The phylogenetic tree reconstruction game: developing reinforcement-learning algorithms for fast and accurate inference of evolutionary trees.

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Abstract

The following two fields have never interacted before: reinforcement learning and molecular evolution. We develop a reinforcement-learning algorithm to solve the challenge of reconstructing phylogenetic trees, which are used to describe the evolutionary relationships among a set of sequences. Current tools for phylogenetic--tree reconstruction integrate heuristic approaches to evaluate only a subset of all potential trees, thus they suffer from the known trade-off between accuracy and running time. Although recent studies have shown the potential of harnessing AI-based methods to reconstruct phylogenetic trees, the question regarding the overall tree-search strategy remains open. In our study, we developed a novel methodology for predicting the maximum-likelihood tree.

Our preliminary results, based on a reinforcement-learning algorithm that was trained using hand crafted features on datasets with up to twelve taxa, demonstrate that the trained algorithm is able to accurately and efficiently reconstruct maximum-likelihood trees. Moreover, we show that our algorithm can often take non-greedy moves in the phylogenetic-tree space.

These results suggest that our proposed paradigm, which uses reinforcement-learning techniques to learn an optimal strategy for the tree search, can boost tree search-heuristics without compromising accuracy.

African origin of a Levantine spider, revealed through molecular phylogeny.

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Abstract

In recent decades molecular phylogeny has been used to infer historical biogeography including geographical origins of various taxa. Specifically, tree topology can be used to infer ancestral origin, based on information of sister taxa. A phylogeny published by Planas *et al*. in 2013 placed the west Mediterranean species of the burrowing spider genus *Lycosa* Latreille, 1804 into closely related lineages, suggesting that each of the five species found in western Europe is nested within a North African clade. Our study aimed at testing how many *Lycosa* species are found in the southern Levant (Israel, Jordan, Palestine and Sinai peninsula), and to explore their phylogenetic relation to the western Mediterranean species. For this purpose we reconstructed a molecular phylogeny based on COI sequences of 18 species from Planas, with the addition of 16 specimens belonging to three Levantine morphospecies, two with burrows that include doors and one with burrows encircled by a turret. We hypothesized that the Levantine morphospecies are closer to one another, than to any of the African lineages, and belong to a separate Levantine clade. Conversely, they could belong to one or more of the North African clades. Our results support the existence of three species in the study area, and reject the hypothesis of a Levantine clade. The Levantine species were found to be nested in two North African lineages: two new door building species are sister taxa within the door building "*oculata*" clade, while a third, turret building species, is nested within the turret building *"baulnyi*"clade. Our findings suggest that in addition to the species from the western Mediterranean, the three *Lycosa* species from the Levant also originated in North Africa. Expanding this updated phylogeny with sequences from species found east to the Levant may help further clarify the origins of the genus *Lycosa*.

Periodical environmental changes and the evolution of senescence

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Abstract

Senescence is a process of phenotypic deterioration that leads to increased mortality risk with age, and eventually to death. Environmental changes and species responses to them are important for senescence evolution. Depending on the environment, the equilibrium between senescence and other life-history properties like reproduction can shift. In environmental conditions that lead to population growth early reproduction is preferred over late reproduction. The reason is that during 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 later reproduction is advantageous. In evolutionary time scales the environment cannot induce indefinite growth or decline, and the more common scenario involves periodical environmental change. Environmental periodicity occurs at different time scales, from multiple years cycles like predator–prey dynamics through yearly cycles like seasons to even single day cycles. I will present a new model that predicts the effect of periodical environmental changes on senescence evolution. I will use the model to compare strategies for dealing with environmental periodicity: synchronized life-history, bet-hedging, and senescence plasticity. I will briefly discuss possible applications of the model results to senescence research.

Comparative metabolite profiling changes during wheat domestication

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Abstract

One of the most important crops worldwide is wheat. Wheat domestication took place about 10,000 years ago. Not only that its wild progenitors have been discovered and phenotypically characterized, but their genomes were also sequenced and compared to modern wheat. While comparative genomics is essential to track genes that contribute to improvement in crop yield, comparative analyses of functional biological end-products, such as metabolites, are still lacking. With the advent of rigorous mass-spectrometry technologies, it is now possible to address that problem on a big-data scale. In attempt to reveal classes of metabolites, which are associated with wheat domestication, we analyzed the metabolomes of wheat kernel samples from various wheat lines. These wheat lines represented subspecies of tetraploid wheat along primary and secondary domestications, including wild emmer, primitive emmer, landraces durum, and modern durum. Our results indicate that underappreciated classes of metabolites that are involved in plant-defense mechanisms significantly increased in association with wheat domestication. We also detected altered changes in the composition of various antioxidants and an increase in the expression of plant hormones. Our data suggest that these metabolites may have contributed to the improvement in the agricultural fitness of wheat. Closer evaluation of specific metabolic pathways may result in the future in genetically-engineered high-yield crops.

Effects of stress on reproduction strategy in a mixed mating system and the inheritance of stress memory in future generations.

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Abstract

Lamium amplexicaule is an annual herb which produces two types of flowers simultaneously: cleistogamic flowers allowing only self-pollination, and chasmogamic flowers allowing both self and cross pollination, and are energetically costlier due to petals and nectar production. The rate of chasmogamic flowers is an indicator for the potential amount of cross fertilization, which impacts genetic variance in the future population.

Fitness-Associated Variation theory suggests that – everything else being equal – stressed individuals would show increased outcrossing rates, allowing the genes responsible for outcrossing to escape from their maladapted genetic background. In this experiment we tested whether *Lamium amplexicaule* plants indeed increase outcrossing rates in response to stress, in the generation of stress exposure and in future generations. To do so, we measured the amounts of chasmogamic vs cleistogamic flowers, and other vegetative and floral patterns, in control and in salt irrigated plants of a genetic line. We continued reconnaissance for multiple generations of stress \ non-stress regimens, in order to assess stress memory occurrence.

Our results suggest that in the first generation of stress exposure, stressed plants decrease outcrossing levels and vegetative growth. This is probably due to survival and growth difficulties, leading to reduced attractiveness to pollinators, and allocation of energy to cleistogamic flowers to assure some level of reproduction. In contrast, we found that offspring of stressed plants show increased investment in reproduction and outcrossing, regardless of present irrigation regimen. The effect lasts so far through the third generation (F2), indicating a possible role for epigenetic inheritance.

We conclude that while stressed plants show decreased outcrossing rates, the pattern is reversed among their offspring that show elevated outcrossing rates leading to higher genetic variation in future generations, mediated by an epigenetic regulation according to parental stress.

Poster Abstract

Rapid adaptation often occurs through mutations to the most highly conserved positions of the RNA polymerase core enzyme

Mutations to the genes encoding the RNA polymerase core enzyme (RNAPC) and additional housekeeping regulatory genes were found to be involved in rapid adaptation, in the context of numerous evolutionary experiments, in which bacteria were exposed to diverse selective pressures. This provides a conundrum, as the housekeeping genes that were so often mutated in response to these diverse selective pressures tend to be among the genes that are most conserved in their sequences across the bacterial phylogeny. In order to further examine this apparent discrepancy, we characterized the precise positions of the RNAPC involved in adaptation to a large variety of selective pressures. We found that different positions of the RNAPC are involved in adaptation to various stresses, with very little overlap found between stresses. We further found that RNAPC positions involved in adaptation tended to be more evolutionary conserved, were more likely to occur within defined protein domains, and tended to be closer to the complex's active site, compared to all other RNAPC positions. Finally, we could show that this observed trend of higher conservation of positions involved in rapid adaptation extends beyond the RNAPC to additional housekeeping genes. Combined, our results demonstrate that the positions that change most readily in response to well defined selective pressures exerted in lab environments are also those that evolve most slowly in nature. This suggests that such adaptations may not readily occur in nature, due to their antagonistically pleiotropic effects, or that if they do occur in nature, they are highly transient.

