Andean populations across deep time, suggesting that sharp regional divides may overstate their demographic independence and instead can be compatible with long-term interaction across ecological zones. The three genetic lineages are further shaped by multiple Holocenemigration waves from North/Central America. Together, this work demonstrates how recent advances in genome quality, sampling, and demographic modeling enable more realistic reconstructions of deep-time human population dynamics in the Americas.

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Epigenetic variation of Y-chromosome palindromic regions across human populations revealed by nanopore sequencing

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The human Y chromosome is enriched in large palindromic and ampliconic regions that harbor testis-specific protein-coding gene families and preserve gene content despite the absence of meiotic recombination. Long-read sequencing has revealed extensive structural complexity and population-level variation in these regions, while comparative analyses indicate that strong selection counteracts high mutability to maintain ancestral amplicon copy number across human lineages. However, how epigenetic regulation operates within this highly repetitive and structurally dynamic genomic environment remains largely unexplored.

Here, we leverage Oxford Nanopore long-read sequencing data from 140 individuals from the Human Genome Structural Variation Consortium (HGSVC) and the Human Pangenome Reference Consortium (HPRC) to investigate DNA methylation patterns across Y-chromosome palindromic regions. Using sample-specific assemblies, alignments, and native methylation calling, we systematically profile methylation levels and variability across palindromic arms and ampliconic gene copies. We find that methylation is largely mirrored between the high-identity palindrome arms, with regional fluctuations, such as two prominent methylation dips on the palindrome 7 (P7) palindrome. Moreover, methylation is the highest on P8, with the general trend of increased methylation on palindromes with low ampliconic gene copy number. Genomic context also plays a role, for example, palindrome 2 (red amplicons) shows distinct methylation profiles depending on whether it is P1-proximal or embedded within P1.

By integrating long-read sequencing, pangenomic assemblies, and methylation, we provide a population-scale view of epigenetic variation in Y-chromosome palindromes and establish a framework for dissecting the interplay between structural variation, copy number, and epigenetic regulation on the Y chromosome.

Project Psyche: A case study of how to embed inclusivity within large-scale genomic projects

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In an era of large-scale genome sequencing projects, high-quality genomes are being rapidly produced across eukaryotic diversity. Expanding genomic resources are opening new frontiers for evolutionary biology, but also present a challenge. Genomic analysis often requires computational power and technical expertise - both of which are unevenly distributed across the globe. This limits inclusion and prevents the potential of genomics to be realised by the global community. To address this challenge, the generation of genomes needs to be partnered with initiatives to build genomics capacity and reduce disparities in access to infrastructure, training, and funding.

Here, we present Project Psyche, a collaborative genomics project that puts inclusivity first. Our community consists of over 150 researchers, conservation practitioners, and industry experts from over 34 countries. Together, we are generating and analysing chromosome-level genomes of all 11,000 species of butterflies and moths in Europe. Currently, we are analysing over 1,000 publicly available genomes as an open-community effort. By sharing the computational load and centrally hosting the dataset to share analytic products, we aim to increase participation. We also organise training workshops, research exchanges, joint sampling trips and in-person meetings across Europe to increase involvement. These activities are funded by a European Cooperation in Science and Technology Action '10kLepGenomes' and we prioritise funding for early-career researchers, researchers from genders underrepresented in the field, and researchers from European Widening Countries. Together, we have built an inclusive consortium that is developing genomics capacity across Europe and beyond, and offers a model for other initiatives.

1603

Comparative inference of regulatory mechanisms driving age-related splicing changes across vertebrate species

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Aging affects many molecular traits, but it remains difficult to separate truly shared regulatory trends from dataset noise. We focus on alternative splicing, a major post-transcriptional regulatory layer that changes with age across many tissues. Our goal is to test how conserved age-related splicing regulation is across vertebrates and whether common mechanisms can explain recurring patterns.

We reanalyze bulk RNA-seq from multiple tissues in human GTEx and additional vertebrates, including mouse, macaque, chicken, and naked mole-rat. Because read coverage per event is often limited, we quantify exon skipping using a count-based probabilistic model that improves sensitivity over PSI point estimates. In human tissues, we recover widespread age-associated exon skipping trends; many events also show age-related increases in inter-individual splicing variability, consistent with reduced regulatory robustness.

We map candidate orthologous events across species using genome alignments and tissue-matched comparisons. These analyses identify a set of conserved age-associated events with consistent age trends across species. Notably, the conserved set is enriched for exons overlapping protein regions implicated in protein–protein interactions, suggesting functional constraint and potential impact on interaction networks.

Finally, we prioritize regulatory explanations by integrating multiple evidence sources: predicted NMD sensitivity of alternative isoforms, age-associated chromatin features where matched data exist, and splice factor involvement inferred from predictive models and supported by splice-factor perturbation datasets in human cell lines. Together, this work provides a comparative, mechanism-oriented view of age-related splicing and an atlas for studying how splicing regulation evolves.

1606

Between fidelity and flexibility: host-specialist and generalist Helicobacter in Podarcis lizards

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Helicobacter bacteria are widely known for infecting mammals, yet beyond a few gastric lineages, their population genetics and gene flow remain poorly understood. Research has largely focused on these species, leaving intestinal and non-mammalian lineages understudied. Consequently, the evolutionary dynamics of Helicobacter in broader host contexts, such as reptiles, remain unexplored. Here, we investigate intestinal Helicobacter diversity across eight European Podarcis species, also known as wall lizards, using 218 metagenome-assembled genomes generated by the Earth Hologenome Initiative. Phylogenomic analyses reveal multiple previously undescribed Helicobacter lineages, substantially expanding known reptile-associated diversity within this genus. These lineages exhibit contrasting host-association strategies. One clade comprises largely host-specific Helicobacter species, each predominantly associated with a single host and showing deep population divergence that mirrors host structure, consistent with long-term co-association. In contrast, we identify a more broadly distributed generalist lineage infecting all eight Podarcis species in our dataset. Although this generalist lineage displays detectable population structure, this divergence is more recent and weaker than in specialists and is frequently disrupted by admixture, particularly among sympatric hosts. To investigate the genomic basis of these contrasting strategies, we performed pangenome analyses across specialist and generalist lineages. We identify both lineage-specific gene content and protein clusters uniquely shared between co-occurring specialist–generalist species pairs, consistent with localized horizontal gene transfer potentially facilitated by co-infection within individual hosts. Together, our results identify reptiles as an underappreciated reservoir of Helicobacter diversity and demonstrate how host specificity, population structure, and gene exchange interact to shape the evolution of gut-associated bacteria.

1607

Evolution of genetic variance and genetic architecture in the context of species' range dynamics

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When does the evolution of genetic variance under joint spatial and temporal change prevent extinction during a rapid temporal change? When environments vary through both time and space, their effects on fitness and genetic variation interact, influencing adaptation rates and the probability of evolutionary rescue. In spatially structured populations, a substantial proportion of genetic variance can be maintained by gene flow. I show that spatial structure can substantially extend the timescales over which recurrent selective sweeps, driven by a temporally changing optimum, elevate local genetic variance -- thereby supporting adaptation to faster temporal change. Furthermore, joint spatiotemporal change alters the expected effect sizes of polymorphic loci: whereas in the absence of temporal change we expect most polymorphic loci to be of small effect, temporal change leads to an excess of alleles of moderate effect.

