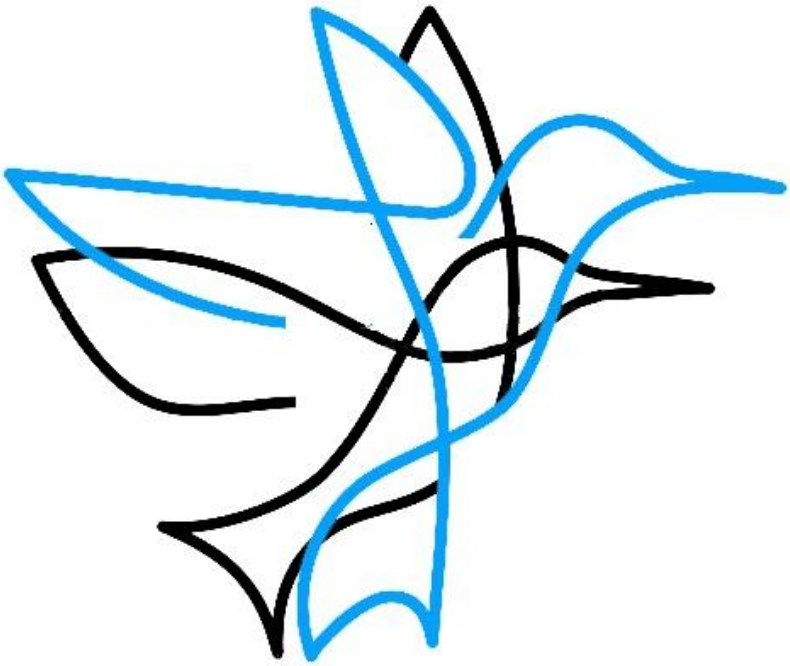
ABSTRACT BOOK

The First Meeting of the Israeli Society for Evolutionary Biology 2019

Dec 11-12, 2019

The Steindhardt Museum of Natural History, Tel Aviv University



Programme overview

Wednesday 11 December 2019				
		Hall	**Room 1**	**Room2**
08:00	09:00	Registration		
09:00	09:15	Opening remarks		
09:15	10:00	**Plenary 1 = Douglas Erwin**		
10:00	10:20	Coffee break		
10:20	12:00	**Genome Evolution (Chair: Tal Pupko)**	**Population Genetics (Chair: Lilach Hadany)**	**Experimental Evolution (Chair: Tzachi Pilpel)**
12:00	13:00	Lunch break		
13:00	13:45	**Plenary 2 = Dieter Ebert**		
13:45	14:05	Coffee break		
14:05	15:30	**Human Evolution & Paleobiology (Chair: Dan Mishmar)**	**Evolution of Behaviour (Chair: Yoav Ram)**	**Virus & Mobile Elements (Chair: Yehu Moran)**
15:30	16:45	**Poster session**		
16:45	17:30	**Plenary 3 = Hanna Kokko**		
17:30		End		

Thursday 12 December 2019				
Hour		**Hall**	**Room 1**	**Room2**
08:00	09:00	Registration		
09:00	09:45	**Plenary 4 = Dan Graur**		
09:45	10:05	Coffee break		
10:05	11:45	**Evolutionary Ecology 1 (Chair: Eran Tauber)**	**Systems Biology & EvoDevo 1 (Chair: Ariel Chipman)**	**Microbial Evolution (Chair: Adi Stern)**
11:45	12:45	Lunch break		
12:45	13:30	**Plenary 5 = Joanna Masel**		
13:30	13:50	Coffee break		
13:50	15:35	**Evolutionary Ecology 2 (Chair: Oren Kolodny)**	**Systems Biology & EvoDevo 2 (Chair: Smadar Ben Tabou de Leon)**	**Phylogeny (Chair: Dorothee Huchon)**
15:35	16:50	**Poster session**		

16:50	17:30	**Society meeting + Poster prizes**
17:30		End

Plenary

Explaining species wide variation: What shapes phenotypic and genotypic diversity?

Dieter Ebert

University of Basel

A key insight of Charles Darwin was that phenotypic variation is the key to understand how evolution works. Genetic and phenotypic variation are now known to be the result of mutation, recombination, gene flow, genetic drift and selection. Understanding the structure of this variation in space and time has become a central topic in evolutionary biology. To understand genetic and phenotypic variation of the crustacean Daphnia, we collected animals from one species from more than 200 populations on 4 continents, assessed diverse phenotypes and sequenced their genome. In my presentation I will show how variation for neutral genetic variation and of diverse phenotypic traits (such as morphology, life history, pathogen resistance, mode of reproduction) can be explained with different evolutionary processes.

