ABSTRACT BOOK

The Fourth Meeting of the Israeli Society for Evolutionary Biology

ISEB 2023

2-3 April 2023, University of Haifa

www.iseb.org.il

Plenary Talk #1

Tal Pupko
The Shmunis School of Biomedicine and Cancer Research, Tel Aviv University

AI and Phylogenomics

For many biological domains, spanning diverse fields such as ecology, genomics, systematics, and epidemiology research, an accurate inference of the underlying phylogeny is indispensable. As such, the development of more accurate phylogeny-reconstruction techniques is an ongoing effort that continuously progresses with the type and size of data analyzed, the computational resources available, and algorithmic developments. Numerous computational techniques were imported from the fields of statistics and computer science in order to improve phylogenetic tree reconstruction. These include treating character evolution as a Markov process, Branch-and-Bound, Markov chain Monte-Carlo, genetic algorithms, and simulated annealing. Despite these improvements, commonly used algorithms still lack the ability to provide an optimal solution. In my talk, I will present our efforts to harness artificial intelligence (AI) for faster and more accurate phylogenetic reconstruction.

Plenary Talk #2

Margarida Cardoso Moreira
The Francis Crick Institute, London, United Kingdom

Origins and evolution of vertebrate organs

My group's research centers on understanding the genetic and developmental bases of organ evolution. By comparing the developmental gene expression programs that give rise to organs across multiple species, we have identified genes, types of mutations, and cellular and developmental processes that underlie the evolution of several mammalian organs. A key challenge in understanding organ evolution is determining how morphological novelties arise, such as new cell types, new tissues, and, ultimately, new organs. To address this challenge, we focus on an organ that has originated independently across many taxa and that exhibits extraordinary phenotypic diversity: the placenta. The mammalian placenta originated once in the ancestor of placental mammals and marsupials and diversified to such an extent that it is the most morphologically diverse mammalian organ. New cell types and tissues have evolved to shape this organ across mammalian species, presenting a unique model to study the origins of these innovations. More broadly across vertebrates, placentas have arisen independently more than 100 times. My group investigates how complex organs originate by studying a family of fish, the Poeciliidae, where placentas have evolved independently multiple times.

Plenary Talk #3

David Gresham
New York University, USA

Copy number variants alter local and global mutational tolerance

Copy number variants (CNVs), duplications and deletions of genomic content contribute to evolutionary adaptation, but can also confer deleterious effects. We investigated *Saccharomyces cerevisiae* (yeast) strains that have CNVs of variable copy numbers and structures. Although beneficial in selective conditions, CNVs typically result in decreased fitness in alternate conditions. We used transposon mutagenesis to investigate mutational tolerance and genetic interactions with CNVs. We find that CNVs confer novel mutational tolerance in amplified essential genes as well as novel genetic interactions. CNV strains have increased mutational tolerance in genes related to translation, and reduced mutational tolerance in genes related to mitochondrial function. We performed RNAseq and found that transcriptional dosage compensation does not affect the majority of genes amplified by CNVs. Furthermore, we do not find that CNV strains exhibit previously described transcriptional signatures of aneuploidy. Instead, CNV strains exhibit downregulation of genes involved in cellular respiration, nucleoside biosynthetic processes, and small molecule metabolism, and upregulation of genes involved in transposition, nucleic acid metabolic processes, and siderophore transport. Our study reveals the extent to which local and global mutational tolerance is modified by CNVs with implications for genome evolution.

Plenary Talk #4

Nina Wedell
University of Exeter, United Kingdom
The University of Melbourne, Australia

Sex, Conflict, and Selfish Genes

Selfish Genetic Elements (SGEs) are genes, organelles, or microorganisms present within the genome or cell of an organism that spread by subverting normal patterns of inheritance to increase their representation in the next generation; hence the term 'selfish'. SGEs such as endosymbionts, transposable elements, and meiotic drive genes are ubiquitous in living organisms and are often associated with fitness costs to the bearer. Despite their impact on the reproduction of their host, their potential role in sexual selection and sexual conflict is largely overlooked. I will discuss some recent work examining the impact of a variety of SGEs showing they can affect the behaviour and reproduction of their host, often with sex-specific effects, and argue they can be important contributors in shaping sexual selection and sexual conflict.

Studying the variation in MS2 bacteriophage evolution during serial passaging experiments

Reem Abu Rass, Moran Meir, Carmel Farage, Uri Gophna and Adi Stern, Tel Aviv University

RNA viruses have high mutation rates, short generation times, and large population sizes, features that allow viruses to evolve exceptionally rapidly. Previous studies in our lab showed that during serial passaging experiments of the RNA virus MS2, cheater viruses emerge under conditions that allow cellular co-infection with two or more different viruses. To test the extent to which cheater viruses emergence, we increased the probability of co-infection even further (high multiplicity of infection MOI). Surprisingly, the results of experiments with high MOI values varied widely. Namely, we found that the founding population of the experiment, despite being genetically homogenous, affected the evolutionary outcome of the experiment. Notably, we verified the genetic homogeneity of each founding population using accurate deep sequencing and found no mutations at appreciable frequencies that could explain these results. We are now focusing on elucidating these perplexing results. We are tackling three different hypotheses, all of which revolve around the idea that there is some form of hidden genetic diversity: (a) our deep sequencing does not allow us to identify mutations at primer positions at the 5' and 3' ends of the genome, and thus we are using 5' and 3' RACE (rapid amplification of cDNA ends) to allow sequencing of these regions across founder populations, these regions are known to have important functions across a variety of viruses. (b) We are examining whether the founder populations may bear RNA modifications by using direct RNA sequencing using MinION. (c) We are examining the possibility that founding populations are composed of haplotypes of differing lengths. Altogether, this study may help uncover how a presumably homogenous viral population leads to very different evolutionary outcomes, and this may have implications for understanding different disease outcomes across different individuals as well.

Discovering the role of tRNA- codon usage adaptation in viral infection

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Regulation of mRNA determines the efficiency, throughput, and accuracy of conversion of the transcriptome into the proteome. A major regulator of translation elongation is the cellular tRNA pool and its coordination with the codon usage of the transcriptome. Recent works demonstrated that the tRNA pool and codon usage change in diverse cell types in a manner that correlates with physiology in health and disease. However, the causal effects of these molecular changes on the physiological state of cells are yet to be demonstrated and understood. Here, I explored the co-adaptation of codon usage and the tRNA pool in viral infection, from both the human and viral perspective. I performed a systematic comparison of the codon usage of human-infecting viruses to the proliferation-differentiation signature and revealed several features that shape the viral codon usage, such as the type of the viral genetic material, the tissue tropism, and the proliferative state of the host cell to which the virus is adapted. Using tRNA deep-sequencing I found dynamic changes in the tRNA pool, both in expression and modification level, of HCMV-infected cells. Intriguingly, some changes occur in response to the infection itself, while others are part of the cellular immune- response, taking place even without the virus. In SARS-CoV-2- infected cells though, the tRNA pool appears not to display regulation in the form of tRNA expression levels and modifications. I further found that viral genes encoded for structural proteins are mostly adapted to the tRNA pool of HCMV and SARS-CoV-2- infected cells. I additionally identified specific tRNAs and modification enzymes whose inactivation upon CRISPR- targeting reduced HCMV infectivity. This study is one of the first studies elucidating the fundamental role of tRNAs in viral infection.

Mutation bias in driver genes reveals the distribution of fitness effects of oncogenic mutations

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Tumor development can be driven by mutations at many genomic sites most of which are still unknown. The probability that an individual site acquires a tumor-inducing mutation is defined by the rate at which this mutation originates, and the degree to which it contributes to tumor development. Here, we design a method for joint estimation of the number of driver mutations and the distribution of their effects at individual genes, and show that accounting for how the observed mutations within a gene are distributed among contexts improves precision of this inference. Using this method, we show that for most oncogenes, the vast majority of driver mutations have already been observed, while for most tumor-suppressor genes, the bulk of driver mutations are still unknown. These results show that tumor-inducing genes vary in the relative roles of mutation and selection in determining the distribution of driver mutations; and inform interpretation of newly detected mutations.

Periodical environmental changes and the evolution of senescence

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Senescence is a process of phenotypic deterioration that leads to increased mortality risk with age, and eventually to death. Senescence (or life-history rate) evolution can be affected by changes in population size: in growing populations, fast life-history (fast senescence coupled with early reproduction) is preferred. The intuition is that during population growth, progeny born earlier can reproduce earlier, and will represent a larger part of the population at the end of the growth period. In a declining population the reverse logic applies, and slow life-history (slow senescence coupled with late reproduction) is advantageous. Natural environments do not allow either indefinite growth nor indefinite decline, and the more common scenario involves periodical environmental change. However, the theory that examines senescence evolution under such conditions is lacking. I will present a new model that predicts the effect of periodical environmental changes on senescence evolution, and use it to compare different senescence strategies. First, we find that synchronization of offspring production with the start of the growth period, if no costs are involved, is always favored. Second, plastic response to environmental changes – namely regulating senescence rate according to the timing of birth with respect to the environmental cycle – is more likely to evolve than bet-hedging under periodical change that occur at the timescale of species lifespan. The model can help explain both within-population variation in senescence and deviations from classic senescence theory in periodic environments.

The differential spread of neutral and adaptive cultural traits among partially connected populations

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Inferring the relations between cultures from their reflection in the archaeological record, as material artifacts at different sites and layers, is one of the major challenges in prehistoric archaeology. Modeling the dynamics of spread of cultural traits, such as tool types and production techniques, is crucial for such inference. Although many studies highlight the extent of inter-population connectivity as a major determinant of such spread, a cultural trait's specific characteristics are rarely taken into account in modeling the probability of its spread. To derive insights about spread of cultural traits, we use analogies with population genetics theory about the spread of genetic traits among partially connected populations as a function of their fitness consequences. The theory, rather intuitively, predicts very different probabilities of spread for neutral and for adaptive traits. Useful perspectives and predictions can be derived from this simple differentiation: (1) One may attempt to predict the range of rates of inter-population connectivity that would have led to uniformity across populations in functional cultural traits, and how this range differs from that for neutral cultural traits. (2) One may use this difference, and the archaeologically observed extent of a trait's uniformity across sites, to infer which cultural traits were neutral and which were adaptive. Using a dynamic computational model, we explore the differential dynamics of traits and demonstrate that even low connectivity rate between populations may suffice for the spread of adaptive traits.