1610

The shifting nature of the SARS-CoV-2 fitness landscape

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Phenotypic fitness landscapes are the drivers of evolution. For pathogens, they link variation in phenotypic traits to differences in growth rates, with the steepest fitness gradients identifying traits under the strongest selection. In general, fitness landscapes are time-dependent, yielding a 'fitness seascape'. As yet, however, few time-dependent fitness landscapes have been quantitatively characterised in natural populations.

Here, we exploit the exceptional availability of public experimental and genomic SARS-CoV-2 data to estimate time-trends in fitness gradients for key viral phenotypic traits. We thus reveal how selective pressures on these traits have changed over time.

Our approach integrates genotype-phenotype and genotype-fitness mappings to estimate the phenotype-fitness relationship. Mutation-level fitness estimates are inferred using a large-scale phylogenetic fitness model applied to public trees containing millions of viral sequences, while phenotypic effects are obtained from deep mutational scanning measurements.

Using this approach, we examine the hypothesis that rising population immunity shifted the phenotypes under selection from intrinsic transmissibility toward antibody escape. In fact, we find persistent selection for increased transmissibility throughout the pandemic. Selection for immune escape intensified after the emergence of the Omicron variant. Selective pressures acting on different antibody-binding epitopes have waxed and waned over time, highlighting the 'Red Queen' nature of virus-immunity coevolution. Furthermore, we establish how the evolutionary pressures we estimate relate to future evolutionary changes. We provide deterministic predictions over timescales of weeks via the Price equation, and forecast the properties of major variants emerging stochastically over years, from the selection pressures on the viral population before their emergence.

1611

Occurrence and potential of inter- and intraspecific gene flow in rapidly adapting butterfly populations

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Human-driven climate change and habitat fragmentation increasingly threaten biodiversity by reducing population sizes and eroding genetic variation required for adaptation. These effects are particularly severe for locally adapted taxa, where limited standing variation constrains adaptive responses. Under such conditions, gene flow hinders local adaptation or provides genetic variation to fuel evolutionary rescue.

A compelling system to investigate these dynamics is the butterfly Euphydryas editha, the first species documented to shift northwards in response to climate change, and one including multiple subspecies of conservation concern despite stable species-wide abundance (Parmesan 1996; Edwards et al. 2025). E. editha exhibits rapid, heritable local adaptation to diverse host plants and strong geographic structure shaped by sedentary behaviour, ecological specialisation, and episodic recolonisation of extinct populations.

This raises questions about the extent to which intraspecific gene flow among ecotypes, and introgression with closely related species, contribute to adaptive potential and population persistence under environmental change.

Using >300 whole genomes, we investigate the genetic basis of potential evolutionary rescue in E. editha by integrating landscape genomics with species ecology. We ask (i) whether incorporating ecological constraints such as phenology and host-plant use improves inference of realistic barriers to gene flow; (ii) how ecotype-specific ecology and recolonisation dynamics shape rescue via natural range shifts; and (iii) whether adaptive introgression contributes to persistence and expansion into novel environments.

By explicitly accounting for ecological barriers and opportunities for gene flow, this work highlights how the genetic architecture of evolutionary rescue is shaped by population structure, hybridisation, and landscape context.

1612

Cross-species chromatin accessibility maps reveal regulatory drivers of mammalian lifespan evolution

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Mammalian species exhibit heritable variation in longevity, ranging from short-lived rodents to exceptionally long-lived clades such as bats and whales. Comparative studies suggest that much of this phenotypic diversity arises from changes in cis-regulatory elements (CREs) rather than coding variants, yet the paucity of cross-species regulatory data has hampered our ability to understand lifespan evolution.

We have compiled longevity datasets for over 200 mammalian species and generated novel, uniformly processed fibroblast ATAC-seq profiles from 40 phylogenetically diverse mammals. Using these data, we train machine-learning models to predict chromatin accessibility in unsampled mammalian species, enabling expansion of functional regulatory information beyond experimentally profiled taxa. We analyze chromatin accessibility across ~149,431 orthologous CREs to distinguish conserved, lineage-specific, and convergently evolved CRE activity. By integrating phylogeny-aware statistical models with predicted regulatory activities, we identify 347 (~0.23%) CREs whose conserved activity patterns are significantly associated with lifespan variation across deep evolutionary timescales. We link these longevity-associated CREs to human longevity phenotypes, identify their target genes using chromatin conformation and proximity-based approaches, and characterize enriched biological processes to understand mechanisms that influence human longevity.

These results provide evidence that changes in regulatory activity contribute to lifespan evolution across mammals, revealing functionally conserved and convergently evolved CREs that would be missed by sequence alignment-based approaches. More broadly, this work establishes a scalable framework for linking regulatory evolution to complex traits, illustrated here through its application to longevity across mammals.

1615

Two decades of yellow-bellied marmot population sampling reveals physiological and regulatory resilience to the metabolic costs of seasonal climate change

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Species confronting global climate change may adapt via flexible evolutionary mechanisms. Leveraging paired phenological, genetic, epigenetic and physiological data from 21 years of individual sampling in obligately hibernating marmots in the western Rocky Mountains, Colorado, USA, we investigated coupled responses to seasonal climate factors that predict mass gain and overwinter survival probability. We observed population genetic structure and inbreeding before integrating high resolution snow and temperature datasets to quantify the association between spring climate conditions to hibernation emergence and DNA methylation. In association with snowmelt timing, we found multiple, differentially methylated cytosines within the putative promoter of Adcy4, enriched for metabolic regulation of cyclic adenosine monophosphate activity. To understand the potential metabolic cost of earlier emergence, we modeled resting metabolic rate and found that physiological cold stress has decreased in June and September over the past two decades. In July, however, recent past and future warming has strongly increased the prevalence of diurnal overheating. Under high emissions anthropogenic forcing scenarios, May will experience the greatest local snowpack loss, positing a future in which marmots emerge earlier overall and remain active while temperatures are below optima. These future outcomes may prolong nutritional limitation in spring, when body mass is already at its annual minimum, while reducing foraging potential under much hotter summers. Our findings offer long-term, mechanistic insights into how seasonal climate factors shape the regulatory genome and metabolic costs of seasonal survival in a hibernating species, supporting climate change as a contemporary driver of molecular evolution in high elevation ecosystems.

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Chromosomal loss trajectories following whole-genome duplication in cancer

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From plants surviving climate shifts to tumours evading physiological constraints, whole genome duplication (WGD) exemplifies extreme genome plasticity. In species evolution, ancient polyploidy events have been followed by rediploidization, the transition of a polyploid genome (usually tetraploid) toward a more stable diploid state through selective loss and reorganization of duplicated genes over millions of years. Whether analogous depolyploidization occurs during somatic evolution in cancer has not been systematically explored.

We developed a computational framework exploiting copy number features to detect and quantify depolyploidization in tumour genomes. Analysis of large cancer cohorts reveals progressive decline in balanced tetraploid genome proportions following genome doubling across most cancer types. Chromosomal loss rates vary substantially: tumour types with frequent WGD exhibit faster breakdown of tetraploidy, while rare-WGD tumours retain balanced states longer. Extensive chromosome loss leading to hypodiploidy is widespread and clinically relevant, typically associated with elevated chromosomal instability, chromothripsis, and poor prognosis. However, complete depolyploidization to a diploid or pseudo-diploid state, though rare, is detectable across most cancer types.

