ABSTRACT POSTER BOOK

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Evolutionary trends in the Insect blastoderm

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Insect embryogenesis is a complex process that varies across different taxa. Despite this variation, all arthropods converge at the arthropod phylotypic stage: the germband. This conservation is reflected in both external characteristics, such as general morphology as well as genetic traits, including conserved gene regulatory networks that control segment polarity. While much attention has been given to segmentation and germband formation, The earlier blastoderm stage has received far less attention. Blastoderm morphology and the cellular behaviors underlying blastoderm formation remain poorly understood. Recent studies have highlighted the crucial developmental consequences of egg morphology and size, suggesting that understanding the evolution of the blastoderm over time and across insect clades could reveal intriguing patterns.

Actomyosin Remodeling Genes and their Role in Sea Urchin Larval Skeletogenesis

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Biomineralization is believed to have evolved independently in different phyla, using distinct minerals, organic scaffolds and gene regulatory networks. Yet, diverse Eukaryotes use the actomyosin network in shaping the biomineral, from unicellular organisms, through echinoderm skeletons to vertebrate bones. However, it is still unclear how the actomyosin network controls biomineral growth. Sea urchin larval skeletogenesis offers an excellent model system to study the role of the actomyosin network and remodelling in biomineralization. Specifically, the inhibition of the Rho GTPase, Cdc42, a prominent actomyosin remodelling protein, blocks sea urchin skeletogenesis and significantly decreases filopodia extension in the skeletogenic cells. However, it is still unknown which effector proteins are activated by the sea urchin Cdc42. Among the best-characterized downstream effectors of Cdc42 are the Paks (p21-activated kinases), a highly conserved group of serine/threonine protein kinases. Paks control the cytoskeleton primarily through the regulation of polymerized actin structures, particularly the formation of filopodia and lamellipodia. Here we investigated the spatial expression and role of Pak in sea urchin larval skeletogenesis using the Mediterranean Sea urchin, Paracentrotus lividus. The gene Pl-Pak3 expression is enriched in the sea urchin skeletogenic cells at early (20hpf) and late gastrula stage (27hpf) and it moves to tips of rods at the pluteus stage (48hpf). To perturb Pak pharmacologically we used the broad Pak inhibitor, PF3758309. Pak inhibition immediately after fertilization results in a much-reduced skeleton at the pluteus stage, with short body rods and no post-oral rods. Addition of inhibitor after skeleton formation results in small-sized embryos with short skeletons and ectopic branching in body rods. These findings suggest that Pak activity is essential for sea urchin skeleton elongation. I expect my studies to illuminate how the common actomyosin remodelling proteins such as Cdc42 and Pak regulate biomineral growth and morphology in invertebrates.

Characterizing the Regulation and Molecular Targets of TGF-β During Sea Urchin Biomineralization

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Living organisms from the five kingdoms of life use minerals to harden their tissues and make teeth, shells and skeletons, in the process of biomineralization. The genetic and molecular mechanisms that regulate biomineralization are far from clear. The Transforming Growth Factor Beta (TGF-β) signaling plays crucial roles in bone formation in vertebrates. The TGF-β pathway is highly conserved in the animal kingdom, which makes it intriguing to study its role in biomineralization in invertebrates' model systems. The sea urchin larval skeletogenesis is a prominent system to test if the role of TGF-β in biomineralization extends beyond vertebrates. Previous studies have shown that the sea urchin TGF-β receptor, TGF-βRII, is selectively expressed in the skeletogenic cells and TGF-β signaling is essential for sea urchin skeletogenesis. However, the upstream regulation and the downstream targets of TGF-β in the sea urchin have not been studied before. Here we study the spatial expression, upstream regulation and the molecular targets of TGF-β in the Mediterranean Sea urchin species, Paracentrotus lividus. The genes TGF-β and TGF-βRII are expressed in the sea urchin skeletogenic cells at the late gastrula stage, prism and pluteus stages. TGF-β inhibition results with a significantly reduced skeleton, in agreement with previous studies in other sea urchin species. Nevertheless, TGF-β inhibition did not affect the spatial expression of the key skeletogenic genes encoding the spicule matrix protein, SM50, and Vascular Endothelial Growth Factor Receptor (VEGFR), or the level of Fibroblast Growth Factor (FGF) at the abovementioned developmental time points. Further studies of the effect of TGF-β inhibition on other skeletogenic genes will hopefully promote our understanding of the regulation and role of TGF-β pathway in sea urchin biomineralization and illuminate its evolutionary origin.

Revision of the gene-culture model for the evolution of human handedness

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It is widely argued that about 90% of humans are right-handed, and that this bias is consistent across the hominin lineage and modern societies. Handedness is commonly attributed to (i) genetic mechanism preserved through a selective regime during human evolution, and (ii) lateralized modalities of the human brain (such as language). However, despite more than a century of research, the etiology of handedness fails to align with these suggestions and remains unclear. To bridge this gap, Laland et al., (1995) incorporated into a genetic model a cultural transmission effect to ascertain the extent to which children acquire their caregivers' handedness pattern rather than genetically inheriting it. A maximum-likelihood analysis indicated that this model aligns with existing data and provides a better fit for observations previous models struggled to explain. The authors predicted that if indeed handedness patterns correspond to cultural bias, variation in the cultural transmission parameters, but not in the genetic one, can be expected across societies and generations. The current study aimed to test this prediction, as this is the only published model integrating the two most discussed factors in the literature (culture and genes). To this end, the analysis was replicated using the original data (sampled from the US and UK). Then, its prediction was tested by applying it to a different sample of 639 independent pedigrees (total of 2018 individuals) from Indonesia, previously collected by Nurhayu et al., (2022) . A Bayesian analysis was further conducted to validate the results. We found similar results to the ones of the original study, indicating its reliability. Furthermore, we validated its prediction and found that in in rural Indonesia genetic predisposition is similar to the one in the UK and US sample, but the cultural component is stronger. To move forward, inheritance pattern among multiple generations from further cultures should be examined.

Oh, the places you'll go: selection on dispersal strategy at the range edge

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At some point prior to reproduction, every individual must decide whether to remain in its natal site or disperse from it. Individuals that stay in their natal site know that it is hospitable, on one hand, but also that they will likely face competition with kin and perhaps others. In contrast, uncertainty awaits individuals that leave their natal area. At the same time, dispersal ascertains avoidance of competition with kin and offers some prospects of reaching an inhabitable site with reduced competition and possibly increased reprodyuctive success. The propensity to disperse is thus an evolved trait whose natural selection is influenced by the chance to find a suitable deme with abundance of resources; this factor changes significantly along a species range. At the range's core, suitable areas are common and continuous, but they are also almost always fully occupied. The range edge is the opposite: the environment is fragmented and harsh, but suitable sites are more likely to be vacant due to extinction and recolonization dynamics. In this study, we investigate the costs and benefits of dispersal in a patchy environment governed by extinction-recolonization dynamics. We use a spatially explicit simulation of core and edge of a species distribution using increasing rates of stochastic catastrophes and chances of death while dispersing. We follow the evolution of dispersal phenotypes to argue that the vicissitudes and increasing patchiness at the range edge create qualitatively different dynamics at the edge, that select for higher tendency to disperse and, counterintuitively, contribute to the genetic pool of the species. These considerations are often underappreciated in studies about core-edge dynamics, even though they might play an important role in the evolution of dispersal and in gene flow patterns.