Genetic diversity, chimerism, and invasiveness in the protochordate Botryllus schlosseri

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The colonial ascidian Botryllus schlosseri, most likely a Mediterranean Sea species, is one of the known human-mediated invaders of coastal marine communities. The species has invaded the Northern and Southern Atlantic and Pacific coasts. This worldwide distribution is primarily anthropogenic in nature, most likely developed during the last millennium. Population genetics studies of B. schlosseri worldwide, using microsatellite markers, point to highest polymorphism level in the native populations of the eastern Mediterranean and southern Europe coasts. The analyses also revealed high genetic differentiation between most invading populations. Invasive populations are established by only a few founders, resulting in low genetic diversity. However, adaptation for invasiveness to various habitats should also comprise a capability to exploit and prosper in diverse ecological niches, thus expected to be associated with a certain level of genetic diversity. A conceivable way of attaining high genetic diversity even when a small number of founders is involved is chimerism, an intra-organismal genetic heterogeneity, resulting from a fusion between different individuals—a common phenomenon found in numerous phyla. The chimera is composed of a mosaic of cells containing distinct genomes. Chimerism is a general phenomenon in Botryllus, and considerable levels of chimerism were detected in the tested invading populations.

The co-option of the mechanosensing and mechanotranduction during the evolution of biomineralization in metazoans

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Embryonic development is driven by the interplay between genomically encoded gene regulatory networks (GRNs) and mechanosensing and mechanotransduction networks (MMNs) that sense and respond to the mechanical properties of the embryonic environment. The evolution of new organs necessitates the coordinated changes in GRNs and MMNs, especially during evolutionary innovations where the stiffness of the extracellular matrix changes dramatically, e.g. in the evolution of biomineralization. Biomineralization is believed to have evolved independently in different phyla, using distinct minerals, organic scaffolds and GRNs. Yet, all biomineralizing cells experience a distinct increase in the stiffness of their environment due to the formation of the biomineral, which is expected to activate the MMNs in these cells. Here we report that the same MMN regulates gene expression and biomineralization in the vertebrates' bone cells and in sea urchin skeletogenic cells, despite the distinct GRNs that control the specification of these cells. In vertebrates' osteoblasts, ECM stiffness activates Focal Adhesion Kinase (FAK), that activate the RhoGTPAse, RhoA, that activates RhoA associated coiled-coiled kinase (ROCK). ROCK activity enhances the strength and activity of the actomyosin network and leads to Erk signaling and to activation of osteoblasts transcription factors. We discovered that sea urchin FAK, ROCK and Erk are active in the skeletogenic cells and their activity is necessary for biomineral growth and skeletogenic gene expression. Perturbations of FAK, ROCK and a reduction of substrate stiffness result with a reduction of skeletal growth and an increase of ectopic branching. We propose that distinct GRNs across metazoans, had employed independently the mechanosensing and mechanostrasduction machinery, in response to the increase of ECM stiffness during the evolution of biomineralization.

Non-violent conflict resolution: a role for microbes?

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Conflicts between individuals are common in nature. A social interaction that describes a conflict (e.g. over a resource, territory, etc.) may be associated with a significant reward or cost, and the outcome is affected by the behavioral strategies and aggressiveness level of the participants. Several theoretical models, for example the Hawk-Dove model (originally defined by Maynard Smith and Price in 1973), have studied the evolution of these strategies from the perspective of the host's genes (where 'hawk' and 'dove' represent aggressive and non-aggressive behavior, respectively). Here we propose that microbes that affect the aggressiveness of their hosts could be favored by selection, and may play a role in shaping the level of aggressiveness among the population. By extending the Hawk-Dove model to include both the hosts and their microbes, we find that microbes inducing non-aggressive behavior are favored under wider conditions compared to genes with similar effects. As a result, the mean fitness of the population is also higher. Our results raise the possibility that changes in the microbial composition within individuals can affect the level of aggressive behavior in the population, and may affect its prosperity over time.

Evolutionary perspective of disease and social solidarity in past populations: the example of a Nabataean Noblemen from Yotvata, Israel

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Sickness in ancient populations might decrease the reproductive fitness of the diseased individual and the population as a whole. Furthermore, ill and disabled people may represent a burden for their group. Nevertheless, not only does evidence of disabled individuals exist since very early in human evolution, but their survival was dependent on social solidarity. This research presents a possible case of Klippel-Feil syndrome (KFS), a rare congenital genetic disease, in a 50-year-old male (H-1) from the Arava desert dated to the Nabataean period (2nd century BCE). H-1 was recovered from an outstanding double chamber mausoleum built on a hilltop and was associated with several valuable artifacts (e.g., high-quality linen and a coffin made of Cedar wood). Altogether, these findings indicated a burial of a high-ranking individual. Following a thorough examination of the skeletal remains, including µCT scans, we identified several pathologies: a cervical vertebrae block (C2-C4), Sprengel's deformity (SD), extensive antemortem tooth loss, and two healed fractures in the distal left forearm. The characteristics of the vertebral fusions - smooth between C2/C3 and irregular between C3/C4 - suggested different etiologies for each segment, i.e., congenital and secondary osteoarthritis, respectively. These conditions, along with SD, are typical of KFS. The poorly healed fractures identified in the left forearm may suggest H-1 suffered from recurrent falls, possibly caused by postural instability. These manifestations resulted in a deformed external appearance and probably some disability. Considering H-1's age, he probably survived owing to the support he received from his community. Moreover, his exceptional burial indicated that he was a nobleman, suggesting that social status among the Nabateans was not dictated by performance and appearance.

Using Multi-Scale Genomics to Associate Poorly Annotated Genes with Rare Diseases

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Next-generation sequencing has revolutionized the identification of disease-causing genes for genetic disorders. However, a definite molecular diagnosis remains elusive in many sequenced patients, where multiple variants are present in genes without a clear connection to the patient's phenotype. In this study, we optimized a multi-scale approach based on phylogenetic profiling (PP) to predict the disease-causing gene in patients. Our approach detects correlated evolution signals among 1,028 eukaryotic genomes to link mutated genes found in patients to their clinical phenotypes. We introduce EvORanker, an algorithm that combines multi-scale PP with additional omics to prioritize disease-candidate genes. In a cohort of previously solved exomes, EvORanker ranked the "true" disease gene as the top candidate in 69% of cases and among the top 5 in 95% of cases. EvORanker demonstrated superior performance compared to existing methods, particularly for poorly annotated genes. The application of EvORanker to two unsolved exomes has led to the discovery of two novel genes as the underlying disease-causing genes for two previously undescribed genetic syndromes. In summary, EvORanker provides an innovative, systematic approach to the discovery of novel disease genes and missing links between genes and phenotypes.

Ancient DNA from a lost Negev Highlands desert grape reveals a Late Antiquity wine lineage

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Recent excavations of Late Antiquity settlements in the Negev Highlands of southern Israel uncovered a society that established commercial-scale viticulture in an arid environment. We applied target-enriched genome-wide sequencing and radiocarbon dating to examine grapevine pips that were excavated at three of these sites. Our analyses revealed centuries long and continuous grape cultivation in the southern Levant. The genetically diverse pips also provided clues to ancient cultivation strategies aimed at improving agricultural productivity and ensuring food security. Applying genomic prediction analysis, a pip dated to the 8th century CE was determined to likely be from a white grape, to date the oldest to be identified. In a kinship analysis, another pip was found to be descendant from a modern Greek cultivar and was thus linked with several popular historic wines that were once traded across the Byzantine empire. These findings shed light on historical Byzantine trading networks and on the genetic contribution of Levantine varieties to the classic Aegean landscape.

Lepidosaur Macroevolution Through Deep Time

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Lepidosauria is the largest clade of tetrapods in the world today comprising over 11,500 known species. To analyze the evolutionary rate of Lepidosaurs' phenotypes through time, we constructed the largest existing dataset of their external morphology (head length and width, body length, limb length and tail length) from both fossil and living species. We collected data from ~23,000 specimens from 3107 species, of which 274 are extinct. We log-transformed the data, calculated evolutionary rates of morphological change, and searched for instances along the phylogeny where evolutionary rates either increased or decreased. The overall evolutionary rate of Lepidsoauria was significantly lower than what would be expected under Brownian motion. We identified rate decreases in the Toxicofera, Gekkota, and Lacertibaenia. On the other hand, we found a rate increase in Scincomorpha. When analyzing body mass alone, we found increased rates in Pythonomorpha and decreases in Iguania, Lacertibaenia, and Gekkota. We then analyzed evolutionary rates, as a function of different forms of substrate use (terrestrial, aquatic, fossorial, etc.), and found, surprisingly, that fossorial and semi-fossorial species exhibited the highest evolutionary rates whereas generalist and scansorial species had the lowest. We hypothesize that fossorial and semi-fossorial species face the strongest evolutionary pressure, with the largest number of morphological solutions, whereas generalist species do not face strong selection pressure as they possess an ecologically flexible Bauplan.