Critically, depolyploidized tumours display genomic signatures distinguishing them from stable diploids. Despite standard ploidy analyses grouping them together, depolyploidized genomes exhibit fundamentally different chromosomal architectures, elevated instability, and distinct loss-of-heterozygosity signatures. As ploidy decreases following WGD, tumours show increased replication and proteotoxic stress, and altered dependencies on ploidy-specific essential genes.

These analyses connect organismal and somatic evolution, exploring shared principles governing genome plasticity and highlighting the potential value of comparative frameworks for understanding what drives and constrains genome evolution following polyploidy.

1627

Predicting Mammal-Wide Variant Pathogenicity, Uncertainty, Gene Essentiality, and Genetic Load

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Biodiversity loss demands tools that translate the surge of genomes into conservation insight. We present a mammal-wide deep learning framework that predicts the impact of missense variants, quantifies uncertainty, summarizes gene essentiality, and estimates individual genetic load by integrating over the most probable sequence carried by each individual. Our approach couples protein language models with calibration to the observed spectrum of mammalian amino-acid variation. This allows placing variants on a continuous pathogenicity spectrum for ranking beyond binary labels, paired with an uncertainty estimate that allows users to filter low-confidence calls.In benchmarks spanning human, mouse, and dog, calibrated scores discriminate pathogenic from benign variants, classify disease versus healthy cohorts, and prioritize variants with severity-consistent ranking. Across four threatened mammals—black-footed ferret, Iberian lynx, vaquita, and clouded leopard—we map deleterious burden, nominate candidate genes concordant with reported health issues, identify variants for targeting in breeding programs, and recover signatures of demography and management. Together, these scores turn raw genomes into actionable hypotheses for monitoring, assisted breeding, and reintroduction planning.

Long-read sequencing reveals the genomic architecture of alternative reproductive tactics in swordtail fishes

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Alternative reproductive tactics exist across the tree of life. In such systems, individuals within the sex under stronger sexual selection can evolve diverse reproductive strategies, including coercive mating or female mimicry. These polymorphic strategies are driven by environmental and genetic variables to varying degrees. When reproductive tactics are strongly genetically linked, loci underlying this variation are predicted to accumulate in regions with reduced recombination rates, creating discrete phenotypic distributions for alternative morphs. Here, we characterize the genomic architecture of alternative reproductive tactics within swordtail fishes (Xiphophorus). Males of different swordtail species can be categorized as having large courting males, small coercive males, or being polymorphic for both male reproductive morphs. Using long-read sequencing, we generated genome assemblies for species exhibiting each of these scenarios. Within one polymorphic species, X. multilineatus, we performed a genome-wide association study for reproductive morph and identified a large, structurally variable region on the Y-chromosome that correlates with reproductive tactic. This region contains expansions of multiple genes, including the melanocortin-4 receptor (mc4r) which regulates feeding behavior in vertebrates. We explored the evolutionary history of this region and showed that across species, small coercive males exhibit marked reductions in mc4r copy number, while large courting males show high variance in mc4r copy number. The non-recombining region of the Y-chromosome containing these structural variants likely acted as a refuge for tactic-specific loci to accumulate, explaining their persistence over time. These results highlight structural variation of the Y-chromosome as a mechanism for driving the evolution of reproductive strategies.

1630

An ancient allele directs epigenetic suppression of a selfish reproductive barrier in maize

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In maize and related plants, a locus called Gametophytic factor1 (Ga1) controls a reproductive barrier that can selfishly prevent ga1 pollen from fertilizing Ga1 zygotes. This selfish element could in theory sweep through plant populations to reach fixation. At fixation the reproductive barrier separating the population from related plants might be reinforced and contribute to speciation. However, the selfish Ga1 allele does not sweep. We find that in over thirty maize genome assemblies the most common allele at the Ga1 locus is actually a ga1 allele that is unable to make or overcome the reproductive barrier. This conserved ga1 allele (ga1-Off), is a specific haplotype containing three full-length gene models that are non-coding due to conserved stop codons. Each non-functional gene model within the ga1-Off allele is between 610 thousand and 1.5 million years old. We show that in developing pollen tissues the ga1-Off allele likely generates 24-nt siRNAs associated with RNA-directed DNA methylation, and these siRNAs map to functional Ga1 alleles. In crossing experiments, the ga1-Off allele was associated with reduced strength of the typically dominant functional Ga1 alleles encoding the reproductive barrier. An allelic interaction between the ga1-Off allele and the Ga1 allele seems to lead to epigenetic suppression of the Ga1 allele across multiple generations. Taken together, this system serves as an example of epigenetic repression of a selfish element that might otherwise contribute to speciation.

1633

From Likelihood to Fitness: Accounting for Phylogeny to Improve Variant Effect Prediction

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Generative models trained on natural sequences are increasingly used to predict the effects of genetic variation, enabling progress in therapeutic design, disease diagnosis and risk prediction, and synthetic biology. In the zero-shot setting, variant impact is estimated by comparing the likelihoods of sequences, under the assumption that likelihood serves as a proxy for fitness. However, this assumption often breaks down in practice: sequence likelihood reflects not only evolutionary fitness constraints, but also phylogenetic structure and sampling biases, especially as model capacity increases. In this talk, I will present our recent advances toward meeting these challenges. I will introduce Likelihood-Fitness Bridging (LFB), a simple and general strategy that improves variant effect prediction by averaging model scores across sequences subject to similar selective pressures. Assuming an Ornstein-Uhlenbeck model of evolution, LFB can be viewed as a way to marginalize the effects of genetic drift, although its benefits appear to extend more broadly. LFB consistently improves predictive performance across model families and sizes, and notably, it reverses the performance plateau observed in larger protein language models. These results suggest that accounting for phylogenetic and sampling biases is essential to realizing the full potential of large sequence models in variant effect prediction.

1639

Diversity of dosage compensation mechanisms in squamate reptiles

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Differentiation of sex chromosomes is typically accompanied by the cessation of recombination and subsequent gene loss from the degenerated sex chromosome (Y or W), resulting in gene dosage imbalances between the sexes. Classical theory, based largely on studies in model organisms, predicts the evolution of mechanisms to compensate for these imbalances. Dosage compensation, or at least dosage balance in the expression of sex-linked genes, has been well documented in lineages with male heterogamety (XX/XY). In contrast, lineages with female heterogamety (ZZ/ZW) are often thought to lack global, chromosome-wide regulatory mechanisms for gene dosage, particularly at the transcriptional level. In this study, we combined high-throughput sequencing with comparative bioinformatics to investigate patterns of transcriptional gene dose regulation in eleven independently evolved sex chromosome systems of squamate reptiles. Our findings provide novel evidence from non-traditional model organisms, revealing the molecular diversity and evolutionary complexity of gene dose regulatory mechanisms across vertebrates.

1646

A herbariomic approach to characterising medicinal black henbane (Hyoscyamus niger) populations in Britain

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Plants have been recognised throughout human history for their diverse medicinal properties and are now embedded within healthcare systems worldwide. Despite being an invaluable resource, the population biology of most medicinal plant species is poorly understood, with many likely threatened with local or complete extinction. Here, we characterise the declining population of naturalised black henbane (Hyoscyamus niger) in Britain. As an opportunistic coloniser of disturbed habitats, it belongs to a unique class of biodiversity associated with pre-historic human migration and agricultural systems. It is therefore a suitable model for investigating a) how land-use changes over time have affected the persistence of archaeophyte populations and b) how ephemerality itself influences population genetic parameters. To interrogate this, we apply a panel of black henbane samples sourced from herbarium collections, supplemented with plants from present-day localities. The analysis is supported by the first assembly of a full draft genome for this species, conducted via long-read sequencing technology. On a species level, our results will provide a foundation for further study of both a) the colonisation and invasion capacity of black henbane in a global context and b) its genetic basis of synthesising known and yet-uncharacterised compounds of medicinal value.