Transcriptome variation in Ommatotriton vittatus during life cycle adaptation to unpredictable habitats

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We investigated differences in gene expression during the life cycle adaptation of banded newts (Ommatotriton vittatus) to unpredictable habitats at the southern border of their distribution. The study identified 9988 genes that were differentially expressed in one of the pairwise comparisons between gene expression patterns of three clustered groups: (1) terrestrial newts (male and females), (2) aquatic newts (male and females), and (3) tadpoles before metamorphosis. Differences in mRNA level were demonstrated by principal component analysis. The total number of differentially expressed genes between aquatic newts (male and females) and tadpoles was 2399, indicating significant differences in gene expression between these two groups. In addition, while the differences between males and females within the same group were relatively small, these differences were more pronounced in the aquatic phase than in the terrestrial phase. Overall, the study suggests that banded newts undergo significant changes in gene expression during different phases of their life cycle, with more significant differences observed between aquatic newts and tadpoles. The results also highlight the importance of considering both sex and habitat when examining differences in gene expression in banded newts.

Quantifying the movement and ecological corridors of the McQueen's Bastard

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Anthropogenic land alterations result in habitat loss. In the northern Negev of Israel, habitat loss and illegal hunting have driven the population of MacQueen's Bustard (Chlamydotis macqueenii), one of Israel's flagship species, to the verge of extinction. An analysis based on a simple stochastic population model indicated that this regionally distinct population is expected to go extinct within 48 years under the current conditions. We explored the movement of MacQueen's Bustard and identified key environmental factors associated with the species distribution in the Negev desert of Israel. This was achieved using GPS data from nineteen males, who were equipped with GSM-GPS devices. During the breeding season, MacQueen's Bustards inhabit the Ezuz area before migrating to the Hatserim air base by walking. We identified dissimilarities in the male movement patterns across distinct activity seasons (breeding and migration season). Specifically, our findings indicate that during the breeding season, male activity is primarily diurnal in nature, whereas, during migration, there is a discernible shift towards nocturnal movement. Those results highlight the dynamic nature of male behavior in response to seasonal changes and underscore the importance of considering multiple temporal frames in the study of animal movement. In addition, We constructed habitat niche models using MAXENT and identified potential migration corridors. These corridors only partially overlap with protected areas. Therefore, we call for designating these entire corridors as nature reserves and preventing their destruction.

Climate change may lead to directional selection in nesting desert chameleons.

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Reproduction is the most important stage in animals' life and is greatly affected by environmental conditions. Many studies discuss the effects of incubation conditions on reptile eggs and hatchlings, but it is not known where most reptiles lay eggs or how they choose nesting sites. The desert chameleon (Chamaeleo chamaeleon musae) is an exception – we found that its nests are at one meter under the surface with burrows 1.5 m long leading to them. Females abandon several nesting attempts before laying eggs in the chosen location. If conditions while excavating nests will not indicate conditions during incubation, nests may become ecological traps. We constructed a dynamic state variable model to understand decision-making in females and predict climate change's impacts on the decisions. The model calculates the decision that leads to the highest fitness and considers the time and state of the individual. The model suggests that chameleons with a high energy state take more risks: they often reject burrows and keep searching for better nesting sites. In contrast, chameleons with a medium energy state dig and lay in the first possible site they find.
The decisions are influenced mainly by the costs of walking and digging. Climate change is predicted to soften soil crusts, causing an increase in the energetic cost of digging the beginning of the nests, but will also decrease the probability of encountering soil that is harder to dig. Climate change will have opposite effects on chameleons in different energetic states. Chameleons with high energetic states will improve their chances of laying, and those with low energetic states will decrease their chances. Assuming that the ability to reach high energetic state before laying has a genetic basis, may lead to directional selection favoring high energetic females.

Using network centrality measures as predictors of gene drive deployment outcomes

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Gene drives are genetic constructs with super-Mendelian inheritance that can spread deleterious alleles in wild populations. Gene drives could potentially be used to suppress or eradicate disease vectors, crop pests and invasive species, with deployment programs expected to commence within a decade. However, prior to deployment, it is crucial to understand how gene drives are expected to spread in order to design safe deployment programs. Previous gene drive models that investigated gene drive spread focused on simple population structures, either in homogenous continuous space or in two-population models. In order to study the behavior of gene drives in more complex population structures, we developed a discrete-space network-based model of gene drive spread with an arbitrary number of populations that are connected by arbitrary gene flow patterns. Under this framework, we studied the relationship between the properties of the network and the release site, and the properties of gene drive spread. By using different generative network models, we studied different network topologies and identified centrality measures of release sites that can predict the outcome of deployment. Our results demonstrate that population structure can crucially alter gene drive spread dynamics. In addition, we highlight centrality measures that are correlated with specific deployment outcomes. Our results identify the key aspects of population structure that should be measured in wild populations that are currently being considered as candidates for gene drive deployment programs, and also demonstrate the ability to develop predictors of deployment outcomes based on ecological factors.

Exploiting the evolution of odorant discrimination in ants to decipher the olfactory code

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Chemical communication is a key component in the life of eusocial insects. It relies, among other factors, on their ability to identify an extensive diversity of ligands using odorant receptors (ORs). Insect ORs are characterized by their massive expansion through gene duplication, where new ORs may develop different ligand specificities, possibly as a result of positive selection and adaptive evolution. Our goal is to infer such events and identify amino acid substitutions that alter OR specificity towards ligands in the carpenter ant Camponotus floridanus. Based on previous results from Saad et al. (2018), we selected candidate ORs that show positive selection after specific-specific duplication in the C. floridanus lineage. We then mapped those mutations on a 3D model of insect ORs, and selected candidates for which positive selection acted on an amino acid around the putative ligand binding site. These sequences are now engineered into mutant flies, and tested for their response to different ligands. Comparing the resulting specific profiles of closely related paralogs shows whether positively selected mutations changed ligand specificity relative to the ancestral protein. Furthermore, we are re-building a gene tree of ant ORs with newly annotated genes from recent high quality genomes, and re-testing for positive selection, to improve the accuracy of our molecular evolutionary data and to add more genes to the gene tree, including both paralogs and more species.

Ecological and demographic drivers of immune-related genetic variation across human populations

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The level of human disease burden varies across populations due to differences in ecology, demographic histories, and epidemiological dynamics. The variation in world-wide disease-burden levels have led to differences in selection pressures on the major histocompatibility complex (MHC), the central component of the human immune system. Here, we investigate how population genomic signatures in the MHC of current human populations could be studied to reflect disease burdens patterns. In addition, we aim to identify the key ecological, historical, demographic and climatic variables that explain the variability in disease burdens. We analyzed the Human Genome Diversity Project (HGDP) dataset, which contains high-resolution genomic data of 53 relatively non-admixed human populations from around the world. We extracted signatures of balancing selection in the MHC by studying genetic diversity and Tajima's D, and controlled for non-immune related signatures by normalizing our results to the flanking regions of the MHC. We identified patterns that differ substantially than the expected genome-wide patterns (i.e., declining genetic diversity with increasing distance from Africa). In particular, we identified substantial signatures of selection in European and East Asian populations, with surprisingly high signals in the Siberian Yakut population. By comparing these signatures with climatic variables, we identified a strong negative correlation between temperature and MHC heterozygosity, with higher normalized heterozygosity levels observed in colder climates. Because climate is correlated with many other factors, it is yet unclear what factor is driving disease burden in humans. Our approach, analysis of world-wide genomic signatures in the MHC, allows us to reconstruct the disease-burden landscapes of the past, and potentially identify the key factors driving them.