A modified reproductive strategy increases parasitic mite adaptivity

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Genetic diversity is essential for populations to adapt to environmental changes. Due to genetic drift, invasive species, and parasites in particular, have low genetic diversity. Yet by definition, to be invasive, a species must quickly adapt to changes: new environment, new host, and in the case of parasites, also pesticides. This paradox raises a fundamental question of how invasive parasites adapt to changes while having low genetic diversity. This is particularly intriguing in haplodiploid systems which have even lower effective population size, as males can inherit and transmit only half of their mother's genome. Here we show that a major global invasive pest of honeybees, Varroa destructor, so far believed to be haplodiploid, is actually not. By investigating the mite's genetic inheritance in a whole genome pedigree experiment across three generations, we discovered that males, while karyotypically haploid, keep both copies of their mother's genome and can equally transmit both copies to their daughters. We suggest that this, along with recombination events, allows a greater genetic diversity than under typical haplodiploidy, by increasing the mite's effective population size. This "cryptic diplodiploidy" could be more common than assumed and potentially explain the remarkable resilience and high adaptivity of varroa and other invasive parasites.

The role of multi-partner protein interactions in the evolution of RNase-based self-incompatibility

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Highly polymorphic genetic loci are the exception rather than the rule. Hence, the few that we know raise theoretical questions regarding the evolutionary forces promoting genetic diversity in these cases. A prominent example is the self-incompatibility (SI) systems of plants, which typically encompass a few dozen of alleles. These systems evolved to reduce the risk of self-fertilization in hermaphroditic plants, which could produce less-fit offspring. Here we focus on the RNase-based self-incompatibility mechanism, which relies on specific molecular interactions between proteins of two families: fertilization inhibiting S-RNase expressed in female organs and fertilization-enabling F-box protein (SLF) expressed in male organs. Thus the combination of alleles an individual possesses determines its mating partners. While it is known empirically that S-RNase and SLFs are highly diverse, previous models failed to pinpoint the evolutionary trajectories by which new alleles evolve, and none of them were able to suggest a stable homeostatic system, demonstrating the natural creation and extinction of alleles over time. Here, we construct a novel theoretical framework, to study the evolutionary emergence and maintenance of S-RNase and SLF alleles. Crucially, our framework allows for multiple distinct partners per protein, as known empirically. A natural consequence of our model is the emergence of fertilization classes, such that all between-class and no within-class fertilizations are possible. We demonstrate a dynamic long-term balance between the emergence and extinction of classes, whereas the equilibrium number of classes depends on population parameters. The emergence of new classes does not require passage through a self-compatible intermediate, or allelic crossover between haplotypes, as previously thought. In summary, our framework is the first to suggest a robust model for RNase-based SI evolution, resolving some open questions. It highlights the role of multi-partner protein interaction, and can also be used to address general questions regarding the size and complexity of biological networks.

Internal tandem duplications in FLT3 and how they lead to gain-of-function of a tumour promoting phenotype

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FLT3 is a tyrosine kinase enzyme that is normally important for development of the blood system and should not be active in adults. About 30% of the patients who suffer from acute myeloid leukaemia (AML) harbour an activating mutation in the FLT3 enzyme. Interestingly, most of these mutations are in-frame internal tandem duplications (ITD) of a stretch of amino acids in the protein. It is not clear why ITDs occur, and how they activate the protein is puzzling. In general, there are very few cases where such mutations are known to be tumourignic except in FLT3. We have studied in-frame insertions in FLT3 from patients, and have characterised their length, sequence and most probable places in which they occur. This analysis, together with computer simulations, helped us to understand why such mutations lead to gain-of-function. It has also suggested that we should not expect differences in response to drugs between patients carrying these mutations. Drugs that aim for inhibition of FLT3 are indeed effective, but additional mutations in the protein lead to drug resistance which will also be discussed.

A mystery in-between: a comparative study on the evolution of intron length

Lior Glick, Gil Loewenthal, Tal Pupko, Itay Mayrose

Introns are noncoding sequences found between exons of eukaryotic genes. In many cases, introns account for the majority of the gene length and thus entail various costs related to their transcription and splicing. Still, introns are present across all eukaryotes. While multiple functional and evolutionary explanations for the abundance of introns have been suggested, to date the impact of introns on the evolution of genomes is still unclear. In this study we approach this question by performing a comparative evolutionary analysis of intron length distributions across hundreds of species from two important taxonomic groups: vertebrates and plants. We report that plant introns are generally an order-of-magnitude shorter than vertebrate introns, and their growth is more tightly constrained. We further found that the effect of the genome size on intron length is considerably stronger in vertebrates than in plants. This results in plant and vertebrate species with comparable genome sizes possessing introns of very different lengths. Since the expansion of genomes alone cannot explain the observed difference, we examined the repetitive content of the studied genomes. We discovered that although plant genomes are more repetitive than vertebrate genomes, plant introns display lower repeat content compared to vertebrates. Moreover, repeats within plant introns are consistently shorter than those found in intergenic regions, suggesting selection favoring their elimination from plant, but not vertebrate introns. This may provide a mechanistic explanation for the distinct intron length distributions observed in plants and vertebrates.

Cell-autonomous evolutionary adaptation

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Throughout evolution, organisms adapt to a wide range of stresses such as high-altitude, extreme temperatures, dietary changes, and pathogens. Well-studied adaptive traits in humans and other multi-cellular organisms often occur in genes expressed in tissues and organs that are relevant to the particular environmental challenge. For example, altered levels of erythropoiesis as an adaptation to high-altitude or thick fat layers in animals living in cold climates. However, we argue that adaptations may also reside in smaller biological units than tissues and organs. Particularly, we hypothesize that some germ-line inherited adaptations may occur in genes that function in cells throughout the body, perhaps within every cell, and may acquire selective advantage to the organism despite their operating in a cell-autonomous fashion. We thus suggest that in addition to organ/tissue-level adaptations, a conceptually novel layer of evolutionary adaptation may be at work in multi-cellular species which we term cell-autonomous adaptation (CAA). Since CAA needs not be organism-specific, it can be shared across distant species, even microbes, living in similar environments. A well-established example of this distinction between cell-autonomous and organ/tissue-level can be found in immunology. While the humoral immune system provides immune protection to the entire body, each individual cell is equipped with cell-autonomous immune mechanisms to ward off the pathogen attack. Through a deep literature-review, we explore the importance of this newly defined concept, particularly in its conservation from humans, to plants and even to unicellular microbes and its implications towards multi-cellular evolution. Further, we explore CAA experimentally via genome-wide CRISPR screens to identify essential genes for the cell's survival under environmental stresses (e.g. hypoxia, UV radiation). Next, we compare the essential genes to genomic regions under selection in human populations adapted to extreme environments (e.g. Tibetans, Greenlanders) to search for CAAs that are adaptive to both the cell and organism.

Not an automatic pilot: The important role of sexual selection on navigation performances of nocturnal moths

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Male moths locate mates based on the female-emitted species-specific sex pheromone. The odor-mediated navigation of male moths in an odorant environment is conceptualized as odorscape. This chemotactic navigation is shaped by natural and sexual selection forces. We tested the effect of two aspects of mate choice on the chemotactic navigation performance of male moths:(1) Availability of one or two odor sources. (2) Quality of the source, either high or low. The source quality was defined as the reproductive potential of virgin females, either fed (high-quality) or starved (low-quality). In wind tunnel experiments, the pink bollworm male moths (*Pectinophora Gossypiella*) were introduced to 3 types of odorscapes: A single odor source of either high- or low-quality females and a pair of odor sources of both high- and low-quality females. The navigation performance of males was tracked using infrared cameras in a steady wind velocity. Two complementary approaches quantified the males' navigation performance: (1) population level- a superimposed spatial distribution of all males' positions, and (2) the individual level, which includes kinematic parameters such as navigational distance, navigation time, and airspeed. We found combined effects of the availability of one or two odor sources and their quality on the navigation performance of male moths. In no-choice conditions, the source quality had no impact on the males' navigation patterns; however, when introduced into choice conditions, the males' navigation patterns differed in relation to the source quality and the number of sources. Interestingly, males who chose the higher quality source had prolonged navigations with higher airspeed than those who chose the poor source, suggesting higher energy costs to males who chose the higher quality females. This is the first study that provides comprehensive evidence for the role of sexual selection on the navigation performance of male moths.

An evolutionary perspective on osteoporosis development

Dr. Helena Gondra and Amit Hadad, De[t. Anatomy and Anthropology, Tel Aviv University

Osteoporosis is a major public health concern, affecting millions worldwide. Its economic burden is rapidly expanding as the world's population ages. Advancing our knowledge regarding osteoporosis etiology is necessary for improving treatments and preventive measures. This study aimed to examine temporal changes in bone health characteristics throughout the last fifteen-thousand years. For this purpose, a non-destructive, valid, and reliable method was developed to study ancient samples. The study included 68 femoral heads housed at the Dan David Center, TAU. These were divided into three main periods: Prehistory (1,000-8,400 cal.BP), Protohistory (11,600–8,400 cal.BP), and History (1st century CE-18th century AD). This division corresponds with significant socioeconomic transitions (e.g., the Agriculture Revolution) that affected humans' way of life, which became more sedentary over time.

All femoral heads underwent a µCT-scan (50µ resolution) at the Shmunis Institute, TAU. Then, osteoporosis was diagnosed from 2D cross-sections, and trabecular bone measures in 3D were obtained (e.g., volume, area, and thickness). We found that the femoral head size was significantly associated with osteoporosis manifestation and increased over time. Furthermore, we demonstrated that the relative trabecular bone volume and thickness were better for diagnosing bone health than its area. Finally, a temporal reduction in bone health was evident. Accordingly, the relative trabecular bone volume and thickness significantly reduced during human history. Thus, in prehistoric times, the risk of osteoporosis was lower than in historic times. To conclude, changes in human lifestyle throughout historical development, including increased sedentism (i.e., reduced physical loadings) and changes in dietary habits, were accompanied by reduced trabecular bone despite the increase in bone size. Hence, the tradeoff of a thrifty skeleton is a risk of osteoporosis in advanced age and could result from a micro-evolutionary process. Consequently, efficient preventive measures for osteoporosis development should focus on encouraging physical activity during early life.