1647

The phylogeography of the Wikstroemia genus – one phylogeny, 50 species, 60 islands, and 250 years of botany

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Herbarium specimes are a wonderful resource for phylogenetics… if you can sequence them. Herbarium specimens are a wonderful resource for biogeographics… if you can figure out where they're from. Through the twists and turns of label identification and geographical mystery solving – featuring squinting, translation tools, speculative interpretation, and the voyages of Captain James Cook – and through a lot of short read sequencing, we leverage 200 herbarium sheets to reconstruct the first ever genus level phylogeny of the Wikstroemia (Thymelaeaceae), a culturally and medicinally significant genus of flowering plants found throughout East, South, and Southeast Asia, as well as on most major Pacific islands. Using this phylogeny and the herbarium records as a backbone, we discuss the biogeographic history of the genus. We ask how the Pacific Island taxa dispersed and diversified from their origin in a common ancestor in Asia, trying to answer the question: How do plants cross oceans? We try to answer another question too, discussing the possibilities and limitations of using herbarium specimens for phylogenomics: How hard is it, actually?

1648

Germline-specific patterns of hypomethylation of previously inaccessible regions of ape genomes

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Telomere-to-telomere (T2T) genome assemblies enable comprehensive analysis of DNA methylation in regions previously inaccessible to short-read sequencing, including abundant peri/centromeric satellite arrays that are among the most rapidly evolving sequences in primate genomes. Here, leveraging complete T2T assemblies and germline and somatic methylation data from human and great apes, we report striking germline hypomethylation of peri/centromeric regions, and that it plays key roles in shaping sequence composition, genomic innovations, and tissue-specific transcription. Integrating whole-genome bisulfite sequencing data, we demonstrate that germline DNA methylation—rather than somatic methylation—best explains patterns of CpG erosion over evolutionary time. Remarkably, peri/centromeric satellites exhibit consistent hypomethylation in sperm across great apes, despite rapid sequence turnover. Moreover, this hypomethylation extends into adjacent non-satellite regions, creating large genomic regions of hypomethylation that are determined by proximity to peri/centromeric satellites rather than intrinsic sequence properties. Genes embedded within these regions show significant enrichment of expression in testis and brain. In addition, these regions are enriched for recently duplicated genes exhibiting distinctive methylation profiles and preferential expression in brains compared to their non-centromeric paralogs. Extending our analysis to other genomic sequences of rapid evolutionary turnover, including lineage-specific insertions and segmental duplications, we show that CpG enrichment and reduced sperm methylation are common features of these evolutionarily dynamic sequences, rendering them resistant to methylation-associated CpG erosion upon emergence. Together, our results reveal a conserved germline epigenetic landscape conferred by the most structurally dynamic regions of ape genomes, linking germline DNA methylation to genome sequence evolution and the evolution of new genes.

1649

Stay in your lane: developing effective approaches to multidisciplinary research and publishing to address twenty first century challenges.

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If traditional research was a long, winding and lightly populated footpath, modern science and information generation is a multi-lane highway with no speed limit. Innovations allow, and increasingly require, investigators to work across fields to tackle complex ecosystem level questions. How, then, can we balance the rigorous standards and practices of slow science with the, “move fast and break things” mentality of contemporary industry? As our molecular acumen grows, we need to better define how, and when science should be implemented. To do that we need to re-define what our professional lanes are and the rules of road.

1651

Homologous recombination in stationary phase bacteria

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During exponential growth bacterial adaptation is fueled by de novo mutations generated during DNA replication. Once nutrients become scarce, cells enter stationary phase and mutation supply ceases. In the absence of replication, the only route to generate new genetic variation is the reshuffling of standing variability by homologous recombination. However, whether and how bacteria resort to homologous recombination under nutrient limitation is unknown. We show how herd immunity to a generalized transducing phage – implemented here via CRISPR immunity – maintains standing genetic polymorphism and stable host-phage coexistence, thereby enabling genome-wide gene flow and accelerating adaptation through homologous recombination up to two orders of magnitude relative to de novo mutations. Recombination occurs in stationary phase and is mediated by recG, which has been previously reported to be regulated by stringent response. Thus, when nutrients become scarce, bacterial herd immunity allows for adaptation by homologous recombination, thereby decoupling evolutionary change from DNA replication. This mechanism helps explain the enigmatic high rates of homologous recombination that have been observed across many bacterial species and suggests a broader evolutionary role for bacterial immune systems beyond defense.

Combining agentic AI with open infrastructure for reproducible analyses

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Here, we introduce BRC-Analytics.org, a platform that combines agentic AI with authoritative data sources and community-curated workflows on freely accessible public infrastructure. BRC-Analytics integrates NCBI Datasets, UCSC Genome Browser annotations, and EBI ENA sequence archives with Galaxy-based workflows for quality control, read mapping, variant calling, transcriptomics, and functional annotation. The platform runs on ACCESS-CI infrastructure, requiring no local installations or funding. Agentic AI tools invoke Galaxy's native analysis functions via API, ensuring every analytical step appears in Galaxy's history with full parameter capture. To demonstrate this approach, we re-analyzed published *Candida auris* datasets encompassing transcriptomic and large-scale surveillance data. However, we show that AI-generated analyses require rigorous validation. In one case, a scientific-sounding AI-proposed method for mapping genes across genome versions yielded an exceptionally high prediction rate but proved only 1% accurate when validated against NCBI mappings—illustrating both the power and the essential safeguards needed when deploying agentic AI in pathogen research. BRC-Analytics provides data-to-publication functionality where agentic AI operates within a framework that enforces transparency, making advanced pathogen genomics accessible to any researcher regardless of computational expertise.

1669

Genetic and transcriptional signatures of evolutionary mismatch in the Orang Asli of Peninsular Malaysia

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In humans, evolutionary mismatch has been popularized to explain high rates of “lifestyle” diseases prevalent in post-industrial contexts where diets, activity patterns, and other factors dramatically differ from recent evolutionary history. Most studies focus on evolutionary mismatch at the phenotypic level, but recent work has provided predictions for the genetic level: mismatched loci should 1) exhibit evidence of past selection and 2) function differently in ancestral versus novel environments, producing genotype-by-environment (GxE) interactions. To test these predictions, we collected whole genome sequencing (n=765) and white blood cell gene expression data (n=894) with the Orang Asli, the Indigenous peoples of Peninsular Malaysia, who live along a gradient from subsistence-based to more urban, “mismatched” lifestyles. Using our WGS data, we first called 5,552,993 SNPs and described genetic variation in this previously uncharacterized population. To identify candidates of past selection, we applied outlier-based tests with the population branch statistic, cross-population extended haplotype homozygosity approach, and integrated haplotype score, identifying several immune and metabolic candidate genes. We then integrated transcriptomic data, finding that lifestyle is associated with coordinated changes in gene expression at 1,829 genes involved in similar biological processes. To test whether genotype interacts with this environmentally-dependent gene regulation, we mapped GxE interactions using a cis-eQTL approach and found 112 significant GxE eQTL. We are now testing whether regions under selection overlap with these environmentally-dependent genetic effects, to understand how past adaptation interacts with current lifestyle change. Overall, this work provides insight into biological consequences of rapid shifts toward “mismatched”, industrialized environments.