A LASSO-based approach to sample sites for phylogenetic tree search

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In recent years, full-genome sequences have become increasingly available and as a result many modern phylogenetic analyses are based on relatively large sequences, often with over 100,000 sites. Phylogenetic reconstruction of large-scale alignments is challenging for maximum-likelihood based phylogenetic inference programs and usually requires using a powerful computer cluster. Current tools for alignment trimming prior to phylogenetic analysis do not promise a significant reduction in the alignment size and are claimed to have a negative effect on the accuracy of the obtained tree. Here, we propose an artificial intelligence approach, which provides a subset of sites and a formula by which one can compute the log-likelihood of the entire data based on this subset. Our approach is based on training a regularized regression model that optimizes the log-likelihood prediction accuracy while putting a constraint on the number of sites used for the approximation. We tested our approach during SPR searches we performed on 55 alignments sampled from the Selectome database and showed that using only around 10% of the alignment sites well approximated log-likelihood values during the search. For the vast majority of the analyzed alignments, using our site-sampling approximation did not result in an inferior tree topology, yet it substantially reduced running times.

An evolutionary-biophysical framework to study the evolution and genetic diversity of self-incompatibility alleles

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Abstract

Hermaphroditic plants are at high risk of self-fertilization, which can produce less-fit offspring. To avoid self-fertilization, plants developed various mechanisms called "self-incompatibility" (SI). We focus on the RNase-based SI mechanism, which relies on specific molecular recognition between highly polymorphic proteins of two families: a cytotoxic ribonuclease (S-RNase) and an F-box protein (SLF), expressed in female and male organs, respectively. The population is then sub-divided into 'mating types', where fertilization is only possible between individuals of different types.

While both SLFs and S-RNases are highly diverse, fertilization of a female, having a new S-RNase requires that a matching SLF already exists at different individuals. Thus, it remains unclear how new alleles evolved. Recent experimental studies revealed a rich picture with fuzzy rather than clear-cut 'mating types'. Yet, previous models only employed simplified descriptions with binary recognition phenotypes and one-to-one relation between female and male proteins.

Here, we theoretically study the emergence and maintenance of genetic diversity among SI alleles. We construct a unique theoretical framework, synthesizing evolutionary and biophysical models.

We represent each allele by a 4-letter alphabet sequence, which stands for the amino acids in the protein recognition domain. The match between particular proteins is determined by the interaction energy between their sequences. This novel approach allows for multiple interaction partners per protein and co-existence of multiple allelic variants, which was not possible in previous binary models.

Asymmetries between SLFs and S-RNases emerge naturally in our model: SLF alleles diversify significantly more than S-RNases; SLFs have a broad distribution of number of interaction partners compared to S-RNases, whereby both dysfunctional and broad-specificity SLF alleles naturally emerge.

In summary, our new framework allows for a much richer picture than was facilitated by previous models. This allows us to recover typical characteristics of this system, as observed in experiments.

The effects of host age at exposure on Daphnia species infected by a yeast

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Abstract

A major challenge of infectious disease epidemiology and evolutionary ecology is to predict why and when a disease will appear and how it will spread in a population. While it is widely accepted that host and parasite genetics, host susceptibility, parasite virulence, resource availability, and variation at the environmental and spatiotemporal levels play a vital role in the establishment of an epidemic, factors related to host demography, such as the age-structure of the host population and age-dependent host susceptibility, are often overlooked in epidemiological analysis. Previous studies using the *Daphnia magna-Pasteuria ramosa* system have shown that juvenile *Daphnia* are more susceptible to infection than older ones, i.e., castration is faster, the production of parasite transmission stages is higher, and coinfections are more common. Furthermore, a study with the microsporidium *Hamiltosporidium tvaerminnensis* showed that *D. magna* susceptibility to infection decreases with age, thereby supporting the hypothesis that host age effects are not limited to infection with *P. ramosa*. In this study, we investigated how general age effects are and if we can detect them in different *Daphnia* hosts. By using three species of *Daphnia*: *D. magna*, *D. similis* and *D. curvirostris*, and their yeast pathogen *Metschnikowia bicuspidata*, we investigated the impact of host age on parasite-induced host mortality and on the relationship between pathogen virulence and transmission in different hosts. Age effects have been detected in all three *Daphnia* species. In *D. magna* and *D. similis* the susceptibility to infection decreased with age, while in *D. curvirostris* it increased with age. These results enhance our knowledge on the relationship between pathogen virulence and transmission in different hosts, reinforces the epidemiological predictions behind it, and improves our response to an epidemic.

The ADAMTS and ADAM metalloproteinase gene families and their role in the development and regeneration of the sea anemone *Nematostella*

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Abstract

We are studying the development and whole-body regeneration (WBR) in the sea anemone *Nematostella vectensis* (*Nv*), which is a basal cnidarian animal model, a close sister clade to bilaterian animals. Besides the obvious interest in exploring the remarkable WBR process and its relation to embryonic development, understanding this phenomenon can shed light on processes like embryogenesis, wound healing and even cancer biology in man.

In order to investigate the WBR process in Nv, we performed a transcriptional screen, in which we defined the genes which respond in their expression pattern during the time course of regeneration. One of the most interesting and conspicuous gene groups that stood out in the screen was that of the metalloproteinases and in particular the family of the ADAMTS (A disintegrin and metalloproteinase with thrombospondin motifs). Another structurally related family are the ADAM genes. These families of enzymes are known to be active in the ECM of cells and play important roles in multiple functions such as the morphogenesis of tissues and cell mobility.

In this project we first define the Nv repertoire of these gene families and explore their evolutionary placement and relation to the mammalian gene families which were the first to be explored. We thus defined 18 ADAMTS genes with only three that could be identified as orthologs of mammalian genes and three ADAM genes, which are orthologs of human ADAM 10, 17 and 28.

In order to elucidate the activity of these genes in Nv and the meaning of the peculiar genomic structure of some, we have started assaying their expression along the developmental stages and in the regeneration time course using qPCR and in situ hybridization (ISH) experiments. Our results to date illustrate a diversity in the spatial and temporal patterns of the genes and interesting cell staining patterns.