Recurring cyanophage infection results in increased fitness rather than changes in host range

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Marine cyanobacteria from the genera *Prochlorococcus* and *Synechococcus* are abundant photosynthetic organisms, responsible for a significant fraction of global primary production. Cyanobacteria-infecting bacteriophages (cyanophages) present large variability in host range, with some infecting as few as one host (specialists), while others infect several hosts (generalists), sometimes from different genera. Host range, and host compatibility in general, was previously shown to be an evolvable characteristic. In order to persist, cyanophage host range must be compatible with the hosts available in the environment, which vary with time and space. Here, we aim to understand which adaptive trajectory is more likely: Adaptation to better infect the original susceptible host, or changes in host range. We explore the adaptive trajectories of one specialist and one generalist cyanophage under different host availability conditions. Upon repeated infection of the susceptible host, we observed a decrease in time to lysis by both specialist and generalist evolved cyanophages compared to the ancestors. This indicates that both phages adapted to better infect the susceptible host. Sequencing of adapted specialist clones, identified by their increased plaque size, revealed three mutated genes that appear to be responsible for the increased fitness. When testing the adaptive trajectory of populations propagated in the presence of a resistant strain, we observed increased fitness during infection of the susceptible host. No change in host range was found for either phage, even though the resistant non-host made up 50-99% of cells. Interestingly, sequencing of the specialist phage populations revealed different mutations to those found in the absence of the resistant strain, indicating that the presence of the resistant strain led to different pathways of adaptation. Our findings suggest that the evolutionary jump required for host range expansion in the interactions tested was difficult to achieve, thus resulting in adaptation to better infect the susceptible host.

Marine zooplankton and associated microbiome as environmental bioindicators

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Ocean water masses hold distinct physical and chemical characteristics and play a crucial role in regulating the climate and maintaining the global ocean circulation system. Different water masses serve as habitats for a wide range of marine organisms, and their movements and interactions can affect the distribution and abundance of these organisms. Within the open sea continuum, mesoscale eddies form unique habitats characterized by distinct physical and chemical conditions, with high or low productivity, supporting and distributing a wide variety of zooplankton, including the larvae and eggs of benthos and fish.

In the Mediterranean Sea, two major thermohaline cells steer the circulation of the western and eastern basins, and a third cell connects the two basins in the deeper waters. The Eastern Mediterranean Sea (EMS) is the hottest, saltiest, most nutrient-poor basin, experiencing rapid biotic transformations due to the influx of alien species via the Suez Canal and further facilitation of the thermophilic aliens by climate change. Due to the ultra-oligotrophic nature of the EMS, eddies are of particular importance, forming productivity islands within the “blue desert”, or facilitating the dispersal of aliens.

Using an integrated approach combining imaging with molecular metabarcoding of Mediterranean zooplankton, we found indications for biotic transformations in the EMS, water mass specific assemblages, and evidence for eddy-derived dispersal and facilitation of Indo-Pacific aliens. We further studied the associated microbiome of dominant copepod species in the EMS and across the Mediterranean. While free-living microbial composition did not present a biogeographic separation, the copepod-microbiome showed clear west-east partitioning and microbial composition gradients. Moreover, we found nitrogen metabolism enrichment in the EMS copepod-microbiota compared with the free-living microbiome, indicating the importance of such associations in oligotrophic environments. We conclude that both zooplankters and their associated microbiome can act as valuable, complementary water mass and environmental bioindicators.

Characterization of polyploidy in plants using extensive ploidy inference based on chromosome number

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Polyploid taxa resulting from genome duplication events are present in diverse groups including Animals, Fungi, and Invertebrates and Plants. Polyploidy is particularly common in plants, with polyploids often exhibiting major phenotypic differences from their diploid ancestors, ranging from morphological, physiological, and life history characteristics to evolutionary rates and adaptive behaviors. These altered characteristics displayed in polyploids may be linked to their success in novel ecological habitats, or to their interactions with their environment. To examine the generality of such hypotheses, the ploidy level of a wide range of plant taxa must be available. However, despite the existence of several methods to infer ploidy levels based on genome size, sequence data and chromosome number information, the ploidy level of most plant taxa remains unknown. We developed PloiDB – a ploidy level database generated using a probabilistic likelihood framework based on extensive chromosome number information and phylogenetic data, that ranges over tens of thousands of plant taxa. We further utilized this framework to determine the effect of phylogenetic scale on ploidy level inference, and to conduct two broad-scale analyses. First, we examined the phylogenetic distribution of polyploids. Our analysis, encompassing 755 plant genera and 22,892 taxa, indicated that polyploidy is a tippy trait. Namely, a trait that appears mostly towards the tips of phylogenies, suggesting of higher extinction risk. Of polyploid lineages. In the second analysis, we studied the consequences of polyploidy on plant-pollinator interactions across 696 ecological networks. Our results demonstrated that, despite prior expectations, polyploids are not more generalists than diploids and do not contribute more to the stability of their community to extinction.

Rapid evolutionary changes in a sexual trait in response to anthropogenic interference: The case of the pink bollworm in cotton fields

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Sex pheromones, released by female moths, provide information on the female species, her mating status, and her reproductive potential and allow conspecific males to choose females advertising their higher reproductive potential. As a part of agricultural control practices, an excess amount of partial blends of the species-specific sex pheromone is applied. The many years of continuous exposure to the synthetic blend enforce mate-seeking males and females to adopt alternative solutions to achieve reproduction. In this study, we demonstrate a change in the ratio of the sex pheromone components in gland extracts of the pink bollworm (*Pectinophora gossypiella*) females in cotton fields treated with the synthetic pheromone for many years. We also demonstrate that males are more attracted to traps baited with the changed ratio of the pheromone components. The change in the female-emitted pheromone and the males' mate preference resulted in the encounters of males and females that escaped the masking effect of the commercial synthetic pheromone. We suggest a possible evolutionary scenario for the evolved changes in the pheromone blend emitted by females and for the directional preference of mate-searching males.

Compensatory frameshifts are common in *Saccharomyces cerevisiae* genes

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Frameshifts result from the insertion or deletion of a nucleotide in a DNA sequence, leading to a shift in the reading frame of the mRNA. This shift causes a downstream change in the amino acid sequence, ultimately resulting in the production of a nonfunctional protein. Compensatory frameshifts refer to a phenomenon where a frameshift mutation is followed by additional mutation(s) that restores the original reading frame and allows for the correct amino acid sequence to be produced. Although functional compensatory frameshifts have been reported, they are infrequent. We looked for Compensatory frameshifts in protein-coding genes of 50 closely related wild-type Saccharomyces cerevisiae strains. These S. cerevisiae genes are highly similar which enables us to identify Compensatory frameshifts based on the differences between the nucleotide and codon multiple sequence alignment. A Compensatory frameshift event was classified if an internal shift was recorded between the nucleotide and codon alignment flanked by identical nucleotide and codon alignment both upstream and downstream to this region. Sixty events that are unique to a specific strain and occurred in non-repetitive regions were identified in addition to events that occur multiple times in repeat regions. Most of the events are composed of two sub-events but some also have three sub-events that are spread over tens of bases. We conclude that Compensatory frameshifts are common over a short evolutionary time.

The disperser dilemma

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In many cooperatively breeding songbirds, individuals of both sexes disperse from their natal group in order to breed, but females disperse more often than males (Kingma et al. 2021, The evolution of delayed dispersal and different routes to breeding in social birds). In such species, adult non-breeding individuals of both sexes face a recurrent dilemma: (1) To delay further their dispersal with the hope that opposite-sex potential mates will shortly immigrate into their natal group, or (2) To disperse immediately into a group with potential mates, and bear the higher risk of perishing on the way. There is an obvious interdependence among the sexes' choices - as individuals of one sex take more risks and disperse more often, opposite sex individuals are further incentivized to wait in their natal group for such incoming mates. What determines the sexes' stable dispersal rates within each social species? To address this question we develop a dynamic, game-theoretic model of differential risk-taking during dispersal. Non-breeding individuals of both sexes who have not yet dispersed recurrently choose whether to wait or disperse; the dispersal hazard is a random variable, partially correlated with the ability of opposite-sex individuals to assist dispersers' integration into the target group. Individuals disperse only when the dispersal hazard falls below a certain threshold, and we analyze the Evolutionarily Stable Strategy (ESS) thresholds of the sexes. We find that the physically weaker sex, typically the females, take more risks in dispersal, and therefore disperse more often. This prediction is corroborated by data on the cooperatively breeding Arabian babbler (Argya squamiceps): Females disperse at a younger age, in smaller coalitions, to further-away groups, and with longer time windows between leaving and joining, despite the lower survival rate concomitant with dispersal (Ostreiher, Mundry and Heifetz, in preparation).

Genomic landscapes of adaptation to future climate: wild barley as a model

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Global climate change poses significant challenges for ecological systems, agriculture and food security. The expected environmental effect is particularly challenging in countries like Israel where demographic processes and accelerated development compete with conservation efforts for the same land resources. So far, the impact of climate change on biodiversity has been studied mainly in an ecological context, yet living organisms are dynamic and can response to environmental change subject to their genetic potential. Here, I will present a new comprehensive wild barley germplasm collection comprised of 300 accessions that represent a wide ecological spectrum including extreme environments. This collection was characterized in a common garden and whole genome sequence data was generated for all accessions. The unique sampling design enabled to identify signals of selection at high resolution despite the strong ecotypic structure among wild barley populations. Moreover, predictive models were developed and the genetic offsets were estimated in a special geographic framework. The main limiting factor for wild barley dispersion and establishment is precipitation where shifts in rainfall are predicted to have a sever impact on the suitability of the current habitats. Desert and eastern populations are equipped with adaptive alleles to future climates while other populations, especially along the southern Mediterranean shore, are at high risk and may fail to cope with climate change unless ecological corridors are kept to allow gene flow.