1672

Machine Learning Reveals Path-Dependent Functional Evolution in Animal Opsins

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Path-dependent evolution—the idea that historical events constrain future evolutionary trajectories—is thought to play a central role in shaping molecular function, yet it has been difficult to evaluate efficiently and quantitatively in natural systems across deep evolutionary time. Opsins, the light-sensitive proteins underlying animal vision, are a classic system for studying functional evolution, with decades of natural history and experimental work documenting repeated shifts in spectral sensitivity across animal lineages. Previous studies suggest that opsin functional diversity is shaped by historical pathways, yet this idea has been difficult to evaluate systematically across deep evolutionary time. Here, we synthesize decades of functional data into machine-learned genotype–phenotype maps and use these models to examine the structure of opsin functional evolution. Starting from reconstructed vertebrate and arthropod visual opsin ancestors, we simulate forward sequence evolution and use our ML models to infer the functional consequences of simulated evolutionary trajectories. We find that path-dependent evolution plays a central role in shaping opsin spectral diversity: the effects of substitutions depend strongly on prior sequence context, as accessible functional trajectories differ between vertebrate and arthropod visual opsins. Together, these results show that machine learning can formalize and scale functional information to test how path-dependent evolution structures molecular diversity.

1673

Eco-evolutionary drivers of the emergence of the major wildlife pathogen, Ranavirus

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Ranaviruses are emerging pathogens that infect a wide range of ectothermic vertebrate hosts, including amphibians, reptiles, and fish, where they contribute to wildlife population declines and cause substantial economic losses in aquaculture. Despite their ecological and economic importance, the genomic diversity and evolutionary history of ranaviruses, and of the broader family Iridoviridae, remain incompletely characterised. Here, we leverage large-scale metagenomic mining of the NCBI short read archive to systematically recover previously unrecognized iridovirus genomes across diverse hosts and environments. Through de novo assembly and validation of recovered observations, we nearly triple the number of available Iridoviridae genomes and substantially expanded their known host range and geographic distribution.

Using this expanded genomic resource, we reconstruct the evolutionary history of ranaviruses and show that their emergence was driven by a deep host-shift event from fish to amphibians, followed by repeated host range expansion. This transition was accompanied by widespread gene loss and horizontal gene transfer. Notably, we identify the acquisition of collagen-like proteins of bacterial origin. Finally, we show that human-associated activities like trade and aquaculture has not led to accelerated viral recombination, contrary to their speculated role in generating novel recombinants that drive disease in wildlife. Together, our findings redefine the evolutionary origins and host breadth of ranaviruses and highlight key genomic processes underlying their emergence. More broadly, we discuss the challenges and value of systematic data mining of existing genomic repositories to uncover unknown viral diversity and to advance our understanding of the evolution and ecology of emerging pathogens.

1674

Ancestral sequence reconstruction reveals simple genetic mechanisms for evolving octocoral bioluminescence

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Enzymes catalyze a variety of biochemical reactions, supporting a diversity of metabolic processes and organismal functions across the tree of life. However, little is known about how new catalytic mechanisms originate. Here we use ancestral sequence reconstruction and biochemical experiments to explore the origin of bioluminescence in octocorals. Octocorals produce light by using a luciferase enzyme, which catalyzes the oxidation of a luciferin substrate. This luciferase evolved from an ancestral haloalkane dehalogenase, an enzyme family with hydrolase rather than oxygenase activity. To investigate the molecular evolution of octocoral luciferase, we inferred a phylogeny using haloalkane dehalogenase and luciferase sequences from octocoral transcriptomes and genomes. By reconstructing and recombinantly expressing ancestral sequences, we identified the historical interval between two ancestral sequences where luciferase activity originated. Of the 38 amino acid substitutions along this branch, nine are found in the walls of the active site cavity. We experimentally dissected the contributions of these nine substitutions and found that the emergence of luciferase activity can be surprisingly simple: deleting a single amino acid residue is sufficient to confer luciferase activity. However, this substitution is not necessary, since we also find that luciferase activity can be conferred via five amino acid substitutions. We also find that the catalytic amino acids used for dehalogenase and luciferase activity are conserved between the two ancestral sequences. Altogether, this work illustrates how ancestral biochemical features may be repurposed in evolution, enabling a few changes in the active site to cause the origin of a new catalytic mechanism.

1679

Parsing nearly neutral theory at the protein level through experimental variation of effective population size and high-throughput biophysical measurements

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The nearly neutral theory of molecular evolution predicts that the extent to which natural selection can overcome the random action of drift depends on a population's effective size (Ne). Comparative work has shown that several phenotypes – including genome size and structure, codon usage, and amino acid composition – vary with Ne, suggesting that differences in mutation-selection-drift balance contribute to phenotypic differences between species. To link such macroevolutionary patterns to the microevolutionary dynamics from which they arise, we employ experimental evolution and fitness assays, with rhinovirus and its protease 3CPro as a model system. We measure the effect of Ne on evolutionary trajectories and outcomes by evolving rhinoviral populations at different Ne across 5 orders of magnitude. We then measure fitness for all 3CPro variants from experimental populations and for a library of single, double, and triple mutants, enabling analysis of the effect of Ne on how populations traverse the local fitness landscape, focusing on dynamics like selective sweeps, clonal interference, and epistasis. Thermodynamic stability (ΔGfold) measurements of these 3CPro variants will allow complementary analysis of how Ne affects the evolution of stability, a universal property of proteins known to be under purifying selection and thus likely sensitive to differences in Ne. These ongoing experiments are supported by our recent results from population genetic simulations. By experimentally varying Ne, the property of populations theorized to tune the balance between mutation, drift, and natural selection, this work aims to illuminate population genetic dynamics and molecular mechanisms underlying the nearly neutral theory.

1682

Nondisjunction and fitness costs in a selfish X chromosome that causes meiotic drive in both sexes in Drosophila testacea

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Meiotic drivers are selfish genetic elements that manipulate the process of meiosis to increase their transmission. Because meiosis fundamentally differs between the sexes, meiotic drivers use different mechanisms and strategies in male and female meiosis. We recently discovered a selfish X chromosome that causes meiotic drive in both males and females in the woodland fly, Drosophila testacea. In this study, we examine segregation distortion through females. We used controlled crosses to ask whether one or two copies of this selfish X chromosome cause higher rates of nondisjunction, or chromosome segregation failure, in female flies. We found that females carrying a selfish X chromosome failed to transmit either of their X chromosomes at a significantly greater rate than wildtype females; this was even more pronounced in females with two selfish X chromosomes, resulting in a large number of sterile sons with an XO genotype. On the other hand, females carrying two selfish X chromosomes almost never transmitted both of their X chromosomes (which would produce XXY offspring). These results suggest that in D. testacea females that are homozygous for the selfish X chromosome, X chromosomes interfere with each other over segregation. Our results show that female meiotic drive is associated with nondisjunction, resulting in negative fitness consequences, and provides insights into the transmission of this unusual selfish chromosome.