Under pressure: selection operating on moths' mate-finding

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Odor-mediated sexual communication has been shaped by both natural and sexual selection pressures. Moths (Insects: Lepidoptera) are notable by their ability to discriminate between fine differences in chemo-sexual cues in airflow, while following the species-specific volatile sex pheromone, emitted by conspecific females. Although moth's sexual communication has been widely studied, the interrelation between the selective forces and the male ability to reach the calling female is still obscure. The study was aimed at exploring the effect of biophysical aspects on the males' ability to locate a mate: (1) Biological aspect– the females' high or low reproductive potential. (2) Source availability – a single source or a choice of two volatile sources. (3) Physical aspect – flying in a steady or an unsteady airflow condition. Male's performance of these three aspects, in different combinations, was tested in a wind tunnel assay; females with high or low reproductive potential were placed in a small cage upwind (in a choice arena or alone). Males have individually released downwind the tunnel. Males that reached one of the volatile sources were scored as successful and those who failed to reach any source were defined as failures. The success rate of males was compared among all treatment combinations. The high rate of failure among mate searching males, suggests a strong selective pressure operates on the male moth. Among successful males, both, the female quality and the flow conditions, had predominant effects on males' performance. We suggest that male moths are subject to two selection forces: natural selection shapes the ability of males to successfully locate a volatile source, and sexual selection, shapes the ability to gain the optimum benefit, locating females having higher reproductive potential. Our finding provides important knowledge for the evolution of

moths' sexual communication, and also to the development of odor-mediated mating system.

Myxozoan infection in thinlip mullet *Chelon ramada* Risso, 1827 a marine species introduced to the Sea of Galilee

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Abstract

Mullets (Mugilidae) are economically important fish in Israel. Two catadromous species of Mugilids (i.e., *Chelon ramada* and *Mugil cephalus*) have been stocked in Sea of Galilee (Lake Kinneret) since 1958 in order to increase fishermen's incomes and lake water quality. The case of the thinlip mullet *C. ramada* is extremely interesting since this species does not reproduce in the lake. Consequently, fingerlings are regularly introduced. Alien species are known to harbor fewer parasites than native ones. Mullets, however, have been found to be more vulnerable to parasitic infections because they are widespread and migrate between marine and freshwater ecosystems. Myxozoans are microscopic parasitic cnidarians that can cause tremendous damage to aquaculture industry. Surprisingly, during a survey of myxozoan infection in the Sea of Galilee, we discovered two myxozoan species infecting the gills, intestine and gall bladder of the thinlip mullet. The prevalence of infection was found to be 17% (4/23). While the first species *Myxobolus exiguus* has been described from mugilid of the Mediterranean, Black and Caspian seas, the second species is novel member of the genus *Myxobolus*. Our study indicated that the parasites infecting *C. ramada* belong to a marine lineage of myxozoans. These results suggest that the infection took place in the Mediterranean Sea, before the introduction of infected fingerlings to the Sea of Galilee. Fortunately, because Myxozoans have an indirect life cycle, which also involve an annelid worm, these introduced parasites are not likely to complete their life cycle in a fresh water environment. *Myxobolus exiguus* is also known to affect other mugilid and its adaptation to the fresh-water environment might have important deleterious impacts. It will thus be important to monitor that its presence does not increase in the environment.

Resistance of Cyanobacteria to Phages under Nitrogen Starvation

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Abstract

Cyanobacteria are important primary producers, and one of the few microorganisms that can perform nitrogen fixation. However, under the right conditions, they proliferate and form harmful blooms. Under nitrogen starvation conditions, the ability to fix atmospheric nitrogen becomes advantageous, and thus such conditions promote blooms by nitrogen fixing strains. A previous study in our lab discovered that when cyanobacteria, grown under nitrogen replete conditions, become resistant to phages, they lose their ability to fix atmospheric nitrogen, and thus they have a decreased ability to survive under nitrogen starvation. Such tradeoff can affect cyanobacteria population dynamics and evolution. These results made us wonder whether during blooms, when nitrogen levels are low, nitrogen fixing cyanobacteria are able to evolve resistance to their phages, or the strong selection will prevent their appearance. Here, we aimed to select for resistance to phages in nitrogen fixing cyanobacteria, under nitrogen starvation conditions. Our results show that strains resistant to phages can appear under nitrogen starvation, though their appearance is much slower than the appearance of resistant strains under nitrogen replete conditions. Unlike the resistant strains isolated under nitrogen replete conditions, these resistant strains are able to fix nitrogen. Some of the resistant strains have shown a decreased growth rate when transferred to a replete nitrogen environment, which may indicate that the cost of resistance prevents them from thriving in rich nitrogen environment. Sequencing the genomes of 68 resistant strains revealed that a wide range of genes are involved in phage resistance. Some of the identified mutations are found in cell surface related genes, however the resistance mechanism is yet to be understood.

Evolution of allosteric features in an enzyme

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Allosteric regulation of protein is so crucial that it is aptly called the “second secret of life”. Despite decades of research on allostery how conserved is allosteric features in a protein across closely related species is not systematically investigated. Earlier we found a unique of mode of enzyme regulation in *B. subtilis* where GudB, the protein of interest was found to be regulated by binding to GltAB. Interestingly, GudB and GltAB catalyze opposite reactions in metabolism. Intrigued by the mode of regulation, we asked how conserved is this in the Bacillus phylogeny. We profiled GudB’s regulatory mode in various Bacillus species representing the major clades in the Bacillus species tree. We find that each clade has evolved a different way to regulate GudB. We argue that the regulatory mode is suited to the metabolic niche in which these organisms thrive. GudB’s regulatory mode thus presents a convincing case that while *enzyme function* can be conserved its *regulation* can be tuned by evolution to suit the metabolic demands of the organism.

Deciphering genetic determinants of sexual mating and its effects on evolution

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Abstract

Sexual reproduction is wide-spread in nature. Major questions in the field are how organisms choose their partners, and how is offspring fitness relates to that of its parents'. We generated and mined massive data on mating choice and fitness inheritance, in unprecedented magnitude, using sexual mating in yeast.

We genetically manipulated and barcoded dozens of haploid strains, originated from wild isolates. The original isolates were collected from diverse habitats and span a broad range of genetic distance (GD) and fitness values.

Following *en mass* mating, progeny of each pairwise combinations were detected by induction of a unique barcode recombination and fusion event in the offspring. Fused barcode regions were amplified, sequenced and quantified.

Using competition assays, we calculated the fitness for each offspring (as well as each parent). We found a decent correlation between the average, the minimum and the maximum fitness of the two parents and offspring's fitness. These results indicate that inheritance of fitness is a complex trait and not a simple function of parents' fitness. In addition, we see a connection between GD of the parents and offspring's fitness; specifically, fitness of the offspring is higher in high GD.

To assess attractiveness of a strain, we counted the number of unique partners it has. This score ranged from 1 to above 60, indicating that some strains mate with many different partners whereas others are more selective. Interestingly, the number of mating partners per strain correlates to the average fitness of its offspring. This result suggests that yeast choose their mating partners to enhance the fitness of their offspring, thus strains that give rise to fitter offspring are being chosen more.