Genetic contribution of Asiatic wild ass males in response to changes in water-source distribution in the Negev highlands

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Genetic diversity is a leading concern in conservation biology due to both its short and long-term implications for species sustainability. Small populations of polygynous species are particularly susceptible to genetic diversity loss because of the limited number of breeding males that contribute to the gene pool. In territorial polygyny, in which males gain reproductive advantage by defending valuable resources, such as food and water. This effect may be stronger when resources are scarce. We estimated the change in breeding males' genetic contribution in the Asiatic wild ass (Equus hemionus) population in the Negev highlands, following active water-source management. This management was implemented by the Israel Nature and Parks Authority to increase water availability in the range of the Asiatic wild ass that has a strong polygynous mating system. We hypothesized that as territorial males tend to establish their territories next to water sources to increase mating opportunities, increasing the number of permanent water sources in the Negev would result in increased numbers of territorial males contributing to the population's gene pool. We established a methodological system to infer genotypes, using hundreds of single nucleotide polymorphisms (SNPs) with a non-invasive sampling approach, to detect relatedness among individuals at a high resolution. Parentage analyses revealed that the number of contributing males increased following the increase in the number of available water sources. Moreover, the geographic locations of breeding males supported a spatial shift in their home ranges toward the new water sources. These findings accord with our research hypothesis. This, in turn, may increase the variance effective size of the population, which is important for the population long term persistence.

Sex, testosterone, and fitness in wild rock hyrax

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Although males and females share traits, their motivations and needs may be different, due to life-history disparities that lead to divergent selection pressures. Proximate mechanisms underlying differences between the sexes include hormones that mediate the development and activation of suites of traits. Testosterone is associated with morphological features, physiological processes, and social behaviors in both sexes. However, even if present in similar concentrations in the circulation, testosterone often affects males and females differently. We combined behavioral mating observations of the wild polygynandrous rock hyrax (Procavia capensis) with hair testosterone that represents long-term integrated levels. We found that whereas copulation success increases with the rise in testosterone in males it decreases in females. We did not find an association between testosterone and choosiness in either sex. However, we found that males with higher testosterone mate-guarded females with lower testosterone. We also found differences in sperm characteristics between males that reside with females and bachelor males. Our findings provide clues to the cost of testosterone and status, in terms of fitness, and open intriguing questions relating to sex and status differences and how they trade off to affect reproductive success.

Computational prediction of divergent ant olfactory receptor binding sites

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Social ants use Olfactory Receptors (ORs) to detect and discriminate between diverse cuticular hydrocarbon (CHC) odorants, large hydrophobic molecules that function as social cues in ants. Ant ORs have diverged to hundreds of distantly related receptors in every species that share a common 7TM architecture and chemosensory functional characteristics. However, our understanding of how evolution shaped the landscape of ant ORs to encode for diverse odorant binding is very limited. Here, we developed a computational pipeline that utilizes Alphafold2 to predict the 3D structures of related ant ORs and their binding sites. Our results show larger and more hydrophobic binding sites for ORs that bind large CHCs, while ant ORs that bind smaller and more polar ligands are also predicted to have smaller binding sites. Residue conservation across the gene trees also validated the prediction pipeline and our results. Our approach provides a molecular basis to decipher how ant ORs were tuned by evolution to detect a wide diversity of chemical signals using a shared 3D scaffold.

The role of the differential tropical-temperate evolutionary potential of tree species on their current global distribution

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The present day distribution of species is affected by their evolutionary history, and is driven by speciation, extinction and dispersal. The evolutionary histories of species have contributed to the well-known latitudinal diversity gradient (LDG) of species richness, but also to other less studied gradients, such as the biome-dependent gradient of species ranges. However, despite a platheore of suggested hypothesis, there is no consensus as to the mechanisms generating these patterns. Here, we study the underlying evolutionary histories leading to the distribution patterns of tree species. We generated and analyzed an extensive dataset of tree species, which includes present-day global distribution dataset and a resolved phylogeny. We identify two trends: (i) an out-of the-tropics trend, wherein most non-tropical species have a tropical origin, and (ii) tropical niche conservatism, wherein tropical species show a higher-than expected phylogenetic clustering. These observations have led us to hypothesize that although tropical special likely experience high environmental filtering, indicated by the phylogenetic clustering, they may have a high adaptive potential and are successfully migrating outwards form the tropics. To further investigate this hypothesis, we tested whether this radiative potential is persistent and continuous throughout time. By analyzing the divergence between tree communities in different geographic locations, we identified a stronger divergent composition between extratropical communities than between tropical communities. This finding suggests that out-of-the-tropics migrations were discrete expansion events, rather than a continuous process. Furthermore, we identified a strong geographical association of phylogenetically related communities in extratropical regions, suggestive of environmental filtering that constrains the expansion of these communities after their formation. Our analysis sheds light on the events leading to the current latitudinal gradient distributions of tree species, and suggests that a similar approach could shed light on macroevolutionary and macroecological patterns in other taxa.

The Role of Segment Polarity Genes in Hemimetabola Segmentation

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Segment polarity genes are an essential part of the segmentation developmental process in all arthropods. These genes were first identified and studied in fruit flies and got their name from the phenotype the flies showed when the genes were inactive; Genes like engrailed, hedgehog, and wingless. Classical studies in arthropod segmentation showed that there is little variation in the expression of segment polarity genes between different arthropod clades. However, recent studies that look at the formation of the anterior head of arthropods, and specifically insects, show that the functions and expressions of segment polarity genes differ in the anterior head's segmentation compared to the rest of the segments. Furthermore, segment polarity genes functions, expressions, and interactions are very thoroughly studied in holometabolous insects like the aforementioned flies, but their roles in segmentation in hemimetabolous insect (insects that have direct development with no pupae phase) is less understood. The lack of studies in non-holometabola insect groups and the discrepancy between the classic and newly shown roles of segment polarity genes in the segmentation of different parts in arthropods drove us to look deeper into their function. In this project we used CRISPR/Cas9 to eliminate the expression of the segment polarity genes engrailed, its paralog invected, hedgehog, and wingless to observe the knock-outs effects on segmentation in different body areas of the hemimetabolous bug, Oncopeltus fasciatus. This study will show the function of segment polarity genes in different tagmata of the bug and can be compared with their functions in other studied arthropods to provide a bigger tapestry of segment polarity genes and their evolution.

What are the genes that make evolution work?

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Evolvability is the capacity of an organism to adapt to the constantly changing environment. Surprisingly, the mechanisms that enable organisms to evolve are not well understood. Some genes are known to restrain evolvability. These mainly include genes coding for DNA repair proteins that decrease the number of mutations and thus limit the speed of adaptation. Yet other genes, such as transposons, and genes involved in horizontal acquisition of foreign DNA from other organisms, may increase evolvability by increasing the mutation rate and gene mixing. In our study we hypothesize that many genes in each organism affect evolvability either positively or negatively and that the regulated interplay between them during evolution governs the rate and nature of evolutionary adaptation. In particular we ask the following questions: what are all genes encoded in a genome that affect the species' evolvability? Is evolvability always linked to the genomic mutation rate? What is the role of phenotypic mutations in affecting evolvability? We combined theoretical, experimental and informatics means to discover the evolvability genes in genomes and characterize their mode of action. Using the yeast S. cerevisiae we conducted a genetic screen for genes affecting evolvability. In this screen all viable single gene deletion mutants were mixed and competed under diverse conditions. Rather than selecting the fastest growing mutants, we developed a method to select the mutants that increased their fitness the fastest. This has culminated in a list of candidate genes that increase evolvability upon deletion. A complementary method further allows us focus on individual evolvability genes and examine how they affect rate of evolution and in parallel rate of mutation. In this talk I will present our current results for several genes for which both assays have been performed, and discuss the possible mechanisms through which they may affect evolvability.

The evolutionary dynamics that retain long neutral genomic sequences in face of indel deletion bias: a model and its application to human introns

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Insertions and deletions (indels) of short DNA segments are common evolutionary events. Numerous studies showed that deletions occur more often than insertions in both prokaryotes and eukaryotes. It raises the question why neutral sequences are not eradicated from the genome. We suggest that this is due to a phenomenon we term border-induced selection. Accordingly, a neutral sequence is bordered between conserved regions. Deletions occurring near the borders occasionally protrude to the conserved region and are thereby subject to strong purifying selection. Thus, for short neutral sequences, an insertion bias is expected. Here, we develop a set of increasingly complex models of indel dynamics that incorporate border-induced selection. Furthermore, we show that short conserved sequences within the neutrally evolving sequence help explain: (i) the presence of very long sequences; (ii) the high variance of sequence lengths; and (iii) the possible emergence of multimodality in sequence length distributions. Finally, we fitted our models to the human intron length distribution, as introns are thought to be mostly neutral and bordered by conserved exons. We show that when accounting for the occurrence of short conserved sequences within introns, we reproduce the main features, including the presence of long introns and the multimodality of intron distribution.

Sib-mating enhances fitness in a haplodiploid beetle

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Inbreeding is generally avoided in animals due to the risk of inbreeding depression resulting from an increase in homozygous deleterious alleles and loss of heterozygosity. Species that regularly inbreed pose a challenge to understanding the effects on fitness of these risks. We investigated fitness consequences of extended inbreeding in the haplodiploid date-stone beetle, Coccotrypes dactyliperda. We hypothesized that persistent inbreeding would result in inbreeding depression while outbreeding would either increase fitness due to heterosis or lower fitness if co-adapted gene complexes are disrupted. We established three breeding treatments with beetles from two geographically separated populations: Sib-mating, outbreeding within the local population, and between-population outbreeding. Between-population outbreeding groups of both populations had reduced fecundity and collapsed before the experiment ended, while sib-mated groups persisted for ten generations and the females had higher fecundity than both outbreeding groups. Average inbreeding coefficients of sib-mated groups were higher than the other treatment groups, yet sib-mated beetles remained genetically polymorphic. Thus, there was no evidence of inbreeding depression, while outbreeding between distant populations led to outbreeding depression. Our findings are consistent with the life history of C. dactyliperda, in which sib-mating predominates within the date seed, but occasional within-population outbreeding likely occurs following local dispersal.