De novo pyrimidine biosynthesis in myxosporea (Myxozoa, Cnidaria)

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Myxozoa is a highly diverse group of cnidarian parasites and is well known for the disease they cause in wild and aquaculture fish stocks. The biosynthesis of pyrimidines plays a pivotal role in cellular processes such as cell signaling, energy metabolism, and nucleic-acid biosynthesis. The metabolic pathways of Myxozoa are poorly characterized. It was previously suggested that the myxozoan Thelohanellus kitauei (Myxobolidea) has lost its pathways for de-novo synthesis of nucleotides. The enzymes involved in the pyrimidine synthesis pathway are encoded by three genes: Carbamoylphosphate synthetase (CAD), Dihydroorotate dehydrogenase, and Uridine 5'-monophosphate synthase. In this work, we mined available genomic and transcriptomic databases from representative of the myxozoan and cnidarian diversity for these genes. Surprisingly, our study revealed the presence of the genes involved in this pathway in all myxozoans for which their genome is available. The only exception was the absence of CAD in most members of the myxobolidea. Orthology relationships were next confirmed by reconstructing maximum-likelihood based gene-specific phylogenetic trees. Our results suggest that analyses based on a single genome may lead to erroneous conclusions and demonstrates the strength of comparative phylogenomic studies, which combine data from multiple species. In the future, we propose extending the suggested approach to characterize additional pathways in these important fish parasites.

Tracking transient gene duplications in natural microbial populations

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Gene duplication is a major force in evolution, with new genes (paralogs) potentially acquiring new functions or losing their function over time. Studies have proposed that prokaryotes have far fewer gene duplication events than eukaryotes, but we suggest that some duplications may have been missed due to technological limitations or rapid genome disappearance. We address this by using long read sequencing of natural microbial populations to capture full genes and their genomic context, allowing us to identify recurring genes with different flanking regions. Our analysis pipeline will also include tetranucleotide frequency analysis and epigenetic modification patterns to sort long reads into species and strains, distinguishing gene duplication events from lateral gene transfers (LGT) and measuring the rate of duplication events per species and environment. This method will promote our understanding of gene duplications in natural microbial populations.

Studying the variation in MS2 bacteriophage evolution during serial passaging experiments

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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.

Antagonistic interactions between cheating bacteriophages during long term evolution

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RNA viruses are the most abundant group of subcellular parasites. Genetic variability has been observed for all RNA viruses, and their potential for rapid evolution is recognized as the basis of their adaptability to novel environments, including the ability to jump between host species and create worldwide pandemics. However, the rapid evolution of RNA viruses comes at a cost to the genetic structure of the population: multiple genotypes are generated during infection and some of them may be defective, i.e., unable to fully complete a cycle of infection. Defective interfering particles (DIPs) which function as molecular parasites of the WT virus are also known as “cheater viruses”. In my research, I use the model virus MS2, a virus that infects bacteria, to understand the mechanisms of cheating. During experimental evolution of MS2, we observed the parallel emergence of different types of single-base cheater mutants. Our findings demonstrate how cheating highlights mechanistic tradeoffs during the viral life cycle and underscore the inherent unpredictability of cheating viruses (Meir et al).

To pursue our findings, we conducted a long-term serial passaging evolutionary experiment and utilized a novel long-read method called LoopseqTM, which allowed us to keep track of the different mutations in the population and their relationships over time. Surprisingly, we observed antagonistic interaction between pairs of mutations at the genomic level. Our findings demonstrate unexpected interactions between viral mutants and highlights that there is some inherent unpredictability in virus evolution. They also demonstrate the different layers of parasitism: viruses parasitizing cells, cheaters parasitizing intact viruses, and cheaters may parasitize other cheaters.

The impact of domestication on the accumulation of transposable element in the wheat genome

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Wheat was domesticated 10,000 years ago in the Fertile Crescent and still one of the main crops cultivated today throughout the globe. The wheat genome is massive, it contains circa 10Gbp of which more than 85% is repetitive sequence. The repetitive fraction of the genome is largely composed of transposomes of which long terminal repeats (LTRs) are the most abundant. Despite their pivotal part of the what genome, little is known about the dynamics of LTRs accumulation in the wheat genome.
Here, I will present our research on LTRs accumulation in the wheat genome and its attribution to domestication. To address this, whole genome shotgun sequence data of a panel of 231 accessions representing wild emmer wheat (n=78), domesticated emmer (n=71), and durum wheat (n=62) were screened for LTRs abundance using a bioinformatic pipeline which was adjusted to deal with the size and complexity of the wheat genome.
Overall, higher LTRs abundance was observed in domesticated types (emmer and durum) compared with wild emmer wheat indicating that domestication has led to an activation of LTRs activity which is common is populations that are under stress or that are recovering from a sever genetic bottleneck. Within domesticated groups, no significant difference was observed in LTRs accumulation indicating that the LTRs activity was mainly affected by domestication rather than by crop evolution.

Reverse transcription of genes by the Ty retroelement and its impact on evolution

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The possibility for Lamarckian modes of evolution rests on the notion that phenotypic changes can either be inherited to the next generation or be converted into the genome. While the first option can be subserved by diverse epigenetic means, the latter requires a back flow of information, e.g. from RNA to the genomic DNA. This reverse flow can be realized by the molecular process of reverse transcription. Retrotransposons propagate in genomes via reverse transcription and here we examine the extent to which they can induce this process in other genes. Reverse transcription can create new copies of reverse transcribed genes and propagate transcription and RT errors back into the genome. Therefore, it can significantly impact their evolution. Specifically, highly expressed genes are more likely to undergo RT, making it a potential agent of Lamarckian inheritance. Ty elements in yeast are retrotransposons that form virus like particles (VLPs) within the cytosol in which cellular mRNA can be contained, and potentially be reverse-transcribed and subsequently incorporated into the genome. High throughput sequencing assays were performed on Ty1 VLPs to determine their mRNA and cDNA contents. Here, we analyze these results and form a list of VLP enriched and depleted genes and of reverse transcribed genes. We see that VLP depleted genes tend to be evolutionary conserved while VLP enriched genes exhibit a high mutation rate. We also see that VLP enrichment and depletion are highly associated with specific RNA localization and that genes with introns are VLP depleted.

Rapid adaptation through microbiome exchange

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In a fast-changing world, understanding how organisms adapt to their environment is a pressing necessity. Research has focused on genetic adaptation, while our understanding of non-genetic modes is still in its infancy. Particularly, the host-associated microbiome strongly influences an organism's ability to cope with its environment. The presence of certain microbes in the gut, for example, can facilitate the utilization of dietary resources, provide protection from pathogens, and increase resilience to diverse abiotic conditions. However, the role that the microbiome may play in species' adaptation to novel challenges is largely unexplored, experimentally as well as theoretically. Here, we study the possibility of such adaptation in invasive species.

We present and explore a new hypothesis: Invasive species may rapidly adapt to local conditions by adopting beneficial microbes of ecologically similar native species. Ironically, due to competition, these native species are also those most likely to suffer from the invaders' spread. We formulate a mathematical framework to investigate how the competitive dynamics between a native and an introduced species can be altered by the transfer of beneficial microbes between the two species.