Phylogenetic regression of sequence embeddings reveals genotypic basis of phenotypes

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One fundamental task in evolutionary biology is to probe the molecular mechanisms underlying the adaptive evolution of functional traits across species, i.e. resolving the genotype-phenotype mapping (GPM) at macroevolution scale. However, such investigation is often challenging due to the high dimensionality of genotype space and the complex, non-linear mapping between sequence and function. Specifically, non-coding elements (NCEs) play pivotal roles in shaping the GPM through regulation of spatiotemporal gene expression. Existing studies on the GPM of NCEs have mostly focused on changes in evolutionary rates, unable to reveal the association between trait states and specific sequence features. Here, we proposed to extract the semantically rich features of NCEs by pre-trained genome language models, and hence detect the GPM by phylogenetic regression of sequence embeddings (PROSE). Taking echolocation in mammalian species as an example, we tested the association between embedding features of promoter-like NCEs and the discrete trait, identifying NCEs and corresponding genes essential for auditory system development. Additionally, multiple candidate genes showed significant differential expression in the cochlea and auditory cortex between echolocating and non-echolocating bats. The candidate NCEs also contain unique motifs associated with transcription factors participating in auditory system development. In a second case study, significant CREs linked to telomere function were found associated with mammalian longevity, a continuous phenotype. In conclusion, PROSE provide a robust framework for resolving the complex GPM between non-coding regions and discrete or continuous phenotypes, demonstrating the power of deep learning in elucidating the molecular basis of adaptive functional evolution.

1692

Modeling regulatory evolution under the assumption of local oligogenicity

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It is generally accepted that genetic effects at most loci are due to multiple somewhat independently acting variants. These are parsimoniously assumed to be reducible to single causal sites. However, relaxation of this assumption, allowing for “local oligogenicity” (haplotype effects in intervals of high linkage disequilibrium) has meaningful implications for our understanding of the genetic architecture and evolution of complex traits. In this talk I will start by reviewing evidence from eCROPseq experiments, namely parallel CRISPR mutagenesis of regulatory variants across credible sets followed by single cell RNA sequencing, that eQTL effects are better viewed as haplotype than single causal variant effects. Next I will show how modeling eQTL with multiple contributing variants in credible sets influences effect size estimates among human ancestry groups. The extent to which this translates into trait effects is dependent on the relationship between eQTL and GWAS variants, which is increasingly appreciated to be highly modified by cell states. Finally, I will report simulation results grounded in empirical haplotype distributions across 1MB intervals, showing how local oligogenicity is predicted to increase divergence in genetic effects relative to single causal variant models. While drift in allele frequencies is the main source of divergence in population attributable risk (realized heritability) at most loci, relaxation of the assumption that causal variants are sparse adds a new layer of complexity to the genetic basis for microevolution of complex traits.

Population Genomics of the Rice's Whale Reveals Long-term Isolation, Admixture, and Genetic Distinctiveness

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Rice's whale (Balaenoptera ricei) is a newly described baleen whale species that was long considered to be a Bryde's whale because the species are difficult to differentiate using external morphological characters. The current abundance estimate for Rice's whales is approximately 51 (95 % CI: 20–130) individuals, making it one of the most endangered baleen whales worldwide. Using whole-genome sequences from 25 individuals, we reconstruct the evolutionary and demographic history of Rice's whale and assess its genetic health. Genomic analyses reinforce its distinctiveness from Bryde's whales, and support that Rice's whale has persisted as a single, small, and geographically restricted population in the northern Gulf of Mexico for tens of thousands of years. Despite having a long-term small effective population size, Rice's whale genomes do not show signatures of recent inbreeding. Runs of homozygosity (ROH) account for a substantial proportion of the genome. However, long ROH are rare, indicating that genome-wide homozygosity largely reflects historically small population size rather than recent inbreeding. We detect clear genomic evidence for a pulse of admixture approximately 500 years ago from a Bryde's whale–like lineage. This admixture event increased heterozygosity in Rice's whale genomes but had little effect on deleterious variation. Our simulations indicate that a recent population collapse to as few as 100 breeding individuals places the species at high risk of future inbreeding unless population growth occurs. However, the effect of these recent demographic events on the genetic load, or overall population fitness, is more modest.

1696

Repeatable genomic responses to climate during global invasion

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Invasive species often spread across broad climatic gradients, with rapid adaptation to local environments playing a key role in their success. Using extensive contemporary and historical collections of Ambrosia artemisiifolia—an aggressively invasive weed and a leading cause of pollen-induced hay fever—alongside a newly constructed pangenome, we investigate the genomic and phenotypic mechanisms underlying recent local adaptation across its native range in North America and introduced ranges in Europe and Australia. By integrating spatial and temporal genomic data, we uncover strikingly parallel allele frequency changes associated with climate across continents, revealing rapid and repeatable evolutionary responses during invasion. Adaptive differentiation is distributed across both single-nucleotide variants and large structural variants, including chromosomal inversions and copy number variants. These genomic regions are associated with key life-history traits and show dramatic shifts in frequency over time and space, consistent with selection acting on standing genetic variation. Together, our results demonstrate how multiple layers of genomic variation facilitate rapid adaptation, helping drive the global spread of A. artemisiifolia across diverse climatic gradients.

1699

Hologenomic signatures of Arctic adaptation in Greenland sled dogs

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The Qimmeq, Greenland's native sled dog, represents a genetically distinct lineage that has supported Inuit mobility and survival in the Arctic for centuries. Shaped by extreme climatic conditions, intense physical activity, and a traditionally protein-rich diet, Qimmit exhibit well-documented genomic adaptations to Arctic life. However, little is known about the microbial communities associated with this unique evolutionary history. We conducted a genome-resolved metagenomic analysis of faecal samples from 385 canids, including 149 novel Greenland sled dog samples and 236 previously published dog and wolf datasets, to test whether traditional dog-husbandry practices in Greenland have maintained Qimmit microbiomes in states resembling their ancestral counterparts and, by integrating host evolutionary history, whether host-microbiome jointly contribute to physiological performance in extreme environments. Qimmit microbiomes formed a homogeneous cluster despite geographic separation exceeding 1,000 km, likely reflecting host genetic and ecological homogeneity. Comparative analyses revealed that Qimmit microbiomes are more similar to wolves than to other domestic dogs. Functionally, they exhibit increased capacity for amino acid degradation and enhanced pathways supporting protein-derived energy metabolism, consistent with cold-adapted dietary and energetic demands. Geographic comparisons identified locality-specific signatures, most pronounced between Sirius military patrol dogs and civilian populations. Despite dramatic seasonal changes in environment, diet, and activity, microbiomes remained remarkably stable, with only modest compositional shifts and no detectable functional changes. Together, these findings position the Greenland sled dog as a compelling system for studying adaptive evolution through a hologenomic framework, in which host genomic and microbiome capacities jointly contribute to adaptation in Arctic environments.

1702

You Don’t Know What You’ve got ‘Til It’s Gone: Using non-biting mosquitoes to understand the evolution of blood-feeding.