Characterizing the mechanisms at the origin of short structural variation across species

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Genome integrity is maintained by molecular mechanisms which repair DNA whenever molecular, physical, or chemical processes inflict damage upon it. One of the most severe types of damage is Double Strand Breaks (DSBs), which can potentially lead to losses of entire chromosomal arms of parts of such, harmful chromosomal rearrangements, and interfere with cell division. DSBs are repaired through different mechanisms, classified to error-free and error-prone mechanisms, such as non-homologous-end joining (NHEJ), microhomology-mediated end-joining (MMEJ) and Synthesis-dependent MMEJ (SD-MMEJ) which leave specific genomic signatures in the genome. These mechanisms have been characterized in experimental systems, where DSBs can be induced using molecular scissors like CRISPR-Cas9, but their footprints have not been assessed in whole genome datasets, due to limitations in the current available methods to infer the DNA repair mechanisms underlying natural variation among individual genomes. Here we report a probabilistic method to characterize DNA repair using short structural variants (INDELs), that enables the analysis and comparison of patterns of DNA repair in experimentally-induced and naturally occurring INDELs. Using this method, we quantify the proportion of different DNA repair mechanisms under different biological scenarios and genomic contexts, providing a better understanding of their role in the evolution of genomes.

The evolutionary root of frequent modern human disorders

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Many of today's physical impairments can be related to the morphological adaptations that occurred during human evolution as well as the mismatch between the human body and our environment. The talk will present two studies relating to these evolutionary risk factors. The first will demonstrate how the transition to an erect stance and bipedal locomotion, among the most fundamental milestones in human evolution, increased our risk of manifesting a hip fracture. The second study will present the impact of fast changes in human behavior on morphological discrepancies of the masticatory system. These could explain the high prevalence of malocclusion nowadays. In both studies, we followed shape changes in the skeletal elements' morphology over time using the landmark-based Geometric Morphometric method. Multivariate statistical analyses and visualization were carried out based on the 3D landmark configurations. These studies emphasized the compromises involved in being a modern human. For example, the changes in proximal femoral morphology which occurred during human evolution and history, i.e., between populations that practiced different lifestyles (e.g., hunter-gatherers and recent humans), resulted in an increased risk for hip fracture, independent of osteoporosis. Hence, hip fracture is a trade-off for efficient bipedal walking in modern humans and is exacerbated by reduced physical activity. Recognizing the elementary risk factors for modern disorders is valuable for improving our ability to predict the risk of these diseases and develop new preventive measures.

Environmental stress leads to mutualism breakdown and biodiversity loss in a simplified bacterial community

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Our current times are characterized by extensive environmental degradation, resulting in significant biodiversity loss and an increased risk of extinction for many species. However, population extinctions can be avoided if species are able to evolve and adapt to their new environment – a phenomenon termed evolutionary rescue (ER). ER has been extensively studied for populations composed of a single genotype, but remains poorly understood for communities of interacting genotypes. Theoretical studies have proposed that populations engaged in obligate mutualistic interactions have reduced adaptability to changing environmental conditions and a diminished capacity for ER. Here, we experimentally study the ER dynamics of an obligate mutualism using a cross-feeding system composed of engineered auxotrophic Escherichia coli strains that reciprocally exchanged essential amino acids. We exposed obligate mutualistic pairs to sudden salinity stress, resulting in a significant reduction in growth rate and overall biomass declining towards extinction. However, mutualistic populations recovered and avoided extinction through the emergence of a single prototrophic strain, leading to the breakdown of the mutualistic interaction. Reversion of the auxotrophy was able to rescue the population, as prototrophic strains were more salt-tolerant than auxotrophic ones. The consistent auxotrophic reversion of the same strain across all replicate populations implies that mutualistic populations' ability to undergo ER may hinge on their capability to revert the auxotrophy, particularly when auxotrophy is more vulnerable to stress than prototrophy. Our results indicate that heightened stress sensitivity resulting from obligate dependencies can facilitate the breakdown of mutualistic networks and lead to biodiversity loss in response to environmental deterioration.

Evolutionary adaptations in microbial microcosms are largely independent of the presence of coevolving species

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During laboratory evolution, replicate bacterial populations often follow similar trajectories, thus their evolution is potentially predictable. However, predicting the evolution of natural populations, which are commonly embedded in multispecies communities, might prove extremely difficult if adaptations are contingent on the identity of the interacting species. The extent to which adaptations typically depend on coevolving partners remains poorly understood, since coevolution is commonly studied using small-scale experiments involving few species, making it challenging to extract general trends. To address this knowledge gap, we study the adaptations that occurred in strains of each of 11 species that were either evolved in monoculture or in multiple pairwise cocultures. While we detect slight but significant partner-specific adaptations, we find that the majority of evolutionary changes that occur are robust across strains that evolved in different biotic contexts; species' growth abilities increase by a similar factor regardless of partners' identity, shifts in community compositions are similar between coevolved pairs and pairs of mono-evolved strains, and the majority of parallelly mutated genes were detected in multiple biotic conditions. We hypothesized that these results might arise from the fact that ancestral strains are maladapted to the abiotic environment, thus having a pool of adaptations that are beneficial regardless of the biotic context. Therefore, we conducted a second experiment with strains that were pre-adapted to the abiotic conditions before being cocultured. We find that even after ~400 generations of pre-adaptation, evolution is surprisingly non-partner-specific. Further work is required in order to elucidate the factors that influence partner-specificity of coevolution, but our results suggest that selection imposed by the biotic environment may play a secondary role to that imposed by abiotic conditions, making predictions regarding coevolutionary dynamics less challenging than previously thought.

Mitochondrial genomics - ancient evolutionary challenges in regulating a bigenomic system with intracellular variation

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Mitochondrial activity is central for metabolism of the eukaryotic cell, and its disfunction leads to both Mendelian and complex disorders. As factors that operate mitochondrial function are divided between the mitochondrial DNA (mtDNA) and the nuclear genome (nDNA) mito-nuclear coordination is imperative. Such mito-nuclear coordination and coevolution play a role in both human diseases and in hybrid breakdown and speciation events. Secondly, unlike the nDNA, the mtDNA resides in multiple copies per cell, which differs in number between cell types and tissues. mtDNA copies frequently diverge in sequence thus creating a mixed population of mtDNA molecules (heteroplasmy). Already during the late 1980's it has been shown that heteroplasmy of deleterious mutations can cause variability in disease phenotypes. However, even highly deleterious mutations can encompass a relatively high proportion of the mitochondrial population per cell without any phenotypic consequences. Another layer of the intracellular variation of the mitochondrial factors stems from RNA modifications and RNA editing of the mitochondrial genome. Here I will touch upon findings that support mito-nuclear co-regulation, the mechanisms and evolutionary forces that modulate heteroplasmy and mitochondrial RNA editing across metazoan evolution.

Exploration of changes in exon number of orthologous genes across the phylogenetic tree

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The availability of the complete genomic sequences of hundreds of eukaryotes opens the way to understand genome evolution at an unprecedented scale. It is commonly thought that genes of higher organisms have more exons. However, there are anecdotal cases of orthologous genes whose number of exons changes in different lineages. The patterns of exon number change across species and the functional effect of that change have not yet been studied systematically.
Here, we have classified genes by their pattern of change in number of exons across the phylogenetic tree. We identified several prevalent patterns of change in number of exons. Some patterns are in accordance with higher organisms having more exons. Other patterns display lineage specific increase in number of exons, hinting that specific functions evolved differently in specific phyla.

A quantitative multi-trait approach is consistent with a major evolutionary transition rather than stepwise increased social complexity in bees

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It is commonly accepted that sociality in insects evolved linearly from a solitary lifestyle through stepwise climbing to complex societies. This “social ladder” theory, based on three traits to achieve “eusociality”, draws a unified framework placing all insect societies on the same evolutionary route. Here, we applied a bottom-up quantitative approach incorporating social and life-history traits to build a multi-dimensional phenotypic space. We used a novel implementation of dimension reduction analyses and phylogenetic inference methods to explore the phenotypic space and the evolution of social complexity in bees. Our analyses are not consistent with discrete sociality phenotypes of accumulative complexity. Rather, our results fit best with two main sociality phenotypes in bees: The monophyletic honeybees, stingless bees, and bumble bees show a high level of social complexity that is distinct from the remaining lineages of orchid bees, sweat bees, and Xylocopinae bees, which form a continuous and flexible gradient of sociality. Our evolutionary reconstruction suggests a major evolutionary transition only for the monophyletic superorganisms and did not support a social ladder in which living species represent a primitive state. The evolutionary route of species through our phenotypic space showed a pattern of directed selection toward superorganismality compared to the rest of the species forming simple societies. Overall, we conclude that bees societies did not evolve in the frequently accepted stepwise manner of increased complexity. The quantitative nature of this approach is specifically powerful for testing relationships between social complexity and "omics" molecular, physiological, and behavioral parameters. Our novel, multi-trait framework sets the stage for studying the evolution of social complexity in additional lineages.

Evolution of supergenes: lessons from social chromosomes

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Supergenes are large genomic regions that determine complex polymorphic traits. The most well known example are sex chromosomes. A large portion of the X and Y chromosomes do not recombine, which allows them to diverge and evolve sex-specific traits. In general, supergenes allow for the evolution of a diverse range of complex traits, including floral morphology in primroses, mimetic wing patterns in butterflies, and morphs with distinct reproductive strategies in birds and lizards. All these examples constitute complex traits of high fitness impact. In social insects such as ants, the social structure and mode of colony reproduction have great ecological and evolutionary consequences. "Social chromosomes" harbor supergenes that determine colony structure in socially polymorphic species, which form either monogyne (headed by a single queen) or polygyne colonies (with multiple queens). Such supergenes were discovered in diverse ant species, suggesting multiple independent evolutionary origins. We discovered a novel supergene in the desert ant Cataglyphis niger, representing a fourth independent origin. Comparative analyses of the four systems reveal general patterns of social supergene evolution, as well as striking variations that may reflect differences in life history and ecology among ant lineages. Interestingly, two of the previously described supergenes act as selfish genetic elements, employing two different mechanisms of action. In the Cataglyphis supergene, we found an unexpected mode of apparently strict maternal inheritance, which may be related to selfish evolution. We are investigating the mechanism responsible for this pattern, including potential mito-nuclear incompatibility.