Plenary

Developmental novelties in the early history of complex life

Douglas H Erwin

Smithsonian Museum of Natural History

The ability for spatial and temporal differentiation of cell types and the generation of multicellular forms is shared among each of the major holozoan clades: Icthysporea, Filastrea, Choanoflagellates and Metazoa. This supports models for the emergence of aniamals based on a transition from temporal to spatial organization of cell types, enabled in part by a suite of regulatory novelties, including distal enhancers, new types of promoters, regulatory RNA and expansion of transcription factors. Further expansion of regulatory capacity arose at the split between protostomes and deuterostomes (including significant changes in chromatin structuring), and within vertebrates. The developmental evidence suggests that the earliest animals were small with diverse cell types, relying largely on proximal regulatory control. More complex developmental patterning arose independently in bilaterian clades during the Cambrian explosion, enabling larger body size and more complex ecological networks. The independent intercalation of regulatory domains for segmentation, a tri-partite brain, sensory systems and appendages mirrors the well-accepted patter for biomineralization. These developmental novelties and the resulting bodyplans can only be understood in the context of the environmental conditions of the time. In particular, the evidence for widespread, independent co-option and intercalation among bilaterian clades strongly implicates external, environmental controls as drivers.

Plenary

Mutational load and the functional fraction of the human genome: It's complicated

Dan Graur

University of Houston

For the human population to maintain a constant size from generation to generation, an increase in fertility must compensate for the reduction in the mean fitness of the population caused by deleterious mutations. The required increase in fertility due to this mutational load depends on the number of sites in the genome that are functional, the mutation rate, and the fraction of deleterious mutations among all mutations in functional regions. These dependencies and the fact that there exists a maximum tolerable replacement level fertility can be used to put an upper limit on the fraction of the human genome that can be functional (f). In a population in which fitness variation is small, it can be shown that f cannot exceed 10-15%. If fitness variation is large, then the upper limit for f can be higher (up to 50%). Of course, mutational load is not the only load to be considered. The substitutional load and the segregational load also depend on f, and they may greatly reduce the proportion of sites in the human genome that are functional. As I said before, it's complicated.

Plenary

Gentlemanly males? Always, sometimes, never?

Hanna Kokko[1], Xiang-Yi Li, Ignas Safari, Wolfgang Goymann

[1]University of Zurich

As someone who studies sexual conflict for a living, I can attest that the twofold cost of sex (caused by the need for a sexual population to produce males) is the cause of many prolonged headaches in evolutionary biology. However, now I will ask the audience to, for once, not be impressed by how different males are (from females) but how similar their body plans generally are. If sexual selection routinely produces flashy males, why do males and females often differ relatively little in their ecological niches? If males refrained from using what the female needs, that'd be quite gentlemanly – but such cases are subtle and/or rare. I will then discuss a bird species, the black coucal, where females keep harems of males, who do all the parenting duties apart from the actual egg laying.

Plenary

De novo genes and the long-term direction of their subsequent evolution

Joanna Masel

University of Arizona

The phenomenon of de novo gene birth from junk DNA is surprising, because random polypeptides are expected to be toxic. However, the evidence that many gene families arise this way has become overwhelming. To persist, a newborn protein must first do no harm, and second, make itself useful. The first imperative shapes the nature of young genes, biasing them toward high levels of intrinsic structural disorder. In the case of de novo C-terminal extensions, disorder can be increased even prior to "birth", when there is a high rate of error in translation termination; this pre-adapts sequences for later mutational co-option. Older proteins are more ordered, such that there is an arrow of protein evolutionary time spanning billions of years. "More evolved" species with higher codon bias are also more ordered, across comparisons of homologous sequences. At the level of individual amino acids, trends as a function of gene age match those predicted on the basis of mean fitness effect on a random peptide expressed in E. coli. Old genes also have their hydrophobic residues more interspersed along the polypeptide chain, reflecting a gradual shift from primitive to subtle strategies for avoiding protein misfolding in the face of a highly frustrated fitness landscape.

Evolution of Behaviour

The evolution of paternal care: a role for microbes?