We find that, non-intuitively, the presence of a related native species may facilitate the success of an invasive species' establishment. This occurs when the invader's fitness is strongly influenced by adaptation to local conditions that is provided by microbes acquired from the natives' microbiomes. Further, we suggest that in such cases a delayed acquisition of native microbes may explain the occurrence of an invasion lag. We discuss biological systems that could lend themselves for the testing of our hypotheses. Overall, our results contribute to broadening the conceptualization of rapid adaptation via microbiome transfer, and offer possible insights for designing early intervention strategies for invasive species management during their lag phase.

Reappraisal of the Middle Pleistocene Homo Fossil Record in Light of the Epigenetically-Reconstructed Denisovan Morphology

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Denisovans were a hominin lineage closely related to Neanderthals who lived during the Middle Pleistocene (MP). They were identified by a genomic analysis of human remains found in Denisova cave. Despite the exceptional preservation of genetic material, the few small and fractured Denisovan remains were mostly unindicative, preventing a significant morphological characterization. At the same time, there are many unclassified human remains from the MP, particularly in East Asia – the Denisovan habitat. Thus, some of these remains might belong to Denisovans .

Previously we have used DNA methylation information obtained from a Denisovan pinky bone and combined this with genotype-phenotype annotations to reconstruct a potential Denisovan morphological profile. Our method has shown >85% accuracy at predicting the morphological features of other species such as chimpanzees and Neanderthals. Here, we present the first unbiased morphological attempt at examining the possibility of Denisovan identity for various MP cranial and mandibular specimens.

Each directional prediction was assigned a fitting craniometric measurement, which was used to compare the test subjects to anatomically modern humans and Neanderthals. The results indicate that several Middle Pleistocene Homo specimens have Denisovan-like morphology, including Bodo, Harbin and Petralona. Since some of the matched crania are dated to around the time of Denisovan-Neanderthal divergence, it might suggest that Denisovans retained the archaic morphology, while Neanderthals developed a more derived face.

A Deep Learning Tool for Predicting Enzymatic Degradation Using Knowledge Graph Embedding

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Human-made waste is polluting water, soil, and air, and is likely to increase in the coming decades. A promising avenue for its treatment is via microbial enzymatic decomposition, which has shown promise in plastic degradation. However, contemporary methods for detecting new enzymatic functions from microbial sources are often limited by culturing, which is restrictive to most microbes. Computational methods tackling these problems often rely on comparison to known datasets and therefore suffer from observational bias, limiting new discoveries. We approach these problems using knowledge graphs, which enable the aggregation of information from multiple sources and the application of AI algorithms to discover new links between them. As a first step, we downloaded multiple datasets of enzymes and their substrates and applied a graph embedding algorithm to detect similarities between certain nodes (e.g., enzymes). The embedding of this massive network enables us to find alternative substrates for enzymes, annotate the function of new enzymes, or find known enzymes that can be applied to new substrates. Our preliminary model was tested against 1000 artificial links (non-existent in the data) for each real link. In 83% of the cases, it places the real link amongst the top 5% links as its prediction. Further developing this network could help us find new enzymes that can degrade human-made waste and potentially reduce worldwide pollution from many different sources.

Exploring the Evolutionary Dynamics of Interspecific Interactions in Microbial Communities

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Microbial communities play a significant role in various aspects of human life and, as a result, there is a desire to manipulate them to meet specific human needs. To do so, it is necessary to understand the processes that shape their assembly and function, as well as their evolutionary dynamics. In particular, interspecific interactions within a community strongly impact its assembly, structure, and productivity, and changes in these interactions can lead to changes in the community's properties. While it is known that interspecific interactions change as communities coevolve, it is not clear how often these changes occur, what factors influence their frequency and whether they are random or deterministic. In order to understand the rules governing the evolution of interactions, I assayed the changes in interactions between ~250 pairs of bacterial species that have evolved for 400 generations under different evolutionary conditions. I found that stronger interactions tend to change more than weaker ones and that effects often change qualitatively (e.g., from positive to negative) during evolution. Examining the evolutionary changes in multiple assemblages of interacting species, rather than in a single pair or community, enabled me to identify general trends in interaction evolutionary dynamics, which can aid in predicting the evolution of communities and improving the design and management of beneficial microbial communities.

Adaptive Laboratory Evolution: A Tool for Prospecting Plastic Degrading Enzymes

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Characterizing evolutionary pathways for adaptation to a weak-link enzyme in bacterial populations

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When important metabolic nodes are inactivated, for example by genetic mutations, long ranging disruptions of a metabolic network can occur, which poses a major adaptive challenge to cells. Former studies have explored the evolutionary trajectories of cells subjected to metabolic disruptions, but have not established a direct link between re-shaping of the metabolic network and organismal fitness.
By replacing the metK gene encoding methionine adenosyltransferase (MAT) in E. coli with an orthologous variant with a distinct mode of regulation, we have turned MAT into a 'weak link' enzyme. MAT is an essential gene catalyzing the formation of S-adenosylmethionine, a metabolite used in myriad biochemical reactions in the cell. After the perturbation a major decrease in the growth rate of the bacteria was noticed, which was reverted during experimental evolution by several adaptive peripheral mutations. To investigate the effect of these mutation we concentrated on the metabolic network of the cells, and specifically on the differences in the relationships between metabolite abundances. Relative amounts of untargeted metabolites were detected in bacterial population pre- and post-laboratory evolution using LC-MS, and the data was used to construct correlated metabolic networks. By comparing properties of the constructed networks marked differences were observed in some, such as the numbers of nodes and links, the density of the network and the number of important nodes (hubs). All of these parameters showed a decrease in the perturbed bacteria and an increase during evolution. The findings suggest that re-shaping of the metabolic networks were triggered by adaptive evolution.

Elucidating the effects of eco-evolutionary feedbacks in a bacterial mutualism

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Coevolutionary forces play an important role in structuring how ecological communities form and function. In particular, eco-evolutionary feedbacks (EEFs), consisting of reciprocal adaptations between interacting species, are thought to be a key mechanism driving coevolution within communities. A well-known example of EEFs is the evolutionary arms race between bacteria and phage, which accelerates their molecular evolution. However, the consequences of EEFs beyond such canonical examples are not yet well understood. Our aim is to address this knowledge gap by investigating the effects of EEFs between bacterial species engaged in a mutualistic interaction, which is a common interaction among microbes. A major challenge in studying EEFs is distinguishing them from differences in selective pressures experienced by species in a community versus alone. To overcome this challenge, we developed an experimental system that allows evolving one species in the presence of another species maintained in its ancestral state, preventing any EEFs. Preliminary results show that a pair of Escherichia coli strains can be used in this experimental system to form a mutualistic interaction through the exchange of metabolites. We (co)evolved these strains with/without EEFs and determined how the presence of EEFs affected the changes in their interaction, amino acid utilization and secretion, and genomes. This research provides a novel approach to studying EEFs between microbes and improve our understanding of the processes shaping the coevolution of microbial communities. This Knowledge can open novel avenues for research and engineering of microbiomes and inform the design of synthetic communities.