The second domestication of cattle- harnessing in-vitro evolution for cultured meat production

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Cellular agriculture could become a major part of our nutrition in the coming decades. In the process of cultured meat production, multicellular organism cells face new challenges, including ex-vivo growth and differentiation toward muscle and fat tissue, which is a very different fate than they were selected for. Can mammalian cells be adapted to thrive and fulfill their destiny in the new environment in order to produce high-quality meat-like products? To address those questions, we are employing a genome-wide CRISPR knockout screen, preformed for the first time in bovine stem cells. In combination with suitable selection pressure, we aim to identify the genes and pathways associated with the proliferation and differentiation of bovine-derived mesenchymal stem cells (bMSCs). This approach will enable us to improve the properties of bMSCs and make them better suited for cultivation in the production of cultured meat.

Aneuploidy can be an evolutionary detour on the path to genetic adaptation

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Aneuploidy is common in eukaryotes, often leading to decreased growth and fitness. However, evidence from yeast and fungi, as well as human tumour cells, suggests that specific aneuploidies can be beneficial under stressful conditions and facilitate adaptation. Yona et al. (2012) have demonstrated in an evolutionary experiment with yeast that populations evolving under heat stress become aneuploid, only to later revert back to euploidy after genetic mutations have accumulated. It has therefore been suggested that aneuploidy serves as a "stepping stone" on the path to adaptation. To test this hypothesis, we developed an evolutionary model with both aneuploidy and mutation, and fit it to the results of the experiment using a Bayesian inference framework. We then predicted the genotype frequency dynamics during the experiment, demonstrating that the majority of the evolved euploid population likely did not descend from aneuploid cells, but rather directly from the euploid wild-type population. Surprisingly, these results agree with DNA sequencing results that show that mutant alleles common in aneuploid cells are uncommon in the evolved euploid population. Our model further predicts that if the experiment was repeated with smaller populations, then a larger fraction of the evolved population would descend from aneuploid cells. Thus, we suggest that aneuploidy can be an inevitable evolutionary "detour" rather than a "stepping stone": it can delay, rather than facilitate, the adaptation of the population, and cells that become aneuploid may leave less descendants compared to cells that remain diploid.

Origin and Regulation of the Vertebrate Kidney

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The anterior-posterior (AP) axis in chordates is regulated by a conserved set of genes and signaling pathways, including Hox genes and retinoic acid (RA), which play well-characterized roles in the organization of the chordate body plan. The intermediate mesoderm (IM), which gives rise to all vertebrates' kidneys, is an example of a tissue that differentiates sequentially along this axis. Yet, the conservation of the spatiotemporal regulation of the IM across vertebrates remains poorly understood. In this study, we used a comparative developmental approach focusing on non-conventional model organisms, a chondrichthyan (catshark), a cyclostome (lamprey), and a cephalochordate (amphioxus), to assess the origin and the involvement of RA in the regulation of chordate and vertebrate pronephros formation.

We show in this study that the intermediate mesoderm and hence the nephric duct origin from a specific domain within the epithelial somite. We also demonstrate that the anterior boundary of early pronephric markers expression (Pax2 and Lim1), positioned at the level of somite 6 in amniotes, is conserved in the catshark and the lamprey. Furthermore, RA, driving the expression of Hox4 genes, similar to amniotes, regulates the anterior pronephros boundary in the catshark. However, this regulatory hierarchy is not involved in the AP positioning of the lamprey pronephros and the amphioxus pronephros homolog, Hatschek's nephridium. We conclude that, while Pax2 and Lim1 are conserved markers of chordate pronephros homologs, the responsiveness of the IM, and hence of pronephric genes, to RA and Hox4-dependent regulation is a novelty of gnathostome vertebrates.

The good, the bad, and the surprising- cholesterol metabolism adds another piece to the puzzle of evolution

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Cholesterol is essential for animal differentiation, growth, and reproduction. Surprisingly, the few invertebrates tested for cholesterol synthesis show complete cholesterol auxotrophy which sparked our curiosity to study the evolution and prevalence of sterol synthesis/ auxotrophy in animals. We found that the cholesterol synthesis pathway (CSP) evolved in basal animals and remains functional in vertebrates but was lost in many invertebrates, including nematodes and most arthropods. But how do sterol auxotrophs thrive without cholesterol synthesis? Using the nematode Caenorhabditis elegans to address this question we have identified a novel metabolic pathway that converts dietary plant and fungal sterols into cholesterol. This pathway relies on the loss of the first three enzymes of the CSP and the repurposed activity of downstream enzymes. Using the loss of the first three CSP enzymes as an auxotrophy signature, we discovered a few species of arthropods, including the parasite Bemisia tabaci (tobacco whitefly), that are predicted to re-acquire cholesterol synthesis by multiple and independent events of horizontal gene transfer. We propose that this intriguing type of horizontal pathway transfer is a general mechanistic principle underlying the acquisition of complex traits during the evolution of animals.

A non-homogenous model of chromosome-number evolution to reveal shifts in the transition patterns across the phylogeny

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Polyploidy, or whole genome duplication, is a remarkable feature in eukaryote evolution. Polyploidy exists in various phylogenetic groups, and is mostly prevalent among plants. Polyploids often differ substantially from diploids in morphological, physiological, and life history traits as well as rates of adaptation and speciation. The development of probabilistic models of chromosome number evolution allows the investigation of various hypotheses related to the dynamics of chromosome number change. While regarded as state-of-the-art, these models are still governed by simplified assumptions, such as rate homogeneity throughout the phylogeny and through time. These assumptions, however, are unlikely to hold in many large phylogenies, since rates of chromosome-number change differ across clades, and may be affected by various phenotypic traits, or by the ploidy level of a lineage. To this end, we developed heterogenous models of chromosome-number evolution that allow multiple transition regimes to operate in distinct parts of the phylogeny. We examined the performance of the developed model using simulations and empirical data and demonstrated its capability to detect shifts in chromosome number evolution. The developed model extends the range of analyses offered by probabilistic methods of chromosome-number evolution and should be particularly helpful for the analyses of large phylogenies that include multiple distinct subclades.

What is the secret of success of the invasive brown widow spider Latrodectus geometricus?

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Invasive species are those that invade new regions, often as a result of human action, and cause damage or threaten the ecological system. Invasive species may possess traits that promote their invasiveness such as high productivity, short development, and high dispersal ability. In addition, they may be less susceptible to natural enemies such as predators and parasites. The brown widow spider L. geometricus, is a highly invasive species globally, including in Israel. One of the main natural enemies of the brown widow spider, as well as of other widow spider species, is the parasitoid wasp Philolema latrodecti, which lays its eggs inside the egg sac of the spider. The wasp larvae feed on the spider eggs until they fully consume it, pupate inside the egg sac and emerge as adults. In the current study we found that the brown widow spider is less susceptible to parasitism by this wasp than a local species, the white widow spider, L. pallidus, under both field and lab conditions. Possible explanations include preference of the spider to human habitats where there might be fewer parasitoids, and better defenses of the egg sac by the female spider. Specifically, in the brown widow females construct spike-like silk structures as a defensive layer around its egg sac. In addition, they defend their nest more actively against the parasitoid than the white widow spider. I will present results of several field and lab experiments supporting these hypotheses. Such knowledge can aid combating this, as well as other invasive species, around the world.

Tracking past human dispersals using sedimentary ancient DNA

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In the past years, DNA retrieved from ancient human remains have been instrumental in furthering our understanding of our own evolutionary past, as well as that of our closest relatives, the Neandertals and the Denisovans. Such studies, however, are inherently limited to sites and timeframes where hominin remains have been found and made available for sampling. A complementary approach to generate genetic data from ancient individuals can be to recover ancient human DNA fragments from sediments – a ubiquitous source material often found in abundance at any archaeological excavation. As such, sedimentary ancient DNA approaches have the potential to elucidate the timing and geographical locations of significant events that influenced our history and the formation of our gene pool.
Here, we screened over 800 sediment samples from 148 Middle and Late Pleistocene archaeological sites in Europe, Asia, and Africa - including caves, rock-shelters, and open-air sites - testing them for the presence of ancient human DNA. This large-scale survey provides the means to evaluate, in a systematic way, the success rates of ancient DNA recovery in archaeological sediments, and to pinpoint factors that may lead to the long-term preservation of genetic material in them. Given sufficient resolution, the identification of ancient human DNA in sediments over such vast geographical and temporal spans could constitute a new way to trace the dispersals of ancient human groups through both space and time.

Modeling the effect of aneuploidy on cancer evolution

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A prime example of evolutionary rescue is the ability of cancer cells to survive treatment. Aneuploidy, the state of abnormal number of chromosomes in the cell, is hypothesized to increase fitness in the presence of anti-cancer drugs, e.g. due to incomplete pathways targeted by drugs. Aneuploidy is highly prevalent in tumours, and certain anti-cancer drugs attempt to combat cancer by increasing chromosomal instability. Here, we focus on the impact of aneuploidy on the fate of a population of cancer cells. We analysed an evolutionary model in which a population of cancer cells adapt to chemotherapy, focusing on the role of aneuploidy in the evolutionary rescue of the population. We use multi-type branching processes to analyse a two-step evolutionary rescue model, where aneuploidy has intermediate fitness between the sensitive wildtype and the resistant mutant. We estimated the probability that the cancer cell population will survive, how it is affected by the population size, the strength of selection imposed by the drug, and the rate of chromosome gain and validated our results using stochastic simulations. We observe that aneuploidy increases the probability of evolutionary rescue even when it is deleterious. We conclude that aneuploidy can play an important role in helping cancer cell populations escape the effects of treatment.