Yael Gurevich[1], Ohad Lewin-Epstein, Lilach Hadany

[1]Tel Aviv University

Paternal care is an evolutionary mystery. Despite extensive research, both theoretical and experimental, the reasons for its ubiquity remain unclear. Common explanations include kin selection, suggesting that the benefits to the offspring outweigh the costs to the father's future reproductive success, and limited accuracy in parentage assessment. However, these explanations do not cover the breadth of circumstances in which paternal care has been observed, particularly in conditions of uncertainty in paternity. Many recent studies presented associations between microbes and complex behavioral traits, including anxiety, depression, and autism spectrum disorders. Here we propose that microbes may play a key role in the evolution of paternal care. Using computational models, we demonstrate that microbes associated with increased paternal care could be favored by natural selection. We find that microbe-induced paternal care could evolve under wider conditions than suggested by genetic models. Moreover, we show that microbe-induced paternal care is more likely to evolve when considering paternal care interactions that increase microbial transmission, such as feeding and grooming. Our results suggest that factors affecting the host microbiome, such as antibiotics or specific foods, could also affect paternal behavior.

Evolution of Behaviour

Using cellular automata to study genome evolution

Keith D. Harris

Tel Aviv University

Cellular automata are useful for modelling complex emergent phenomena that are derived from simple components, and their application to biological systems ranges from ecological models to the formation of body patterns in development. However, most of these models employ agents the behaviour of which has a limited range of plasticity. Here I propose a number of cellular automata of increasing complexity in terms of behavioural plasticity, to demonstrate additional applications of cellular automata, in particular to genome evolution. I begin with a simple evolutionary model in which agent behaviour within a two-dimensional space is defined by a finite number of parameters which are under selection; these form behavioural functions which translate environmental inputs to behavioural outputs (e.g. food availability into movement or reproduction). In this model, adaptations are based on random variation of these parameters. Increasing the number of parameters or the complexity of the environment, in terms of food distribution, increases the number of evolutionary steps required to reach fitness optima. It is also possible to map the evolutionary steps to each optima: this process lacks “fitness valleys” given that changes in parameters are linearly related to behavioural outputs. In the next stage, I introduce a pseudo genome by bit-encoding a string representation of parametric data; mutations are no longer graded alterations of behaviour, while rearrangements and deletions can lead to the loss of environmental inputs with severe impact on fitness. The evolutionary landscape of this model consists of discrete states, most of which are unviable. While the probability of mutations increasing fitness is reduced, less evolutionary steps are required to reach fitness optima. In addition, reversible loss-of-function in the pseudo genome can evolve as a behavioural switch, adapting agents to periodic environmental changes. Finally, I replace predefined behavioural functions with sets of basic mathematical operations encoded by the pseudo genome. This increases the depth of fitness valleys while increasing the potential of behaviour coding. Further elaborations of this model, such as allowing behavioural functions to alter the pseudo genome, make it applicable to questions of evolvability and parasitic DNA.

Evolution of Behaviour

Host-microbiome coevolution and cooperative behavior

Ohad Lewin-Epstein[1], Ranit Aharonov, Lilach Hadany

[1]Tel Aviv University

Cooperation is a fundamental behavior observed in all forms of life. However, the evolution of cooperative behavior is intriguing – how can a trait for helping others, while also conferring a cost to the actor, be favored by natural selection? The evolution of cooperation has been widely studied, but almost all theories focused on the cooperating individual and its genes. We suggest a different approach, taking into account the microbes carried by the interacting individuals. Accumulating evidence reveal that microbes can dramatically affect their host wellbeing and behavior. We thus propose that host-microbe coevolution may favor microbes that induce their host to cooperate. Similarly to genes, microbes can be transmitted vertically, from parent to offspring, but differently from genes (in multi cellular organisms) microbes can also transfer horizontally, between interacting hosts. Hence, considering both transmission abilities yield new and interesting results. Using computational modeling we find that microbe-induced cooperation can evolve in a wide range of conditions, including when facing hosts' resistance to the microbial effect. We show that host-microbe coevolution leads the population to a rock-paper-scissors dynamic, that enables maintenance of cooperation in a polymorphic state. This theory may help explain occurrences of cooperation in a wide variety of organisms, including in cases that are difficult to explain by current theories. This study offers a new perspective on the coevolution of hosts and their microbes, and on the role of horizontal transmission in evolution.