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Mosquitoes are blood-sucking insects with a worldwide distribution that transmit pathogens causing multiple diseases, such as malaria and dengue. In mosquitoes, blood-feeding is a sex-specific trait with only female mosquitoes requiring a bloodmeal before producing eggs. Interestingly, some lineages of mosquitoes have lost the ability to bite, rendering them unable to transmit pathogens. In this study, we compared the genomes of biting and non-biting mosquitoes to help identify genes that are important to blood-feeding, as these should follow different evolutionary trajectories in the non-biting mosquitoes. To do so, we examined patterns of gene family evolution, selection, and expression. We predict that genes that are important to blood-feeding, such as those that influence host-seeking behavior, will be lost or will be undergoing relaxed selection in the biting lineages. We also predict that the head transcriptomes of the non-biting lineages will have less pronounced sex-specific differences. We found that non-biting lineages had a high number of convergently lost orthologs. However, there was little evidence of relaxed selection across the genomes of non-biting mosquitoes, suggesting that if genes involved in biting were retained, they may have other important functions. As expected, the head transcriptome of female mosquitoes in non-biting lineages had more similar gene expression to their male counterpart when compared to biting lineages. Taken together, our results suggest that biting genes were lost quickly after the transition from biting to non-biting and that changes in sex-specific gene regulation are important drivers of this transition.

1703

Genomic reconstruction of the bacterial toolkit for plastic biodegradation

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Microplastics and nanoplastics (MNPs) have become pervasive pollutants across global ecosystems. Microbial communities in plastic-rich environments face selective pressures that promote genomic innovations supporting plastic biodegradation and other adaptive functions. To investigate how genome plasticity contributes to this process, we constructed a comprehensive dataset of plastic-degrading orthologous groups in prokaryotes and identified 51 protein families with potential MNP-degrading activity. Using BLASTP-based functional annotation, we mapped the 51 putative Plastic-Degrading Orthologous Groups (PDCOGs) onto geolocated protein sequences worldwide. Overall, PDPPs account for about 3.5% of prokaryotic proteins and are broadly distributed, occurring in most species and environmental niches worldwide. These enzymes are remarkably widespread, present in ~50% of prokaryotic species (range: 3–95%), suggesting that plastic-degrading capacity is embedded within evolutionarily dynamic genomic architectures across bacteria and archaea. Remarkably, more than 95% of prokaryotic (archaea and bacteria) species appear capable of degrading at least one type of polymer. We also analyzed plastisphere biofilms from macro-plastic fragments collected in Finland and Spain. Pure isolates were cultured, identified by 16S rRNA, and their polymer types determined by FTIR. Integrating these isolates with PDCOGs annotations shows that plastisphere taxa putatively possess diverse enzymatic repertoires that may have been shaped by exposure to synthetic polymers. Further experiments are needed. The PDCOGs dataset (https://phylobone.com/microworld/PDCOG) highlights the eco-evolutionary significance of genome plasticity in enabling microbial adaptation to anthropogenic substrates. Moreover, this work provides a strong foundation for future studies on the genetic mechanisms for MNP biodegradation and its association with other adaptive traits.

1708

Increased survival of low-frequency lineages during fluctuations in resource abundance

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Bacterial evolution is likely strongly influenced by the need to survive periods of extreme resource scarcity. Many bacterial species can enter a state of growth termed long term stationary phase (LTSP), which enables them to survive for many years and even decades, under resource exhaustion. We previously showed that Escherichia coli LTSP populations are dominated by high-frequency lineages that continuously adapt genetically, despite resource exhaustion. By combining whole-genome sequencing (WGS) with barcode-guided lineage tracking we show that many more lineages survive within LTSP populations than previously observed. LTSP lineages are most often seeded by genotypes that segregate at low frequencies immediately following exponential growth, suggesting that slow growth or dormancy during exponential phase increases the likelihood of surviving death phase and entering LTSP. Similarly, when LTSP population samples are made to re-adapt to growth in fresh media, most surviving lineages are ones that segregated at extremely low frequencies during LTSP. Thus, while they are often overlooked in standard analyses, low frequency lineages contribute disproportionally to the pool of genotypes that survive fluctuations in resource abundance.

1710

Multilevel drift and selection in the evolution of prokaryotic plasmid

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Extrachromosomal genetic elements are widespread across all domains of life, including prokaryotic plasmids, fungal accessory chromosomes, and eukaryotic organelles. These elements often occur in multiple copies within individual host cells, contributing to the emergence of intracellular genetic diversity (heteroplasmy). As a result, their evolution is shaped by processes acting at two levels: within host cells and across host populations. However, incorporating multiple levels of biological organization into classical population genetics theory remains challenging. Focusing on bacterial plasmids, we supply empirical data and theoretical formulations for the effect of genetic drift and selection on plasmid allele dynamics within the host and the bacterial population. Our resarch uncovered segregational drift – genetic drift acting on the intracellular plasmid pool – that suppresses the establishment of novel plasmid alleles, including those beneficial for the host. Furthermore, studying the determinants of plasmid fitness, we characterize effective strategies for the evolutionary success of low-copy extrachromosomal elements. Together, our findings provide insights that may extend to the evolution of other extrachromosomal elements with similar population structures. By focusing on plasmids, our research reveals general principles in the evolution of autonomously replicating genetic elements.

1711

Convergent Evolution in Tumor Genomes Targets Functional Domains from Ancient to Lineage-Specific

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Tumor evolution is shaped by selective pressures that repeatedly favor similar functional outcomes across genetically distinct cancers. While convergent evolution in cancer has been studied at the gene level, this work investigates selection on smaller functional units, namely protein domains. Using >10,000 primary tumor exomes from TCGA, we quantified selection strengths acting on missense and truncating mutations aggregated by protein domain. This analysis identified 561 domains under significant positive selection across tumor types, spanning 841 genes. Notably, 122 of these genes would be difficult to detect using gene-centric approaches due to low mutational recurrence or mutations outside functionally critical regions. We classified positively selected domains by evolutionary antiquity. The most ancient domains trace back to pre-eukaryotes and are involved in core cellular processes (e.g., DNA mismatch repair and metabolism), and tend to accumulate the highest numbers of mutations. The majority of positively selected domains originated in early eukaryotes and are enriched for regulatory control and cellular organization, whereas metazoan-specific domains are primarily associated with signaling and cell–cell communication. In contrast, <4% of positively selected domains emerged after the vertebrate radiation and are mutated at low frequencies. These results suggest that cancer preferentially exploits deeply conserved biology, with regulatory complexity driving tumor adaptation, while recent evolutionary innovations are relatively fragile and dispensable. Furthermore, domains under strong convergent selection are enriched in genes associated with therapeutic response and druggable protein families. This redundancy highlights a framework for drug repurposing, prioritization of functionally convergent therapeutic targets, and interpretation of resistance and relapse mechanisms.

1712

Origin and host diversification of giant viruses infecting eukaryotes

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Giant viruses (phylum Nucleocytoviricota) are large dsDNA viruses that infect a wide range of eukaryotes, including vertebrates, invertebrates, diverse algae, amoebae, fungi, and other microbes. To better understand these viruses of ecological, evolutionary, and economical importance, we combined phylogenomics, dating, and protein homology detection to elucidate their origin and virus-host interactions. Our host-constrained dating indicates that the last Nucleocytoviricota common ancestor (LNCA) dates back to 700 million years ago in an aerobic environment with comparable oxygen levels to the present, suggesting a role of oxygen and eukaryotic oxidative energy production for the early evolution and later genome gigantism of giant viruses. Virus-host phylogenetic comparisons show that giant viruses underwent extensive host shifts since their origin. Mapping of host taxa distribution indicates that LNCA infected amoebal hosts from the eukaryotic supergroup Amoebozoa. LNCA already possessed two families of entry-fusion complex proteins that were originally known from the endocytic entry pathway of animal-infecting poxviruses. Critical to entry into endocytosing host cells, these proteins likely facilitated the infection of amoebae by LNCA and repeated shifts of giant viruses from amoebal to animal hosts, including those that eventually led to the emergence of iridoviruses and African swine fever viruses. In contrast, the loss of these proteins is associated with transitions from amoebae to algae and other eukaryotic hosts where giant viruses evolved other cell entry pathways. Together, our works illustrate the virus-host-environment interactions through the geological timescale for one of the most widespread lineages of viruses.