Deciphering genetic determinants of sexual mating and its effects on offspring fitness and evolution

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Sexual reproduction is wide-spread in nature, allowing combination of beneficial alleles. Many papers show that species choose mating partners, possibly to optimize offspring fitness. Major questions in the field are how organisms choose their partners, and how is offspring fitness relates to that of its parents'. Using a collection of 1000 natural isolates of S. cerevisiae strains (Peter et al. Nature 2018) we have generated and mined massive data on mate choice and fitness inheritance, in unprecedented magnitude, using sexual mating.
In our experiments, all yeast strains were allowed to mate with one another while progenies were detected using barcode recombination system (Yachie et al. MSB 2016) and next generation sequencing. This method allows the detection of mate choice as well as the fitness of parents and progenies by competing all strains in a test tube.
While in fermentable carbon source, offspring fitness was mainly dependent upon parents' fitness, in non-fermentable carbon offspring fitness increased with parents' genetic distance. In addition, we have looked upon mating efficiency and found the it declines with parental mating efficiency in both carbon sources. As for mate choice, en masse experiments suggest that yeast choose mating partners, possibly to avoid low fitness offspring.
Together our finding suggests that mate choice is exercised in low eukaryotes such as yeast and it contributes to fitness inheritance and evolution.

Unravelling the role of venom in predator-prey interactions using natural populations and transgenic approaches in Nematostella vectensis

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Recent advancements of the sea anemone Nematostella vectensis as a venomous model organism provide us with the opportunity to test for the first time how toxin genotypes impact predator-prey interactions at the organismal level. Previous work has revealed a striking phenomenon in which a natural population of Nematostella from Florida (USA) has undergone a gene loss event resulting in the significant reduction of Nv1, the most dominant toxin in adult Nematostella. This led us to develop a novel genetic manipulation tool to precisely reduce both RNA and protein of Nv1 at significant levels. We show that animals lacking Nv1 have a significantly reduced ability to defend themselves against grass shrimp (Palaemonetes pugio), a known predator of Nematostella. Unexpectedly, mummichogs (Fundulus heteroclitus), fish which share the same ecological niche, are significantly more attracted to Nematostella with wildtype levels of Nv1, hinting that Nv1 affects the fish's behavior. We further tested this by exposing mummichogs to water incubated with transgenic Nematostella animals overnight. We see that mummichogs exposed to water coming from transgenic control Nematostella (CTRL), which have wildtype-levels of Nv1, move significantly more than the Nv1-knockdown animals (KD). We hypothesize that accumulation of high Nv1 levels in the water can affect fish behavior, highlighting the potential role of Nv1 in chemical ecology. Finally, using a randomized feeding trial we see that KD animals grow significantly more when food is restricted compared to the CTRL animals. This provides clear evidence that Nv1 is metabolically expensive and can affect the physiology and fitness of an animal. Overall, by utilizing transgenic Nv1-knockdown animals that phenocopy a population that has naturally lost Nv1, we demonstrate for the first time that a single venom component has essential ecological roles that can shape interspecific interactions and contribute to the physiology and fitness of the animal.

Accumulation of deleterious alleles may be slower in r-selected species than commonly predicted

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Anthropogenic processes are increasingly causing fragmentation of habitats and populations around the globe, resulting in small populations vulnerable to various risks. Inter alia, small populations are vulnerable to fixation of deleterious alleles, due to increased genetic drift and ineffective selection. However, a species' life-history may influence the efficacy of selection acting upon it. If a species is highly r-selected (producing many offspring per reproduction event), the population of offspring in each generation may outnumber the adult population by several orders of magnitude, potentially increasing the efficacy of selection during the juvenile life stage. We used computer simulations to explore the force of selection experienced by a population as a function of the number of offspring produced by each adult. The results of our simulations suggest that provided that a deleterious allele is expressed during the juvenile life stage, selection against it in an r-selected species may be more effective than in a K-selected species (which produces few offspring per reproduction event), when adult population sizes are equal. Notably, our results were highly sensitive to the exact implementation of selection in the juvenile population, highlighting the importance of making assumptions explicit when exploring such dynamics. We conclude that in certain ecological scenarios, r-selected species are predicted to show greater resilience in the face of genetic bottlenecks, a factor that should be considered in the context of nature conservation and particularly when prioritising conservation efforts.

A single-cell view of a rapidly evolving morphology

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One of the major challenges of evolutionary biology is to uncover the molecular mechanisms underlying morphological divergence. To address this question, we use a model system with a huge interspecific variety, Drosophila male genitalia. Male genitalia are among the most diverse and rapidly evolving organs in the animal kingdom, probably due to sexual selection. This trend extends to the model organism D. melanogaster and its close relatives, which display dramatic morphological differences that are predicted to contribute to reproductive success. We focus on two closely related species, D. melanogaster and D. simulans, and the genetic and developmental basis of their morphological divergence. First, we generated 3D confocal microscopy images of the developing genitalia of both species at 8 different time points and demonstrated when the interspecific differences arise. Second, we performed a single-cell RNA sequencing on the D. melanogaster and D. simulans developing genitalia at the 3 most representative time points of mid pupal development and mapped the analyzed cells to different genital substructures. Thus, we revealed the expression profiles specific to each substructure in both species. These data will allow us to identify new genes that are involved in genitalia development and evolution, and the mutations that contributed to the morphological differences between these species.

Behavioural adaption of the pink bollworm moth in response to the mating disruptive technique used in cotton fields

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The pink-bollworm moth (Pectinophora gossypiella) is one of the most destructive cotton pests. Mating disruptive technique is an environmentally friendly control tactic, used worldwide for many years to control its population. In this tactic, the target field is permeated with the synthetic sex pheromone of the pest, to prevent males from finding females and mating. Like other anthropogenic interference, this control tactic may induce relatively rapid environmental change for the organisms it is applied against. It often alters the interactions of the organisms in the changed environment, causing population decline or driving evolutionary changes, including adaptive evolutionary responses. We hypothesized that due to the intense selection pressure on the moths to mate when treated with mating disruption, a change in the moths' mating behaviour might evolve. We compared the mating behaviour of naïve populations (who did not experience mating disruption) to that of field moths (collected from a field treated with mating disruption for many generations) and found two significant behavioural differences: 1. Males from the field increasingly interfere with mating couples in attempt to mate the receptive (copulating) female. When the synthetic pheromone was added, a negative interaction was detected: naïve moths reduced disturbing couples, and field moths increased this strategy. 2. Naïve males delay mating with small, inferior females, awaiting the receptivity of larger females. Field-collected male moths are less choosy and readily mate with smaller inferior females. We conclude that field-collected male moths have developed adaptive mating strategies to overcome the masking effect of the synthetic pheromone.

Adaptation under prolonged resource exhaustion is characterized by high levels of convergence and frequent historical contingency

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Escherichia coli are non-sporulating bacteria that possess an ability to enter a state called Long-Term Stationary Phase (LTSP), which allows them to survive very prolonged resource exhaustion. In July of 2015 an LTSP experiment was launched in our laboratory, in which five independent populations were established via inoculation into fresh media and have not been provided with any external nutrients ever since. We found that genetic adaptation under LTSP occurs in an extremely convergent manner, across independently evolving populations. Within each population, we observe the early establishment of lineages - subpopulations that descend from a common ancestors and co-exist within a population, alongside other lineages, evolving independently from them. The high convergence with which mutations occur, as well as the observed lineage structure has provided us with an opportunity to ask how contingent evolution under LTSP is. In other words, we could ask how often a certain locus is significantly more likely to be mutated on the background of specific or non-specific mutations in a second locus. We found very high levels of contingency with approximately a third of convergently mutated loci participating in contingent loci pairs. Contingent pairs of loci are significantly more likely than expected by chance to have known functional relationships. This indicates that the contingencies we identified are likely biologically meaningful, and that pairs of contingent loci are more likely to be functionally related, even when no such relationship is currently known.

The second domestication of cattle: Evolving bovine mesenchymal stem cells for cultured meat applications by genome wide CRISPR screen

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How can in-vitro evolution help us improve the cultivation of meat? Cultured cell-based meat is a rapidly growing alternative to traditional meat, aiming to mitigate adverse effects associated with live animals; it is more efficient, sustainable, and humane and has a smaller ecological footprint compared to live cattle. However, to achieve efficient and economical production of cultured meat on a large scale, several aspects must be improved, including the development of cell lines adapted for cellular agriculture. In particular, faster proliferation rates, improved differentiation efficiency, and adaptability to environments and conditions of cultured meat cultivation are essential traits for such cell lines. One approach to improve these phenotypes is to naturally evolve cells under appropriate selective pressure. However, limited divisions and the relatively long doubling time of mammalian cells make this approach extremely challenging. Instead, we aim to identify major genes and pathways associated with the desired traits of bovine-derived MSCs for cultured meat using a genome-wide loss-of-function CRISPR screen in conjunction with directed evolution. We isolated MSCs from bovine adipose tissues and confirmed that they retained their proliferation potential, multipotency, and ability to incorporate foreign DNA by lentiviral transduction. We curated a 3,000 sgRNA CRISPR KO sgRNA library targeting candidate genes, packaged the library into lentivirus, and transduced bMSCs. With appropriate selective pressure, each cell's fitness will vary based on the contained sgRNA, ultimately changing the composition of sgRNAs in the population, which is quantifiable by high-throughput sequencing. This enables us to discover and manipulate important genes and pathways affecting traits important for cultured meat cultivation. Our study provides a new perspective on the role of directed evolution in advancing the field of cellular agriculture. The identification and, ultimately, harnessing of said genes and pathways in bMSC will lead to more economical and efficient cultured meat production.