Evolution of Behaviour

Crowd wisdom enhanced by costly signaling in a virtual rating system

Ofer Tchernichovski, Lucas C. Parra, Daniel Fimiarz, Arnon Lotem[1] and Dalton Conley

[1]Tel Aviv University

Costly signaling theory was developed in both economics and biology and has been used to explain a wide range of phenomena. However, the theory's prediction that signal cost can enforce information quality in the design of new communication systems has never been put to an empirical test. Here we show that imposing time costs on reporting extreme scores can improve crowd wisdom in a previously cost-free rating system. We developed an online game where individuals interacted repeatedly with simulated services and rated them for satisfaction. We associated ratings with differential time costs by endowing the graphical user interface that solicited ratings from the users with "physics," including an initial (default) slider position and friction. When ratings were not associated with differential cost (all scores from 0 to 100 could be given by an equally low-cost click on the screen), scores correlated only weakly with objective service quality. However, introducing differential time costs, proportional to the deviation from the mean score, improved correlations between subjective rating scores and objective service performance and lowered the sample size required for obtaining reliable, averaged crowd estimates. Boosting time costs for reporting extreme scores further facilitated the detection of top performances. Thus, human collective online behavior, which is typically cost-free, can be made more informative by applying costly signaling via the virtual physics of rating devices.

Evolution of Behaviour

Nocturnal and diurnal Drosophila: insights into the genetics of diurnal preference

Mirko Pegorao, Bengisu Subaşı, Eran Tauber[1]

[1]Haifa University

Most animals restrict their activity to specific part of the day, being either diurnal, nocturnal, or crepuscular. The genetic basis underlying this diurnal preference is largely unknown. Under laboratory conditions, Drosophila melanogaster is crepuscular, showing a bi-modal activity profile. However, a survey of strains derived from wild populations indicated that high variability among individuals exists, including diurnal and nocturnal flies. Using a highly diverse population we have carried out an artificial selection experiment, selecting flies with extreme diurnal or nocturnal preference. After 10 generations we obtained highly diurnal and nocturnal strains. We used whole-genome expression analysis to identify differentially expressed genes between diurnal, nocturnal and crepuscular (control) flies. Excepting one circadian clock gene (pdp1), most differentially expressed genes were associated with either the clock output (pdf, to) or input (Rh3, Rh2, msn). This was congruent with behavioural experiments indicating that both light masking and the circadian pacemaker are involved in driving nocturnality. The diurnal and nocturnal selection strains provide us with a unique opportunity to understand the genetic architecture of diurnal preference.

Evolutionary Ecology 1

The evolution of floral host preference in longhorn bees of the genus Eucera (Hymenoptera, Apidae, Eucerini): is association with pollen from bee-flowers advantageous?

Achik Dorchin[1], Dana Langgut, Frank Neumann, Nicolas Vereecken

[1]Museum of Natural History

Flowers with specialised pollination mechanism with concealed pollen, such as in the Fabaceae and Lamiaceae, are pollinated primarily by bees and often referred to as 'bee flowers'. While some long-tongue bees show preference to bee flowers with restricted pollen, other species specialize on pollen accessible flowers or are floral generalists. Recent studies suggested that pollen is not an easy-to-use resource, such that changes in floral host preference would strongly depend on physiological and neurological constraints of bees. It can be therefore hypothesised that exploitation of restricted pollen from bee flowers consisted a significant event in bee evolution, opening a new ecological niche that has resulted in increased diversification of the associated bee lineages. So far, no empirical evidence for increased diversification rates has been demonstrated in bees in association with exploitation of restricted pollen from bee flowers. This study uses phylogenetic inference and determination of pollen grains collected by ca. 390 females from ca. 80 species to trace the evolution of floral host preference in longhorn bees of the widely distributed genus Eucera. Based on the pollen spectrum collected, each species is assigned to one of the floral preference categories: 1. pollen accessible flowers; 2. pollen restricted flowers; or 3. generalist with regard to pollen accessibility. Reconstruction of ancestral floral preferences using Bayesian methods show that early diverging Eucera lineages are mostly associated with accessible pollen whereas more recently diverging lineages are capable of utilising both accessible and restricted pollen or prefer restricted pollen. We use both character state dependent speciation-extinction (SSE) approach, and a complementary nonparametric method to test the hypothesis that switching from utilising accessible pollen to restricted pollen from bee flowers has increased the rate of diversification in Eucera bees.

Evolutionary Ecology 1

Evolution of plant defenses along an invasion chronosequence

Michal Gruntman[1], Udi Segev, Gaetan Glauser, Katja Tielbörger

[1]Tel Aviv University

The success of invasive plants has often been attributed to rapid evolution, and in particular an evolutionary shift in resource allocation from herbivore defense to increased size, which could be selected for due to release from native enemies at the introduced range. However, such evolutionary processes can take place not only between the native and invasive ranges but also within the invasive range over time. In this study we examined the potential for post-invasion evolution in herbivore resistance in the invasive plant Impatiens glandulifera, by comparing plants from its native populations and from populations across its invasion chronosequence. Results of a common-garden experiment revealed that plants from native populations or older populations within the invasive range show greater resistance to a generalist herbivore, coupled with greater production a secondary defense compound. Results from a field survey suggested that older populations within the invasive range incur greater attack rates from local herbivores compared to recently-established populations. These findings support the idea that the selection pressure of enemy release at the introduced range might attenuate over time, leading to the evolutionary recovery of enemy resistance.