Predicting ant olfactory receptor structures, binding sites and odorant specificity

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Understanding olfactory space and perception is challenging because of its multidimensionality, discontinuous stimuli, and widely different types of odorant molecules – resulting in a large repertoire of olfactory receptors (ORs). We focus on how social ants use ORs to detect and discriminate between cuticular hydrocarbon (CHC) odorants, which function as social cues in ants. Insect ORs are 7TM proteins that function as hetero-tetrameric complexes that form a single cation channel. While these ORs are distinct from GPCRs, evolution diverged them to hundreds of distantly related receptors that nevertheless share a common architecture and functional characteristics. However, our understanding of the sequence-structure-function relationships between receptors and ligand binding is very limited .

We used Alphafold2 to predict the 3D structures of related ant ORs. We then used these models to compare their sequence-structure relationships and to predict which residues form a putative ligand-binding cavity. These predictions were validated by comparison to experimental data, showing the utility of our approach. Our results show that CHC-binding ORs have larger and more hydrophobic predicted binding sites compared with non-CHC binding ORs, which have smaller and more polar predicted binding sites. Our results contribute to a better understanding of the structure-function relationship between ORs and their ligands and lay the basis to decipher how ant ORs were tuned by evolution to selected CHCs.

Target complementarity in cnidarians supports a common origin for animal and plant microRNAs

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MicroRNAs (miRNAs) are short RNA sequences that post-transcriptionally regulate gene expression in many organisms. They are important for normal development and physiology of both plants and animals; however, their mode of action, biogenesis and target recognition differ between the two kingdoms.
miRNAs anneal to mRNA transcripts and activate silencing mechanisms. In bilaterians, which include most animal species, miRNAs bind their targets with positions 2-8 of the miRNA called the 'seed'. This causes translational inhibition or deadenylation, promoting degradation. In plants, miRNAs match their targets with nearly full complementarity that results in cleavage of the mRNA between positions 10-11 of the miRNA. Interestingly, miRNAs exhibit similarities between plants and Cnidaria, the sister group to Bilateria that diverged over 600 million years ago and includes sea anemones, jellyfish, corals, and hydroids. It was previously shown that in the model sea anemone Nematostella vectensis, similarly to plants, miRNAs fully match their targets and cause mRNA cleavage.
In this study, we characterized the complementarity requirements of miRNAs to their targets in Nematostella. We utilized transgenic anemones ubiquitously expressing mCherry and designed miRNAs based on an endogenous miRNA template to target mCherry mRNA. We altered the miRNAs sequence and tested how complementarity patterns affect silencing efficiency at the RNA and protein levels, by microinjecting them to zygotes. We reveal that bilaterian-like 'seed-match' and seed with 3' supplement matches have no silencing effect in Nematostella. Moreover, when positions 10-11 are mismatched, no silencing occurs; however, only mismatching position 10 or 11 cause partial silencing. Finally, we assayed miRNA silencing of synthetic mCherry mRNA with three miRNA binding sites in the 3' UTR to mimic typical miRNA targeting and received similar results.
To conclude, this study reveals more similarities between plants and cnidarian miRNAs and contributes to growing line of evidence for common evolutionary origin of miRNAs.

Investigation of antiviral pathway in the sea anemone Nematostella vectensis reveals clues of functional conservation of innate immune system

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Animals adopt complex and multi-component molecular mechanisms to protect themselves from viruses, and this constant reciprocal competition has resulted in an evolutionary arms race between the viruses and hosts. However, the mechanisms of arms race between viruses and animal hosts has been mostly limited to vertebrates and have been less elucidated in marine species. Given the lack of data regarding innate immune system of marine invertebrates, the present study aims to characterize host evolution utilizing the starlet sea anemone, Nematostella vectensis, which is a representative and well-studied model of the basally-branching Cnidaria, and to empirically identify host evolution in the laboratory and the field. This will enable characterizing the ecology and evolution of host-virus dynamics. Based on comparative genomics and positive selection signals of antiviral proteins obtained by comparing the transcriptomes of geographically-isolated anemones, we will functionally characterize these antiviral component by state-of-the-art genetic manipulation methods. In addition, we will conduct quantitative studies on adaptation to specific virus communities as well as identification of the specific gene expression through a combination of laboratory and microcosm. Our project will shed light on the innate immune system of non-bilaterian animals and its co-evolution with viruses, providing new insight into animal adaptation to viruses in natural populations.

The whole genome variation between the sexes of Russian sturgeon (Acipenser gueldenstaedtii)

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The Russian sturgeon (Acipenser gueldenstaedtii, AG) is an ancient and endangered fish species increasingly raised on fish farms for black caviar. Understanding the process of sex determination in AG is, therefore, of scientific and commercial importance. AG lacks sexual dimorphism until sexual maturation and has a predominantly octoploid genome without a definite sex chromosome .

A conserved short female-specific genomic sequence (ALLWSEX2) was recently described, leading to the development of a genetic sex marker. However, no biological function has been reported for this sequence. Thus, the mechanism of sex determination and the overall inter-sex genomic variation in AG are still unknown .

To comprehensively analyze the inter-sex genomic variation and assess the overall inter-species variation between AG and A. ruthenus (AR, sterlet), a related tetraploid sturgeon species, we performed whole-genome sequencing on DNA from 10 fish-farm-raised adult AG (5 males and 5 females). We produced a partially assembled, ~2390 MBp draft genome for AG. We validated in AG the female-specific region previously described in AR. We identified ~2.8 million loci (SNP/indels) varying between the species, but only ~7400 sex-associated loci in AG. We mapped the sex-associated AG loci to the AR genome and identified 15 peaks of sex-associated variation (10 kb segments with 30 or more sex-associated variants), 1 of which matched the previously reported sex-variable region. Finally, we identified 14 known and predicted genes in proximity to these peaks .

Our analysis suggests that one or more of these genes may have functional roles in sex determination and/or sexual differentiation in sturgeons. Further functional studies are required to elucidate these roles

Distant structural homology among receptor tyrosine kinases in relation to ligand interactions

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Cellular signaling cascades are based on accurate recognition between partner components. In particular, signaling cascades initiated by receptor tyrosine kinases (RTKs) control cellular processes such as proliferation, differentiation, and cell survival. RTKs can be activated by diverse protein ligands outside a cell, leading to stimulation of downstream signaling pathways inside the cell. Understanding the basis for such selectivity and how it evolved is a major goal for basic research and drug design. Moreover, pinpointing specific residues that influence protein-protein interactions (PPIs) can help identify how evolution built functional PPIs and guide the engineering of novel interactors .

We combined sequence and structure-based approaches to analyze a large dataset of RTK structures and pinpoint domain-level and per-residue contributions to the relevant PPIs. We developed a new geometry-based approach to compare the structural building-blocks of different receptor-ligand complexes, identifying subgroups within and across the RTK superfamily that are unexpectedly structurally similar. Our approach presents a generalizable and accurate method to map the structural building blocks across entire protein families and identify distant evolutionary relationships among them.

Seasonal and depth distribution of Synechococcus sp. in the Red Sea at the clade and subclade level

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Synechococcus sp. is a globally distributed marine cyanobacterium with high intragenus diversity. Various Synechococcus phylogenetic groups, currently divided into 18 clades, and more than 30 subclades, co-exist in the same environment. However, these lineages differ in their abundances and distribution patterns. Gene content also varies within and between lineages. Here we present the analysis of 85 metagenome from the Gulf of Aqaba, Red Sea, collected at three depths (20, 60, 100 m) during spring, summer, and fall in 2015 and 2016. We found recurrent seasonal patterns in clade and subclade distribution for the two years suggesting the presence of some beneficial genetic adaptations in the most dominant lineages to certain conditions. Whole-genome sequencing was performed for 22 Synechococcus isolates, all belonging to the most abundant clade in the Gulf of Aqaba, and their gene content was compared. These results, although preliminary, contribute to our understanding of Synechococcus biodiversity and the evolutionary processes driving the diversification of its lineages.