Deciphering the complete mitochondrial genomes of *Oikopleura dioica* (Chordata: Tunicata: Appendicularia)

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Abstract

Appendicularians are solitary tunicates, which form an important part of the planktonic biomass. They are the only tunicates known to retain their tail as adults. Since tunicates are the closest relatives of vertebrates, appendicularians are model organisms to understand the evolution of chordates. Although the nuclear genome of the appendicularian Oikopleura dioica has been sequenced, no complete mitochondrial genome of Appendicularia has yet been published. The reason for this absence is, most probably, the fast evolutionary rate of appendicularian mitochondrial genomes combined with unusual characteristics such as RNA editing. We here present our preliminary results regarding the sequencing of the complete mitochondrial genome of O. dioica. In particular, we aimed to determine its structure and gene content. To decipher the mitochondrial genome of this species we have re-sequenced its genome using both short Illumina reads and long Nanopore reads. We also analyzed cDNA reads and EST sequences available in public databases. While we could assemble complete protein-coding genes based on cDNA and EST, no such assembly was possible for DNA reads. Mapping DNA reads to RNA contigs revealed RNA editing events in TTTTTT (6T) regions in the mitochondrial RNA (in a 5'-3' orientation). These editing sites reside within regions composed of numerous T and few C (i.e., polypyrimidine regions). Specifically, the nanopore reads indicate that these polypyrimidine regions are about 50 bp long. Using both short and long reads we successfully assembled three mitochondrial contigs. Among these contigs only ten protein-coding genes, two rRNA and one tRNA, could be identified, indicating important mitochondrial tRNA gene losses in this species, as well as the loss of few protein-coding genes. We expect that this mitochondrial genome will become a reference for comparative studies aiming at understanding the evolution of mitochondrial editing and gene loss in Appendicularians.

An evolutionary arms race between nitrogen fixing cyanobacteria and their viruses

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Abstract

Cyanobacteria perform a substantial part of photosynthesis and nitrogen fixation in nature, and thus play a central role in various ecosystems. Under certain conditions, some cyanobacteria strains proliferate and form seasonal blooms that can become harmful to the environment and to the people using these waters. Cyanophages (viruses that infect cyanobacteria) have a long-term coexistence with their cyanobacterial hosts in nature. One of the models that may help explaining this coexistence is a continual arms race between cyanobacteria and their phages. To gain insight into the cyanobacteria-cyanophage arms race, we used two nitrogen fixing cyanobacterial host strains and their phages. We isolated and characterized (phenotypically and genotypically) cyanobacteria substrains resistant to these phages, as well as phage substrains that coevolved with the resistant substrains.
Resistance to phages came with a reduced ability to fix nitrogen and with a limited growth under nitrogen starvation conditions. Resistance conferring mutations were found in various genes related to the cell surface of the host, which may affect the ability of the phage to adsorb and infect this potential host. Moreover, the completeness of the cyanobacteria cell surface is important for efficient nitrogen fixation, and thus modified cell surface may explain the reduced nitrogen fixation in the resistant substrains. Considering an arms race model, indeed, many of the phages displayed mutations in genes related to the phage tail structure, which is responsible of the recognition of the host and the attachment to its cell surface.
Our results suggest that cyanophages can potentially affect the cyanobacterial populations both by killing them and by selecting for resistant strains with a substantial reduced ability to survive under nitrogen starvation conditions, in which the susceptible strains proliferate and bloom. Understanding the mechanisms that drive this coevolution can help in understanding of cyanobacteria-phage populations dynamics.

Behavioral variation according to feeding organ diversification in glossiphoniid leeches (Phylum: Annelida)

Hee-Jin Kwak

ABSTRACT

Adaptive radiation is a phenomenon in which various organs are diversified morphologically or functionally as animals adapt to environmental inputs. Leeches exhibit a variety of ingestion behaviors and morphologically diverse ingestion organs. In this study, we investigated the correlation between behavioral pattern and feeding organ structure of leech species. Among them, we found that *Alboglossiphonia* sp. swallows prey whole using its proboscis, whereas other leeches exhibit typical fluid-sucking behavior. To address whether the different feeding behaviors are intrinsic, we investigated the behavioral patterns and muscle arrangements in the earlier developmental stage of glossiphoniid leeches. Juvenile Glossiphoniidae including the *Alboglossiphonia* sp. exhibit the fluid ingestion behavior and have the proboscis with the compartmentalized muscle layers. This study provides the characteristics of leeches with specific ingestion behaviors, and a comparison of structural differences that serves as the first evidence of the proboscis diversification.

Competition within the microbiome may promote dysbiosis and exacerbate host addictive behaviors

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Accumulating studies have revealed mechanisms by which the microbiome affects its host brain, behavior and wellbeing, and demonstrated how the host, in turn, affects the microbiome composition. Much effort is currently devoted to investigating the role of the microbiome in the onset and progress of various chronic diseases, including addictive behaviors. Nevertheless, understanding of the ecological and evolutionary processes that shape the host-microbiome ecosystem and affect the host state is still very limited. Here we propose that competition dynamics within the microbiome, intertwined with host-microbiome mutual regulation, may promote dysbiosis – persistent imbalance in the microbiome associated with disease states – and play a significant role in aggravating addictive behaviors. We constructed a mathematical framework, considering the dynamics within the host-microbiome ecosystem in response to host-induced alterations, such as consumption of new substances. First, we find that selection may favor microbes that influence host condition, encouraging states that are advantageous for them. We next find that substantial host alterations may lead to a new microbiome-composition that would reinforce the new host state, restraining attempts to return to the initial equilibrium, and thus promote relapse episodes and prolonged addictions. Finally, we find that lower microbiome richness and functional diversity may further intensify dysbiosis and exacerbate addictions. This framework provides novel evolutionary and ecological perspectives on host-microbiome interactions and their implications for host behavior and health, while offering verifiable predictions with potential leads for clinical treatments.

Competition within the microbiome may promote dysbiosis and exacerbate host addictive behaviors

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Accumulating studies have revealed mechanisms by which the microbiome affects its host brain, behavior and wellbeing, and demonstrated how the host, in turn, affects the microbiome composition. Much effort is currently devoted to investigating the role of the microbiome in the onset and progress of various chronic diseases, including addictive behaviors. Nevertheless, understanding of the ecological and evolutionary processes that shape the host-microbiome ecosystem and affect the host state is still very limited. Here we propose that competition dynamics within the microbiome, intertwined with host-microbiome mutual regulation, may promote dysbiosis – persistent imbalance in the microbiome associated with disease states – and play a significant role in aggravating addictive behaviors. We constructed a mathematical framework, considering the dynamics within the host-microbiome ecosystem in response to host-induced alterations, such as consumption of new substances. First, we find that selection may favor microbes that influence host condition, encouraging states that are advantageous for them. We next find that substantial host alterations may lead to a new microbiome-composition that would reinforce the new host state, restraining attempts to return to the initial equilibrium, and thus promote relapse episodes and prolonged addictions. Finally, we find that lower microbiome richness and functional diversity may further intensify dysbiosis and exacerbate addictions. This framework provides novel evolutionary and ecological perspectives on host-microbiome interactions and their implications for host behavior and health, while offering verifiable predictions with potential leads for clinical treatments.

Ciliogenesis in the basal sea anemone *Nematostella vectensis*

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Abstract

The sea anemone *Nematostella vectensis* is a member of the Cnidaria phylum, a sister group to Bilateria that has become an important model system for developmental and evolutionary studies. *Nematostella* larval stage of a free-swimming planula utilizes cilia that cover its entire body for locomotion. Having arisen early in eukaryotic evolution, cilia are found across a broad phylogenetic spectrum in cells of different tissues and organs. Moreover, ciliary structure is highly conserved from protists to multicellular organisms. In mammals, ciliary malfunction causes severe disorders known as ciliopathies. Here, we demonstrate that planula ciliogenesis is affected by GABAB receptor signaling. Addition of GABAB agonist baclofen caused reversible arrest of planula mobility, development and metamorphosis. Comparative transcriptomic profiling of baclofen-treated and untreated control planulae revealed changes in expression of genes associated with ciliary structural and transport. Further analysis showed down-regulation of known ciliopathy genes, including *foxj1* transcription factor, a master regulator of ciloigenesis. Our findings open new avenues for comparative studies of cilia function and evolution.