1713

Tracing Protein Fold throughout Evolution using Synthetic Biology and Protein Design

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All extant life relies on a canonical 20-amino acid alphabet, yet the evolutionary transition from prebiotic chemistry to this fixed code remains a central mystery. Was this specific alphabet a prerequisite for life, or could early functional protein folds emerge from a simpler, "primordial" set? We utilize synthetic biology and de novo protein design to explore the structural landscape of reduced amino acid alphabets. We demonstrate that structural order can emerge spontaneously from random sequences composed of "early" prebiotic amino acids. By reconstructing small, ancient folds using a strictly acidic, reduced alphabet, we show that a lack of positively charged and aromatic residues does not preclude protein folding. Instead, we find that this "early" alphabet is uniquely optimized for structural propensity. Additionally, our results indicate that early acidic peptides and folds could have served as functional sites, capitalizing on ligand and metal-binding interactions. Our work suggests that the protein folding landscape was a driver in the evolution of the genetic code, providing the design principles for engineering synthetic proteins from reduced alphabets.

1714

The functional impact of adaptive variants in South Asian populations

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South-Asians present a higher risk of developing Type-2 Diabetes (T2D), and South Asia hosts about a quarter of the world population. With an overgrowing population, the potential number of persons afflicted by this disease is set to increase. Despite some recent meta-analyses, South Asians samples were still largely outnumbered by European and East Asian ones in genome-wide association studies (GWAS). An alternative solution to identify disease-associated variants is through selection mapping. In fact, the rise of “lifestyle” diseases, including T2D can be due, to a degree, to an evolutionary mismatch. To test this hypothesis, we performed a genome-wide scan for signals of recent positive selection in a wide-cohort of South Asian populations. We identify a substantial proportion of selection signals in metabolic-associated genes. By fine mapping their functionality and disease-association, we are able to highlight genes and variants whose role in the aetiology of T2D has never been explicitly introduced before. Our results highlight the importance of evolutionary studies in the identification of the genetic basis of complex diseases in human populations.

1716

170 million years of Y chromosome evolution

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This project entailed assembling the complete Y chromosome sequences of three distant lizard species from the pleurodont clade, whose lineages diverged more than 100 million years ago. Over 170 million years of evolution, this enigmatic sex chromosome underwent severe genomic decay, resulting in a Y chromosome with, on average, only seven remaining genes and the emergence of a lncRNA-mediated (MAYEX) dosage compensation mechanism. The structure of these Y chromosomes differs from that of mammals. Despite being rich in repetitive elements, their protein-coding genes are single-copy, and remarkably, only two genes are conserved across all three species. We are now investigating its functional genomics using transcriptomics and mapping active and repressive epigenetic marks, examining its 3D architecture with Hi-C, and applying CRISPR to decipher the essential functions of the few genes that have persisted through this extensive decay.

Positive Selection Across Scales: Genetic Architecture of Adaptation and Connectivity in Wild Sunflowers

Zhiqin Long

Background

Positive selection is a key evolutionary force driving adaptive evolution across multiple biogeographic scales, with different evolutionary consequences. At local scales, positive selection can promote local adaptation by accumulating advantageous mutations within populations, thereby contributing to local divergence. At broader scales, it may facilitate the spread of advantageous alleles across populations, thereby connecting populations in geographically widespread species or even between closely related species. Moreover, positive selection may underlie parallel adaptation among species exposed to similar abiotic or biotic conditions. The genetic architecture underlying these adaptive processes is expected to vary. Migration–selection balance theory predicts that genes involved in local adaptation will exhibit concentrated architectures and higher pleiotropy to counteract the homogenizing effects of migration, whereas genes repeatedly involved in species-wide or interspecific sweeps may show reduced pleiotropy, as complex architectures can slow adaptive responses. Species-wide sweeps are also predicted to be enriched for genes involved in genetic conflict. In this study, we ask: (1) how positive selection contributes to the adaptation and connectivity of species across multiple biogeographic scales, including local, species-wide, and interspecific scales, and (2) how genetic architecture varies with adaptive process and geographic scale.

Methods

We analyzed a whole-genome resequencing dataset of 1,229 individuals from four Helianthus species, with distributions ranging from narrow (H. argophyllus, 297 individuals) to intermediate (H. petiolaris ssp. petiolaris, 144; ssp. fallax, 199) to wide (H. annuus, 589). To detect locally adaptive loci, we applied Wavelet Spatial Genetic analysis (Lasky et al., 2024), which captures spatial patterns of genetic relatedness across multiple scales without discretizing populations or knowing selective pressures in advance. To identify species-wide and interspecific selective sweeps, we integrated a haplotype-based statistics with a site frequency spectrum–based method. Tissue specificity of genes was evaluated using RNA-seq data from five tissues in H. annuus to estimate levels of pleiotropy. Gene family duplication events were inferred using OrthoFinder3 based on chromosome-level genome assemblies.

Preliminary Results

Our results identified thousands of locally adaptive genes across all four species. Functional annotation reveals strong enrichment for genes involved in abiotic stress responses. These candidates significantly overlap with genes identified in previous genotype–environment association (GEA) analyses (Todesco et al., 2020), supporting the interpretation that heterogeneous patterns of genetic relatedness often arise in response to local environmental pressures. These genes also show higher pleiotropy than genomic background genes, consistent with theoretical expectations. At species-wide and interspecific scales, globally adaptive genes are enriched for functions related to chromosomal segregation, cell cycle regulation, defense, and reproduction, and are strongly shared across species, supporting pervasive parallel evolution. Contrary to expectations, globally adaptive genes exhibit elevated pleiotropy and are enriched in low-duplication gene families, suggesting selection may favor genes with larger effects. Notably, globally adaptive genes overlap substantially with locally adaptive genes at broader scales, indicating that positive selection may facilitate the spread of beneficial alleles and promote connectivity among populations and species.

Overall, our results highlight positive selection as a key evolutionary force shaping diverse biological processes, with strong parallelism across species. The genetic architecture of adaptation is consistent across multiple geographic scales.

Potential for alleviating inbreeding depression using gene editing

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Humans are devastating biodiversity on the planet. While conservation management is slowing extinction rates for many threatened species, the battle is being lost as more species are becoming threatened. Gene editing has revolutionized the genetic manipulation of domestic and laboratory species and has the potential to make major contributions to conservation. This presentation will consider how gene editing may contribute to conservation by alleviating inbreeding depression. For species down to a single population (usually critically endangered) and suffering inbreeding depression, there are no current genetic management options to alleviate their problems. This proposal involves identifying homozygous harmful alleles of large effects contributing to inbreeding depression and “curing” them by gene editing. The recently announced “de-extinction” of the dire wolf by gene editing 14 gray wolf loci represents a technical proof of principle for such a proposal. Crucially, gene editing to alleviate inbreeding depression needs to avoid population size bottlenecks at foundation that lead to additional genetic problems. Thus, after removing individuals with harmful off-target edits, there needs to be at least 25 reproductively contributing, independent homozygous edited individuals (or 50 heterozygous ones).