Effects of different foraging strategies in different climate conditions on the reproductive success in the desert harvester ant Pogonomyrmex barbatus

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Foraging strategies are crucial for the survival and reproduction of animals. Foraging of ants is manifested through collective behavior, the coordinated behavior of group without central control. To understand how this collective behavior responds to changing environmental conditions, a long-term study has been conducted using the red harvester ant Pogonomyrmex barbatus as model organism. Harvester ant colonies have been monitored on a study field site for over 30 years, and their foraging behavior was measured in fluctuating weather conditions . The main food source of harvester ants are seeds, which are also the main source of water. Living in a desert, the ants forage under harsh weather conditions and desiccation risk. We hypothesized that the regulation of foraging in response to humidity has fitness consequences for this population. We used restriction-site associated DNA sequencing (RAD-seq) to generate a genome-wide map of polymorphism at 9824 single nucleotide polymorphisms (SNPs). Based on these genotypes, we inferred kinship between 488 colony samples, to detect mother-daughter pairs of colonies. Thereby, we assess the reproductive success of colonies over 30 years. We use this large dataset to test whether colonies that reduced foraging on dry days have higher reproductive success.

Anatomy of miniature arachnids: a case study of four-legged mites Achaetocoptes (Eriophyidae) and spiders Rayforstia (Anapidae)

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The miniaturization of arachnids is almost unexplored despite the fact that mites are supposedly the smallest terrestrial arthropods. Works devoted to the anatomy of small spiders are also extremely rare. Using methods of histology, confocal and transmission microscopy and three-dimensional computer modeling we study the anatomy of some of the smallest arachnids: four-legged mite Achaetocoptes sp. (Trombidiformes: Eriophyoidea) and spider Rayforstia sp. (Araneae: Anapidae). It is shown that the characteristics of insects associated with miniaturization are also characteristics of the smallest arachnids. The mite has a closed digestive system, absence of circulatory system, oligomerization of nervous system, and compactization of organs. Most of the body is occupied by gonads with few eggs. The spider exhibits oligomerization of the nervous system, a significant increase in the brain volume relative to the body volume, reduced branching of the midgut - it does not branch in the prosome, and the absence of lung books, as in many miniature spiders. Nevertheless, arachnids have differences related primarily to their ontogenesis. They do not have a pupal stage and it would be interesting to see how different the anatomy of mature and immature mites and spiders is. We suggest that the miniaturization of mites is primarily limited by the size of the gonads and eggs, whereas the size of spiders also depends on the volume of the abdomen with digestive system and silk glands, which are an important evolutionary acquisition of this group, as well as on the brain size because among spiders there are no parasites and hunting is important for them. The data obtained allow us to supplement our understanding of the convergent pathways of structural transformations associated with miniaturization in different arthropod groups .

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Exploring the regulatory linkage between the Drosophila Svb and Osi genes

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Animals adapt to their ecological niche by evolving specialized morphologies, physiologies, and behaviors. Various studies have revealed adaptive variations between species but very little is known about their genetic and molecular basis.
Drosophila sechellia is an endemic species to the Seychelles archipelago that belongs to the D. melanogaster group of species. D. sechellia feeds and reproduces exclusively on the ripe Morinda citrifolia fruit (noni fruit), a fruit that is toxic to other species in the group. Previous studies suggested that the resistance of D. sechellia to the noni fruit toxicity involves genes of the Osiris family. D. sechellia is also distinguished from its related species by its naked first instar larvae. While larvae of other species are covered with cuticular trichomes, D. sechellia larvae have lost many trichomes due to the loss of expression of the shavenbaby gene in D. sechellia embryos. Shavenbaby encodes a pleiotropic transcription factor that regulates trichome production and other developmental processes. While the genetic and molecular mechanisms underlying the loss of trichomes in D. sechellia are well understood, the selective pressure that led to this evolutionary transition remains a mystery. Here, we hypothesize that Shavenbaby regulates the expression of the Osiris genes and that this regulatory relationship serves as a strong selective pressure for the loss of shavenbaby expression in D. sechellia embryos. We combine genomic analyses, reporter gene assays and genetic studies to test this hypothesis and to reveal the adaptive benefits that prompt the loss of trichomes in D. sechellia larvae.

The genetic basis of trichome loss in D. sechellia.

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Morphology evolves predominantly by changes in gene regulation due to mutations in developmental enhancers. However, only few studies have identified the causal mutations in evolved enhancers that contributed to morphological differences between species. Here we address these issues by studying evolved enhancers of the Drosophila shavenbaby gene.
Shavenbaby encodes a transcription factor that controls the development of cuticular hair-like projections called trichomes. Trichome patterns have repeatedly evolved in larvae of the genus Drosophila through changes in the shavenbaby regulatory regions. Seven enhancers, located in the cis-regulatory region of shavenbaby, control its complex embryonic expression. In D. sechellia, a sister species to D. melanogaster, five of these enhancers have evolved reduced embryonic activity, leading to the evolution of naked larvae. We have previously identified the causal mutations and revealed the complete molecular mechanisms underlying the loss of one of these enhancers, named E6, in D. sechellia, but the genetic basis underlying the loss of function of the other enhancers remains unknown .
Here, we use reporter gene assays to identify the causal mutations that altered the function of all the D. sechellia shavenbaby enhancers. We find that, like the D. sechellia E6 enhancer, two additional D. sechellia shavenbaby enhancers have evolved through gain of repression. In contrast, the D. sechellia shavenbaby Z1.3 enhancer accumulated a 120-nucleotide deletion in the core enhancer that eliminated most of its embryonic activity. Our future studies will reveal how many and what type of cis-regulatory changes underly a simple evolutionary transition such as the loss of trichomes.

The multiple roles of the gap genes network and its evolutionary versatility in hemimetabolous insect development

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The current hypothesis in the evolution of early insect development proposes that the spatial expression patterns of segmentation genes in developing embryos are established through a wave-like mechanism, in which the expression of one gene activates the next gene in a cascade-like fashion .
This hypothesis has been supported by studies in various model organisms, including Drosophila melanogaster and Tribolium castaneum .
In this study, we aimed to investigate the expression patterns of gap genes in O. fasciatus embryos and test whether they follow the wave hypothesis .
We used in situ hybridization to visualize the expression patterns of the gap genes Giant, Krüppel and hunchback during early embryonic development .
Our results demonstrate that the expression patterns of these gap genes in O. fasciatus do not follow the wave-like pattern that has been observed in D. melanogaster .
Specifically, we found that the expression domains of Krüppel and hunchback are not restricted to alternating segments, as would be expected if they were following a wave-like pattern. Additionally, we observed that the expression of giant is not initiated by the expression of hunchback, which is inconsistent with the wave hypothesis .
Overall, our results suggest that the wave hypothesis may not be a universal mechanism for establishing the spatial expression patterns of segmentation genes in all insect species.
Further studies are needed to explore the mechanisms underlying the establishment of segmentation gene expression patterns in O. fasciatus and other non-model insect species.