Contribution of allele frequency classes to inference of population structure

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Abstract

Analysis of population structure in natural populations using genetic data is a common practice in population genetic studies. While many inference methods focus on a single level of structure, in most natural populations population structure is highly hierarchical, with genetic clusters spanning from fine- to broad-scale across many levels. Typically, methods for inference of population structure aggregate information from thousands to millions of SNPs. However, the information contribution of SNPs to population structure inference is non-uniform, and it is unclear how SNPs with different allele frequencies contribute to inference of population structure. In particular, SNPs with different allele frequencies may contribute differently to population structure inference because evolutionary processes at different hierarchical scales are often characterized by different typical allele frequencies. Here, we use a network-based inference methods, which can account for many levels of hierarchical structure, in order to quantify the information-contribution of SNPs with different alleles frequencies to inference of population structure. We measure information contribution using a customized information-theoretic measure suited for comparing hierarchical population structures. To understand information contribution in humans, we analyze the Human genome Diversity Project data set, containing 929 individuals and over 32 million SNPs. We find that the extremely low-frequency classes, below 1%, which typically contain many more SNPs than higher frequency classes, nevertheless contribute much less information to broad-scale structure analyses, but not to fine-scale analyses. When normalizing for per-SNP contribution of information, we demonstrate a non-monotonical contribution of information with increase in the frequency. These findings contribute to our understanding of the importance of particular SNPs to population structure inference, and can help in design of SNP panels. Moreover, our analysis can help in characterizing and illuminating the evolutionary roles of different loci at different levels of the population structure hierarchy.

Cross-species identification of cancer resistance genes uncovers their association with human cancer risk

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Abstract.

Cancer is an evolutionarily conserved disease that occurs in a wide variety of species. We applied a comparative genomics approach to systematically characterize the genes whose conservation levels significantly correlates positively (PC) or negatively (NC) with a broad spectrum of cancer-resistance estimates, computed across almost 200 vertebrate species. PC genes are enriched in pathways relevant to tumor suppression including cell cycle, DNA repair, and immune response, while NC genes are enriched with a host of metabolic pathways. The conservation levels of the PC and NC genes in a species serve to build the first genomics-based predictor of its cancer resistance score. We find that PC genes are less tolerant to loss of function (LoF) mutations, are enriched in cancer driver genes and are associated with germline mutations that increase human cancer risk. Furthermore, their expression levels are associated with lifetime cancer risk across human tissues. Finally, their knockout in mice results in increased cancer incidence. In sum, we find that many genes associated with cancer resistance across species are implicated in human cancers, pointing to several additional candidate genes that may have a functional role in human cancer.

Prediction of Conservation Categories for Data Deficient Species from Genomic Data

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Abstract

The International Union for Conservation of Nature (IUCN) Red List aims to contain information on the conservation status of all animal, fungi and plant species. However, more than 15% of the Animalia species are currently defined as Data Deficient (DD) due to the difficulty and cost of collecting sufficient ecological information to categorize them. Consequently, efforts are made to predict their conservation category using computational tools. While for many DD species ecological data is lacking, genomic information is much cheaper to obtain and is available for a significant proportion of them, usually in the form of a single sequenced genome. In previous studies, genomic data has been used to predict conservation categories in two ways: (i) using location in the phylogenetic tree; (ii) using population genetic statistics, such as effective population size and heterozygosity, extracted from a population dataset. Recent computational methods, such as the Pairwise Sequentially Markovian Coalescent (PSMC) model, succeed in inferring demographic histories from a single high-resolution sequenced genome, suggesting that conservation-relevant demographic trends can be extracted from single genomes. We utilize these genomic signatures of demographic histories to predict conservation categories. To generate such predictions, we adopt a deep learning approach, a computational method which has shown success in extracting information on evolutionary processes from genomic data. Under this approach, we construct a convolution neural network and train it on genomic data labeled with IUCN categories. In addition to enabling cheap and efficient putative assignment of conservation categories to DD species, affording them inclusion in conservation prioritization plans and legal protections, our project will also enable us to investigate the relation between evolutionary signals in the genome and risks of extinction.

Parasite resistance *vs*. tolerance: insights on transgenerational effects of immunity in a *Daphnia*-yeast system

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Abstract

Parasites impose different selection regimes onto their hosts, which respond in return by increasing their resistance, i.e., reducing the infection rate, or their tolerance, i.e., altering epidemiologically related life-history traits. Parasite challenge may impact the challenged generation as well as their offspring, a mechanism known from invertebrates as transgenerational immune priming (TGIP). In this study, based on findings from the *Daphnia-Pasteuria* host-parasite system, we hypothesized that parental exposure to the yeast parasite *Metschnikowia bicuspidata* will induce increased resistance to the offspring generation. We exposed two parental generations of the model organism *Daphnia magna* to the horizontally transmitted yeast parasite *M. bicuspidata* in a fully cross-factorial experiment, and recorded life-history traits in the offspring generation. Our susceptibility assays revealed no impact of parental exposure on offspring resistance. Nonetheless, different life-history traits were altered, with maternally primed offspring producing more offspring than the unprimed ones in the presence of the parasite, which supports the "environmental matching hypothesis". We further found strong grandmaternal effects in early life-history traits, which may affect the fitness of the offspring. Interestingly, primed *Daphnia* for two sequential generations had no competitive advantage over unprimed ones, indicating anticipatory maternal and grandmaternal effects. While we observed a short decrease in survival for animals primed for two sequential generations, we did not find clear evidence for an adaptive TGIP response. Our findings increase our knowledge regarding TGIP responses in invertebrates and show that TGIP is not a consistent mechanism even within the same species. Thus, it is likely driven by different selective regimes.

From solitude to eusociality: a multi-dimensional quantitative approach to study the evolution of social complexity

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Abstract

The diversity and richness of social insects make them an excellent model for comparative studies on the function and evolution of complex societies. The current approach for research on the evolution of insect sociality is based on a qualitative and crude classification and suffers from several limitations: (i) It assumes that social traits always evolve together and in synchrony, which may falsely imply that social evolution always progresses along a single linear stepwise trajectory that can be deduced from comparing extant species; (ii) It pools species differing in social complexity into a single level; (iii) It limits our ability to test the association between the level of sociality and quantitative "omics" molecular, physiological, and behavioral parameters. We are developing a novel approach that is based on quantitative indices for social complexity using bees as a model. Bees exhibit diverse levels of sociality – from solitary living to highly complex social organization, and it has evolved independently in several lineages. As a first step, we conducted an extensive literature review to extract numeric data for many social traits and species. We compiled a comprehensive database of traits using meta-analysis techniques for quality control. Next, we performed data-driven statistical analyzes, which account for phylogenetic relations between species. Our approach enables quantification and mapping of sociality in species based on multiple types of data. Our preliminary results indicate a spectrum of social complexity types in bees, which is wider than appreciated with the classical approach. We identified multiple axes that characterize regions of interest in the multidimensional trait space, suggesting non-trivial relations between different social complexity traits. Our approach is not taxon-specific, and can be useful for comparative studies of other taxa – from ants to primates.

gUMI BEAR, an unsupervised population barcoding system to track evolution at high resolution

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Abstract

Lineage tracking methodologies have opened up the possibility to witness previously unknown heterogeneity in the internal dynamics of populations, allowing exploration of the forces underlying adaptability and evolvability. However, current methods are labor-intensive, highly specific, not sufficiently reproducible and expensive. To address these issues, we developed gUMI-BEAR (genomic Unique Molecular Identifier Barcode Enriched Associated Regions) – a versatile method for tracking evolution at high resolution. The system includes donor-DNA, containing a barcode coupled to sequence-ready adapters, that can be inserted into any locus in the genome when co-transformed with a CRISPR-Cas9 plasmid.