Functional characterization of venom as a complex trait and elucidation of its contribution to animal fitness

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Venoms are complex cocktails characterized by a high diversity of components, which cause a physiological and biochemical imbalance in the target organism after infliction of a wound using a specialized delivery mechanism. Venom is a functional and ecological trait, typically used for predation and defense. This functional gamut emphasizes the importance of venom as a key innovation underpinning the evolutionary success of many animal lineages. However, it is also metabolically expensive, which negatively affects fitness. Thus, it appears to be evolving under strong selective pressure that balances its negative and positive contribution to fitness. Venom can be considered a complex trait as it is made of many proteins shaping the phenotype. This characteristic together with the expected direct relationship of gene-toxin-phenotype make it an appealing system for studies at the functional level. In this work we propose to study the contribution of venom to organismal fitness which have been rarely studied experimentally. It now can be directly tested by the genetic manipulation methods available for the sea anemone Nematostella vectensis. We are generating knockout animals for the toxin genes: Nep3, Nep3-like which are examples for abundant nematocyte neurotoxins present in the animal from the planula stage to the adult and may serve both in defense and in catching prey and NvePTx1 which is a gland cell toxin restricted to the egg and larval stages and absent from adults, hence used primarily for defense as Nematostella larvae do not feed. Several single guide RNA (sgRNA) species targeting the 5’ and 3’ regions of each toxin-encoding gene were synthesized and microinjected with the endonuclease Cas9 into zygotes to produce double-strand DNA eventually resulting in frameshifts. Knockout animals will be subjected to tests measuring their fitness as well as their ability to catch prey and defend from predators.

To mistranslate or not to live

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Traditional view on organismal adaptation postulates that mutations in genotype drive the phenotypic variation allowing to sample diverse adaptive strategies towards the environment. In our work we explore different modes of adaptation where protein phenotypic variations arise directly from the frequent ribosomal mistranslations. Gene mistranslations might increase the adaptive capacity of the organism by sampling multiple phenotypic variations at the same time. Additionally, error sampling of phenotypic variants in combination with the genetic variation might explain the rise of complex epistatic molecular traits, emergence of which would be exceptionally rare otherwise. Here we present the significance of mistranslations on organismal fate on the example of E.coli TEM-1 beta lactamase enzyme. The protein was engineered in such a way that only mistranslations will rescue organism from the presented antibiotics. We report that mistranslation frequency directly correlates with the organismal fitness allowing us to speculate on predictability of sequential mutation events through phenotypic “look-ahead” effect and “quantum-tunneling” the protein fitness landscape through genetically non-viable but phenotypically accessible variants.

The effect of the social system on mitochondrial diversity in killer whales.

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Killer whales have an extremely low diversity in the mitochondrial control region, the reasons for which are not yet known. Among the different explanations for this phenomenon, we can find low mutation rate, historical bottlenecks, small effective population size, cultural transmission, and social system .
One explanation is due to the unique social system of killer whales, a combination of matrilineality—offspring remain with their natal group throughout their life—and outcrossing—mating with individuals outside of the natal group. We developed a population-genetic simulation using SLiM, which simulates the killer whale population dynamics and genetics. We use this simulation to examine the effects of social systems on the mitochondrial and nucleic DNA diversity by changing parameters such as male/female dispersal rate and inbreeding vs outcrossing rate. A few key aspects of the simulation are that the diversity is compared between different populations rather than within a population and that the simulation allows extinction of pods and therefore reduced diversity.
Our goals are to explore the boundaries of a sustainable population and how different parameter regimes lead to extinction or expansion of the population. Our results will provide a foundation for further research on the mechanisms affecting mitochondrial diversity and reflect on further processes in killer whales, such as their long post-reproductive life span and their ongoing speciation.

To interact or not to interact: a toy model for the evolution of the protein-protein interaction network in RNase-based self-incompatibility system

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More than 40% of flowering plant species evolved a self-incompatibility (SI) mechanism to promote outcrossing and prevent inbreeding. Here we focus on one SI mechanism found in Solanaceae and Rosaceae families. There, fertilization is conditioned on specific molecular recognition between highly diverse proteins of two families: RNase (female) and SLF (male). A male (SLF) should then recognize and fertilize most foreign females (RNases) but not the self RNase. Both RNase and SLF are highly diverse, but it remains unclear what the likelihood of a new allele integrating into an existing network is. In this work, we focus on the biophysical parameter of RNase-SLF interaction threshold energy, determining which proportion of random alleles interacts. We construct an evolutionary-biophysical model of SI haplotypes, representing alleles by sequences of amino acids. Fertilization is possible if the SLF-RNase interaction energy is below the threshold. The haplotypes evolve under a combination of different selection pressures: avoiding self- while simultaneously maximizing non-self fertilization. Crucially, our model allows for multiple partners per allele, as known empirically. We then investigate the effect of the threshold energy on the evolved network and allelic characteristics. We find that the total allele count, the number of partners per allele, and the amino acid content of RNase alleles strongly depend on this parameter. By tuning the energy threshold our model bridges between two extremes, thereby shifting the balance between the two selection pressures: for a low threshold the interaction between random sequences is rare, hence SLFs mostly evolve to enhance between-haplotype interactions, whereas, for a high threshold, interactions are ubiquitous and thus SLFs evolve mostly to avoid within-haplotype interactions. It would be interesting to study where the actual proteins lie in this range of possibilities.

Exploring the role of genome size variation in evolution

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Genome size variation within a species has been described in several plant species, yet the biological essence remains elusive. Evolutionary theory predicts that increased genome size can have an advantage by improving the efficiency of selection when effective population size is low. However, contradicting evidence in different plant species has challenged this adaptionist view on genome size variation in nature. To address this, two wild barley species, namely Hordeum spontaneum and H. Bulbosum were sampled along environmental gradients and screened for genome size variation. Genome size varied dramatically in both species with up to a 185Mbp difference between the smallest and largest haploid genome. In the self-fertilizing species, H. spontaneum, a significantly larger portion of the variation was maintained within populations while in the outcrossing species H. bulbosum most of the variation was observed between populations. Moreover, both collections were characterized genomically and phenotypically under common garden conditions. Significant correlations were observed between genome size, phenotypic (flowering time), and environmental variation (precipitation and soil structure) in both species. Overall, larger genomes are more common among the desert ecotype, thus genome size increases with increased temperatures and decreased precipitation. Most of the variation in genome size is attributed to mobile elements (LTR-type) which are likely activated under water deficit conditions. We conclude that increased genome size can compensate for the loss of genetic variation and that adaptation to the environment has contributed mildly to genome size variation.

More than skin deep: signs of divergence in populations of Lycosa piochardi Simon, 1876 (Araneae, Lycosidae) in Israel

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The genome of a species is rarely uniform throughout its distribution range. Differential selection pressures, as well as genetic drift, alter the allele frequencies in parts of the species' distribution, and make the population evolve in different directions. Such divergence can be, but isn't necessarily, a prelude to speciation, without the need in a geographical barrier. The speciation through cladogenesis requires restriction of gene flow between populations of the parent species, which in sympatric populations necessitates the development of reproductive barriers: either behavioral, physical or ontogenetic. Lycosa piochardi Simon, 1876 is a burrow-dwelling wolf spider common throughout western Asia. In the southern Levant it is found in most of the terrestrial habitats, including desert, Mediterranean scrubland and subalpine ecosystems. Lycosa piochardi exhibits great phenotypic diversity, in size, coloration and genital morphology, both within and between localities. In order to understand whether the population structure of this species is correlated with environmental factors, we used ddRAD sequencing on L. piochardi from throughout the southern Levant and analyzed the species' population structure. There are at least three populations in our sampled data, each is correlated to a different climatic region and exhibits unique phenotypic diversity. The two main populations (desert and Mediterranean) show very little intermixing, despite the geographical proximity. The partial isolation of the populations in the study area may represent an initial stage in sympatric speciation.

Inferring migration rates from Fst matrices

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Migration rates between pairs of populations are important for many evolutionary and ecological studies,
but directly measuring them from observations is often difficult. When genetic data is available, genetic differences between population can be summarized using Fst matrices. In order to relate the evolutionary
process to migration patterns, the connection between Fst, coalescent times, and migration rates of populations can be described mathematically: given a pair-wise migration rates matrix M, the pair-wise coalescent times matrix T can be computed, and given a pair-wise coalescent times matrix T we can calculate the pair-wise Fst matrix F. Therefore, combining these two transformations, M → T and T → F, we can construct the transformation M → F. However, the reverse transformation M → F is more difficult to study, and potentially generates identifiability issues which prevent direct inference of migration from Fst; in other words, the full reverse transformation F → M can in some cases produce a unique solution, but in most cases the solution space is infinite or empty. In this project, we characterize the solution space of migration matrices that correspond to Fst matrices, and show that it can be drastically narrowed down by first analyzing the possible T matrices produced from the transformation F → T, and using coalescent theory to filter out a large portion of these matrices. We then investigate the M matrices produced from the reverse transformation as networks, and analyze our result in terms of
network metrics. The goal of this project is to develop a formal method for inferring and characterizing the range of migration matrices that correspond to genetic data summarized as Fst matrices, and to develop a tool that would allow gaining insight into migration patterns between sub-populations.

Inferring evolutionary dynamics on incomplete fitness landscapes

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Fitness landscape mapping and the prediction of evolutionary trajectories on empirical landscapes are major tasks in evolutionary biology research. It is hoped that the advent of experimental evolution, now enabling the detailed fitness characterization of many genotypes should shed light on the evolutionary trajectories that led to the specific genotypes found in natural populations. Yet, fitness landscapes have astronomical dimensionality, and even current measurements of tens of thousands of different genotypes, facilitate the study of only tiny bits of the actual fitness landscapes. Thus, inferences of evolutionary trajectories on empirical landscapes should properly account for missing data due to the inevitably incomplete coverage of the landscape.

This project aimed to characterize biases in the inference of empirical landscape occupancy due to its incompleteness and develop computational methods to handle such biases. We used a stochastic evolutionary simulation to calculate the genotype occupancy of a given landscape. Such a simulation is useful because it enables comparison between predictions over full and sampled landscapes. We used either the NK model or a uniform fitness landscape as our model. We found that even on a flat landscape, if incomplete, genotype occupancy is proportional to the number of its single mutants included in the dataset, rather than being uniform as expected. We then continued by designing a scheme that will correct for such imbalances in the numbers of mutants of different genotypes and tested it on both the flat landscape and the NK model. Our preliminary results show that this scheme correctly accounts for incompleteness for the uniform fitness landscape, but only partially corrects if the fitness is not uniform. As fitness landscape measurements become more common, further development of such computational methods is required and we expect them to be applicable in various evolutionary studies.

Inference of CNV rate and fitness effect from yeast evolutionary experiments using neural networks and evolutionary simulations

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Selection and mutation are two forces that heavily affect adaptive evolution. The ability to evaluate those is key in understanding population dynamics. In this study, we show the assess of adjacent genes' knockouts on CNV formation and fitness. We modeled the evolution of CNVs in the GAP1 gene in the yeast Saccharomyces Cerevisiae through 116 generations using a Wright-Fisher model.
Then, we used a novel locus-specific fluorescent CNV reporter to measure the proportion of cells with multiple GAP1 loci. We applied this technique to five wildtype populations and to 21 knockout populations from three different knockout lines.
To estimate the differences between the populations, we use recently developed neural-network simulation-based inference algorithms (nnSBI). We obtain a joint posterior distribution of the four model parameters: fitness effects and mutation rates for both adaptive CNV formation and other adaptive mutations. Our preliminary results show meaningful differences among the studied cell lines. Overall, the Maximum A-Posteriori (MAP) values for the GAP1 fitness effects vary from 0.08 to 0.2, while the mutation rate varies from 1e-6 to 1e-3.5. For SNVs we found similar yet broader ranges of MAP values. Our study demonstrates the suitability of neural-network likelihood-free methods for inferring key factors in evolutionary processes from empirical observations. We also describe interesting properties of nnSBI that may help its application by other researchers.

A new analysis of translation errors in human reveals negative correlation between translation fidelity and genes evolution rate

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As with other processes in cell, translation can result in more than one outcome for the same RNA. While errors can potentially damage the cell, they could also create new phenotypic variation that could be subject to natural selection. In this study, we investigated whether the occurrence of errors in translation is a stochastic process or a well-directed process that benefits the cells. Specifically, we examined the sequence context of amino acid substitutions and the conservation of translation error sites and patterns across different organisms and human tissues. Our findings suggest that translation errors are not entirely random, but instead reflect an interplay between stochastic and deterministic processes. Furthermore, we detect a positive correlation between the tendency of human protein sites to be translated with error and their rate of evolution as assessed by comparison to their orthologs across vertebrate species. Thus it seems that the rate of phenotypic mutations correlate with the rate of genetic mutations per site. This appears to suggest selection for translation fidelity in human. By shedding light on the role of synonymous mutations in translation errors, we can gain a better understanding of the mechanisms that underlie protein evolution and adaptation.

Mapping genotypes of microbial cooperation

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Cooperation complicates microbial evolution. At the absence of cooperation, individuals try their best to survive. In contrast, cooperative individuals sacrifice themselves to prosper the community. Cheaters are the extreme forms of non-cooperators. In theory, when they arise, cooperators and the whole community are endangered. Intriguingly, in nature, cooperation stands the test of time. Current studies apply a binary YES/NO decision for cooperation depicted by secretion of public good proteins. However, in reality, various cooperative strategies can be realized, due to regulation of protein production and secretion on a continuous scale. Our lab co-discovered a cis regulatory mRNA motif for protein secretion (SECReTE). Here we study this motif, alongside Signal Peptide (SP), to understand various genotypes of cooperation. We separately manipulated the 2 motifs and generated 2 synthetic yeast libraries. Each library includes thousands of motif variants for the secretion of Suc2, a well-characterized public-good yeast protein. The variants in each library competed all together. We isolated colonies from the libraries at the beginning, middle, and the end of the competition and found that more SP colonies isolated from the end have cheater-like monoculture growth. Consistent to this, we found that depleted SP variants have less efficient translation and might have higher protein secretion. On the other hand, with thousands of SECReTE sequence variants, we investigated detailed sequence signatures for RNA localization of SUC2 mRNA. We revealed two motifs for high and one motif for low ER localization. We are now working to understand the relationships between their sequence features, secretion behaviors, and fitness and ability to cooperate and cheat.