To demonstrate the system's capabilities, we applied our method, in two different ways, to the *Saccharomyces cerevisiae* strain BY4741; In the first application, gUMI-BEAR was used as a means to study evolutionary dynamics in populations with no prior fitness differences. In the second, we conjugated the gUMI system to *hsp82* variants, creating an identity between barcode and mutant. This allowed us to screen together a virtually unlimited number of random variants. In both implementations, we were able to track thousands to millions of lineages across multiple generations (250-450), revealing lineage-specific adaptations to environmental changes and observing subtle dynamics with high resolution and accuracy. Due to the robust nature of the libraries created using this methodology (99.9% population similarity between replicates), one can compare the dynamics among repeats in the same and in different experiments to reveal the interplay between stochastic and deterministic outcomes. While the identity of adapted lineages in the unbiased populations varied between replicates, lineages with the same *hsp82* variant behaved consistently within and between experiments even when replicate experiments were conducted months apart.

gUMI-BEAR provides the means to examine evolution at previously unattainable depth by providing a scalable, modular, reproducible and cost-effective experimental system that can easily be implemented in a range of setups.

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Decoding the functional importance of sparse highly conserved short motifs in lncRNA genes

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Abstract

Thousands of long noncoding RNA (lncRNA) genes have been identified in animal genomes, a growing fraction of which have been implicated in the regulation of numerous cellular processes. This functionality has often been attributed to short conserved stretches, disguised in sequences that change rapidly, that facilitate interactions with other RNAs, proteins or genomic loci. Consequent to their rapid evolution, it is often impossible to detect significant sequence similarity in lncRNAs from species separated by >50 million years. This substantially hinders the use of comparative genomics to identify functional lncRNAs and to uncover conserved sequence elements that modulate biological function. Here we present lncLOOM, a novel graph-based framework that uses integer linear programming to identify combinations of short conserved motifs that are constrained within a set of rapidly evolved sequences. The significance of the motifs is empirically determined and the motifs are mapped to known binding sites of miRNAs and RNA binding proteins. We show the power of lncLOOM to uncover biologically relevant motifs in lncRNAs that are conserved between mammalian and fish species, even in cases where no sequence similarity is detectable by traditional alignment programs. As a case study, we used lncLOOM to identify deeply conserved motifs that are essential to the function of *Chaserr*, a lncRNA that acts in *cis* to repress the expression of *Chd2,* the dosage of which is critical for embryonic development and brain physiology. We show that targeted blocking of these conserved motifs with antisense oligonucleotides is sufficient for boosting CHD2 levels, thus providing a potential therapeutic approach for treating CHD2 haploinsufficiency.

Plastic increase in recombination rate in response to environmental shifts as an evolving strategy: a numerical model

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Abstract

Numerous empirical studies have witnessed a plastic increase in meiotic recombination rate in organisms experiencing physiological stress due to unfavorable environmental conditions. Yet, it is unclear which aspects of an ecological factor (e.g. intensity, duration, variability) are critical for inducing changes in recombination. Previous theoretical models proceeded from the assumption that organisms increase their recombination rate when the environment becomes more stressful and demonstrated the evolutionary advantage of such a strategy. Here we explore another stress-associated recombination strategy, implying a reversible increase in recombination rate in response to environmental shift. In our model, we assume such plastic changes in the organisms, grown in an environment different from that of their parents, and, optionally, also in their offspring. We show that such a shift-inducible recombination strategy is favored over the intermediate optimal constant recombination under the entire parameter space of the model. Moreover, plastic recombination sometimes outcompetes also zero and free optimal constant recombination, thus making selection on recombination less polarized. It appeared that the most informative characteristic, which defines the fate of shift-inducible recombination, is the within-period range of the population mean fitness values. These results hold for both panmixia and partial selfing, although selfing makes the dynamics of recombination modifier alleles faster. Our results suggest that epigenetic factors, presumably contributing to the environmental plasticity of recombination, may play an important evolutionary role.

Using computationally inferred genealogies to study differentiation of closely related Warbler species

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Abstract

Golden-winged warblers (*Vermivora chrysoptera*) and blue-winged warblers (*V. cyanoptera*) are hybridizing songbirds that differ in plumage coloring and breeding range. Both species are declining in numbers due to habitat loss over the last 150 yrs and the golden-winged warblers are currently of conservation concern, in part due to hybridization with the blue-winged warblers. Despite their clear visual phenotypic differences, their genomes are nearly identical, save for six small nuclear regions, as well as considerable difference in their mitochondrial genome.

In this work we are interested in identifying and characterizing genomic regions of differentiation that occur despite extensive hybridization. To this end, we use genealogies represented by the ancestral recombination graph (ARG). We employ ARGweaver, a computational method for probabilistic inference of the ARG from whole-genome sequence data. ARGweaver infers a local tree for each position in the genome and we use these local genealogies to extract useful statistics that are informative about the mode of speciation. Using these tree-based statistics, we wish to investigate the selective forces acting on genomic regions that keep them from homogenizing. In particular, we detect genomic islands of divergence, examine the timing of divergence and the dynamics of speciation. In addition, we show that tree-based statistics can be applied and are useful in studying selective forces in a species-complex that is comprised by as little as two species. We envision this approach being applied to other species complexes in studying modes of speciation.

Foraging efficiency in the face of predation risk: a comparative study of desert rodents

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ABSTRACT:

Question: What is the adaptive significance of the heteromyid cheek pouch?

Organisms: Two heteromyid rodents (Merriam's kangaroo rat, *Dipodomys merriami*, and desert pocket mouse, *Chaetodipus penicillatus*) from the Mojave Desert, and two gerbils (greater Egyptian gerbil, *Gerbillus pyramidum*, and Allenby's gerbil, *Gerbillus andersoni allenbyi*) from the Negev Desert, Israel.

Site: An outdoor vivarium on the Sede Boqer campus of Ben-Gurion University of the Negev, Israel.

Methods: We measured foraging time in seed trays for heteromyids and gerbils. We also measured the number of trips to food patches, and giving-up densities (GUDs, the amount of seed left behind when an individual left a seed tray).

Predictions: We expected cheek pouches to confer improved heteromyid foraging efficiency by reducing the number of trips between food patches and caching sites. We further expected that, compared with the other species, kangaroo rats would be less inhibited by barn owls, by moonlight, and by risky microhabitats.

Results: The two heteromyid species harvested more food per trip than the two gerbil species. Kangaroo rats had lower GUDs than any other species, particularly in risky microhabitats and at the full moon. Harvest rate curves for greater Egyptian gerbils and kangaroo rats indicated that these two larger bodied species were more vigilant than the two smaller bodied species.

Conclusion: Adaptations such as body size and the external cheek pouch appear to allow kangaroo rats to manage risk and harvest food more effectively than smaller and non-heteromyid rodents.
Keywords: foraging efficiency, gerbil, giving-up density, heteromyid.

Identification of novel biological pathways through co-evolution analysis

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Abstract

The evolutionary history of a gene, as conveyed in its conservation pattern throughout phylogeny, holds a lot of information on the gene's function. Phylogenetic profiling is a straightforward method of elucidating a gene's functional interactions from its conservation pattern in multiple species. Given the extensive growth in genomic data, phylogenetic profiling is a powerful approach. Despite the sequencing revolution, most human genes are poorly annotated. We aim to use phylogenetic profiling to annotate uncharacterized genes and uncover novel biological pathways. Although identifying uncharacterized pathways represents an extremely difficult challenge, novel pathways were recently identified after extensive analysis of gene groups showing similar phenotypes, interactions, or expression.

Recently, we established that integrating information from different clades can optimize co-evolution signals and improve gene function discovery. We generated a network of all genes divided into paralogous groups for 12 clades containing almost 2000 species and identified clusters. We found several known pathways, but the annotated clusters corresponded to only 22% of the overall clusters. The remaining clusters may represent undiscovered biology. Using data integration and biological validation we intend to identify novel biological pathways. *Characterization of even a single novel pathway is of paramount importance.*

A-to-I RNA Editing: An overlooked source of temporal mutations that could be beneficial in the life cycle of an organism

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Abstract

Traditionally, DNA mutations are considered to bear the sole responsibility for alterations in genomic information. Creating diversity at the level of the DNA is costly for the organism, as the majority of mutations are not advantageous. Moreover, changes in the DNA are transmitted between generations, and an adaptive response to an environmental change may result in lower fitness once the environment changes again. Here we suggest that RNA editing enzymes, which modify individual nucleobases within RNA molecules are additional powerful mean for inner transcriptome diversity. In A-to-I RNA editing, genomically encoded adenosines are transformed by the Adenosine Deaminases Acting on RNA (ADAR) protein family and recognized as guanosines in the RNA sequence. When editing occurs within mRNAs, it can recode specific codons, leading to changes in protein structure and function. In addition, RNA editing can create temporal diversity, that unlike DNA mutations does not leave mutation burdens in the genome for many generations of cells.
To test our hypothesis, we created a selection-neutral in vivo system to investigate the effects of massive RNA editing on evolution. This was achieved by the exogenous expression of the ADAR proteins in the yeast Saccharomyces cerevisiae, an organism whose origins precede the emergence of ADARs, but can expresses ADAR from different organisms. Remarkably, we identify extensive (thousands) A-to-G changes, genome-wide, without leaving any traces on DNA. Exploration of the proteomics profile changes in response to ADAR activity reveled that RNA editing events are manifested at the proteomic levels and are a source of protein heterogeneity. Using the sophisticated experimental tools available in yeast, revealed that creating massive transcriptome diversification only at the RNA level, and only at a certain stage in the life cycle of an organism, could be much more beneficial in specific scenarios.

Selection shapes metazoan mitochondrial DNA gene organization and impacts transcription boundaries

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Abstract

Unlike mitochondrial gene content, which is widely perceived to be conserved among metazoans, the gene order and topology of the mitochondrial genome (mtDNA - circular, linear, fragmented) are drastically more variable. Nevertheless, it is yet unclear whether mtDNA organization has any functional effect on the mitochondrial genes' transcriptional pattern and regulation. By employing an in-house algorithm to analyze annotated mtDNAs from ~8000 different metazoan species, we found that gene order across the entire mtDNA sequence is selectively constrained in a phylum-specific manner. Secondly, we found that certain short gene clusters are deeply conserved across metazoan phyla. These two findings led us to suggest that such constraints may affect mtDNA regulation. As a first step to assess this possibility we analyzed new available precision run-on transcription data (PRO-seq) from *Drosophila melanogaster* and corroborated previous observations that the drosophila mtDNA harbors 3 heavy strands and 2 light strand transcription start sites (TSS), in contrast to a single TSS per strand in mammals. While analyzing available RNA-seq data from a variety of metazoans we found that the drosophila pattern of mtDNA transcription corresponds to the boundaries of gene clusters across nearly all tested insects, as well as in other arthropods. This indicates that the drosophila pattern of mtDNA transcription is highly conserved across the phylum of Arthropoda, similarly to the conservation of human mtDNA transcriptional pattern across mammals. Our results suggest that evolutionary changes in mtDNA organization are selectively constrained, and likely lead to functional differences in mtDNA regulation across metazoans.

Recurrent recruitment of a family of toxins within and across the venom system of *Nematostella* during development

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Abstract

Gene duplication has been a major force in the evolution of venomous animals. Animal venoms are mixtures of various bioactive molecules and are usually heavily based on peptide and protein toxins. A major trend in venoms is the generation of new toxins by duplication of non-toxin proteins and the recruitment of one of the paralogs into the venom-producing cells. The convergent recruitment of Membrane Attack Complex and Perforin Family (MACPF) protein domain has been reported in the venom of various lineages including fish, snails, and cnidarians. Here we systemically investigated the spatiotemporal expression and function of genes encoding single domain MACPF proteins in the model cnidarian *Nematostella*. We find that four genes encoding MACPFs are expressed at measurable levels during development with varying dynamics. while only one paralog is expressed exclusively in ectodermal stinging cells that are related to envenomation, another paralog is expressed only in endodermal cells during a very short period at the planula stage, strongly suggesting it has a non-venom function. Strikingly, two additional paralogs have an expression pattern in the early planula also during a very short period and are weakly expressed in stinging cells, while strongly expressed in endodermal cells. This result suggests these two paralogs might represent a "transitional form" between a toxin and a non-venom protein-encoding gene that still present some residual expression in stinging cells. Phylogenetic analysis suggests that the ancestral MACPF was probably a toxin expressed in stinging cells. Such an evolutionary history would provide strong support for the reverse recruitment of a cnidarian toxin for the first time.

Evolved transcriptional responses and their regulation after long-term adaptation of *Bemisia tabaci* to a marginally-suitable host

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Although generalist insect herbivores can migrate and rapidly adapt to a broad range of host plants, they can face significant difficulties when accidentally migrating to novel and marginally-suitable hosts. What happens, at both the genome-wide regulatory and transcriptional levels, if these marginally-suitable hosts must be used for multiple generations before migration to a suitable host can take place, largely remains unknown. In order to study this, we established a multi-generational experimental setup that compared the differences between populations of the whitefly *Bemisia tabaci*, a generalist phloem-feeding species, subjected to cotton (a suitable host) and habanero-pepper (a marginally-suitable host on which the initial survival is 5%). We used reciprocal host tests to find the differences in gene expression and to examine the possible role of DNA methylation in their regulation. Our transcriptomic data revealed that most transcriptional changes in the habanero-pepper adapted population (survival increased to above 60%) were changes in three molecular functions/biological processes: enhanced formation of cuticle structural components, reduced activity of cysteine-type peptidases, mainly cathepsin B proteins that activate plant defenses, and carbohydrate metabolic processes. Our methylation analyses of the DNA of the differentially expressed genes, did not find correlation between the gene's expression levels and direction of change, and their promoters and first exons methylation status. Further studies are required to identify the molecular regulatory mechanism/s that control the distinct transcriptional signature of adaptation to habanero-pepper in *B. tabaci* and test the possible involvement of selection for a subset combination of alleles, complex gene-regulatory networks, molecular chaperon hubs and regulatory microRNAs in the regulation of the process.

Allopatric mimicry in Eurasian vipers?

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Abstract

A basic premise in mimicry theory is that all participants in the mimicry system must be sympatric, as the predator must encounter both model and mimic in order to confuse the two. Though it has been suggested that mimicry may arise between allopatric species through mediation of migratory predators, this question awaits examination. Many species of Eurasian vipers display variations of a dorsal zigzag pattern, which has apparently evolved several times independently as an aposematic signal. We hypothesise that various species of Eurasian vipers participate in an allopatric complex of Müllerian mimicry, mediated by migratory birds of prey. Bird migration, particularly in large soaring species likely to prey on snakes, is not geographically uniform. Rather, migration routes typically circumvent large bodies of water, and are therefore funneled above specific areas that constitute "migration bottlenecks". Hence, while certain species of vipers are exposed only to migratory birds at the ends of their migration routes, other species of vipers are exposed to numerous different species of migratory birds that are funneled above their distribution. We predict that while vipers at the ends of bird migration routes will display regular patterns, vipers at migration bottlenecks will display irregular patterns, comprising different elements displayed by vipers throughout bird migration routes. We intend to analyse and quantify the regularity of patterns belonging to various different species of vipers found throughout Europe, the Middle East and north Africa, and correlate pattern regularity with position along bird migration routes. Here we present preliminary data and discuss their implications.

The role of two cuticular proteins in post-larval development of endoparasitoid wasp *Microplitis mediator*

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Abstract

Microplitis mediator belongs to the endoparasitic wasps from the Braconidae family that have the potential to become a widespread type of biological biopesticide in agriculture. Egg hatching and all larval stages occur inside of the host insects from a range of Lepidoptera agricultural pests. Right before pupation the pre-pupa emerges from the host and ends up in a completely different environment with a range of hazards, such as UV, drought, etc. Our study focused on proteinaceous changes of the cuticle during this challenging time for parasitoid wasp, in particular structural cuticular proteins (CPs) that are an indispensable part of cuticle organization. Our study revealed that only 12 (out of 70) CPs genes were transcriptionally active during late larval stages of *M. mediator*. Among them, the transcription patterns of two CP genes *MmCPR5* and *MmCPR6* coincide with the emergency from the host body and pupation processes. Immunohistochemical analysis showed that these proteins were located within the whole procutile so probably not involved in cuticle specialization. We used dsRNA injection into the parasitized host cavity to reveal the functional role of these genes during the chosen developmental period. The results clearly showed that these two genes were crucial for parasitoid survival right before and after an emergency from the host body. The total number of survived wasps with succesful adult eclosion decreased under 20% compared to 90% of the control group. The ultrastructural analysis showed the decreased thickness and changes in laminae organization in MmCPR5- and MmCPR6-deficient prepupa. The results of the dye penetration test and qRT-PCR of genes involved in cuticle melanization and hardening suggested the disruption of cuticle barrier function in experimental groups. In a conclusion, this study revealed two CPs that are involved in cuticle adaptation to the rapid environmental changes after exiting the protection of host larvae.

Co-option of genetic interaction across different developmental pathways

Judith Wexler and Ariel Chipman

Signaling networks are redeployed across different developmental times and places to generate phenotypic diversity from a limited genetic toolkit. Hormone signaling networks in particular have well-studied roles in multiple developmental processes. In insects, the ecdysone pathway controls critical events in late embryogenesis, such as trachea formation and deposition of cuticle, the timing and type of molts throughout post embryonic development, and even the acquisition of memories in adulthood. While this pathway is absent in the earliest stage of embryonic development in the well-studied *Drosophila melanogaster*, one component of the network, the nuclear receptor *e75a*, is necessary for proper segment generation in the milkweed bug *Oncopeltus fasciatus*. Published expression data from several other species suggests possible conservation of this role across hundreds of millions of years of insect evolution. Previous work also demonstrates a second nuclear receptor in the ecdysone pathway, *ftz-f1*, also plays a role in segmentation in multiple insect species. However, up until this point, no study has investigated the functional relationship between *e75a* and *ftz-f1* in the context of insect segmentation. Here, we use RNAi and in-situ hybridization in the German cockroach *Blattella germanica* to examine the functions, expression patterns, and regulatory interactions of *ftz-f1* and *e75a* in early embryogenesis.

Convergence and Historical Contingency in *E. coli* Adaptation to Prolonged Resource Exhaustion

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Abstract

Escherichia coli are non-sporulating model bacteria that possess an ability to enter the state called Long-Term Stationary Phase (LTSP) which allows them to survive prolonged resource exhaustion. In our laboratory we carry out evolutionary experiments aiming to provide a deeper insight into dynamics of bacterial evolution during LTSP. The data obtained so far suggests that the adaptation of *E. coli* populations is highly convergent since it seems that there is a number of common ways for bacteria to adapt to resource exhaustion. We seek to determine the extent of this convergence and to what degree this phenomenon might be driven by contingency – the dependency of the way bacteria adapt on which mutations they previously acquired. We have identified a number of bacterial subpopulations that descended from common ancestors – lineages. These lineages established in the early time points of the experiment and are defined by different mutations in *rpoB* and *rpoC* loci. The bacteria seem to adapt to prolonged resource exhaustion via soft sweeps with some lineages dying out and others persisting throughout the experiment. We observed similar lineages across independent populations demonstrating alike patterns of mutation acquisition which suggests a strong convergent pattern of adaptation driven by historical contingency.

בס"ד

The effect of assortative mating on gene drive dynamics

Royi Zur

Supervisor: Dr. Gili Greenbaum

Abstract

Gene drive is an emerging biocontrol technology that enables the rapid spread of engineered genes in wild populations by violating the rules of Mendelian inheritance. Because gene drives can severely suppress or eradicate populations within several generations, it has been proposed to use this technology to deal with vector-borne diseases and invasive species. Due to the risks associated with gene drives, mathematical models are the primary method with which the behavior of gene drive designs and strategies are evaluated. However, so far, gene drive models have focused on random mating populations, and have paid little attention to the possibility that non-random mating may affect the dynamics of gene drives. Assortative mating is particularly relevant for gene drive dynamics because there is a possibility that wild-type individuals will be able to distinguish between gene drive individuals and wild-type individuals and consequently avoid mating with them. In such cases, assortative mating may be generated. Under Mendelian inheritance, assortative mating affects the genotype frequencies but not allele frequencies, whereas with non-Mendelian inheritance the change in genotype frequencies may induce changes in allele frequencies. Therefore, assortative mating may affect the evolutionary behavior of gene drives. Here, we present a gene drive model that incorporates assortative and disassortative mating. We formulate a mathematical model of the dynamics and study the equilibrium points and their stability under different scenarios. We find that, in general, assortative mating increases the range of scenarios for which gene drives are driven to loss. On the other hand, we find that disassortative mating increases the range of scenarios leading to fixation of the gene drive allele, as well as to a scenario in which the outcome is frequency dependent, meaning that the gene drive allele can be driven to either fixation or loss depending on the initial condition.