Evolutionary Ecology 1

Anti-herbivory plant coloration

Simcha Lev-Yadun

Haifa-Oranim

Plants use many types of defensive plant coloration: camouflage, aposematism, undermining insect herbivore camouflage, masquerade, dazzel coloration, Batesian and Mullerian mimicry, mimicry of animals, signalling that leaves are going to fall. In certain cases the visual defense operates simultaneously with chemical signaling. Experimental data about herbivore responses are accumulating slowly, mostly because this is a new scientific arena, therefore challenging scientists that wish to discover new scientific territories.

Evolutionary Ecology 1

Newly-established brown widow spiders are more dispersive and less fecund across multiple invasion fronts

Monica A Mowery[1], Yael Lubin, Andrew C Mason, Maydianne CB Andrade

[1]Ben-Gurion University of the Negev

As invasive species spread around the world, understanding the factors underlying invasion success has become increasingly important. Using an evolutionary perspective to examine biological invasions, we investigated how selection on phenotypic traits changed over population establishment time. Here, we studied how behaviour and morphology have evolved in invasive populations of brown widow spiders (Latrodectus geometricus) with known establishment dates. Using temporal and spatial variation across four populations from the United States and four populations from Israel, we tested predictions about changes in trait distributions over establishment time. We predicted that selective filters during the invasion process would result in larger, more fecund, more dispersive, and more exploratory spiders from recently-established populations, and that if tradeoffs occur, they would favour dispersal at the expense of fecundity and size at the invasion front. After common-garden lab rearing, we measured dispersal tendency, web building behaviour, size, and reproductive output. We found that recently-established invasive spiders dispersed more quickly and with higher frequency than spiders from longer-established populations. Spiders at the invasion fronts were larger, yet had lower fecundity than expected based on body size. However, despite lower fecundity, invasion-front spiders showed more plasticity in egg investment, consistent with predictions of higher plasticity in newly-invasive populations. Across considerable environmental heterogeneity in the eight populations studied on two continents, we found consistent patterns in dispersal propensity and speed depending on population history. These patterns of behaviour and morphological differences, seen across independent invasion fronts, suggest that fast dispersal and larger size promote invasion success and are under positive selection in invasive populations. We infer that common traits may underlie success for species spreading past the point of introduction. This work expands our knowledge of how evolutionary processes affect the spread of invasive species through selective filters in the invasion process.

Evolutionary Ecology 1

Metaplasticity: fine tuning and curbing the costs of plasticity

Ariel Novoplansky

Ben-Gurion University of the Negev

Organisms exhibit a plethora of plastic traits to cope with their ever changing environmental challenges. However, the complexity and costs of plasticity suggest the involvement of higher-order metaplastic controls and coordination of plastic responsiveness. To use a known example, while the shade avoidance syndrome (SAS) in plants is a manifestation of multiple first-order phenotypic plasticities, the circumstances, timing and magnitude of these responses are expected to be further modulated by higher-order metaplasticities reflecting the specific advantages and costs of SAS under specific conditions. Accordingly, metaplastic control may rely on a variety of regulatory genes and morphogenetical contingencies that reflect the organism's evolutionary background, maternal and concurrent physiological state, ontogenetic stage, size, phenology, and various external cues correlated with concurrent and anticipated stresses, disturbances and biotic interactions. Studying the functional implications and controls of higher-level plasticities is expected to shed light on the functional tradeoffs involved in the manifestation of multiple plastic traits and their evolutionary implications.

Evolutionary Ecology 1

Less fit Lamium amplexicaule plants produce more dispersible seeds

Eyal Zinger[1], Ariel Gueijman, Uri Obolski, Yoav Ram, Eliya Ruby, Mor Binder, Nivi Yechieli, Nir Ohad and Lilach Hadany

[1]Tel Aviv University

Theory predicts that less fit individuals would disperse more often than fitter ones (Fitness Associated Dispersal, FAD hypothesis). To test this prediction under laboratory conditions, an entire life cycle of Lamium amplexicaule plants and the preferences of its dispersal agent, Messor ebeninus ants, were tracked. Characterization of individual L. amplexicaule plant revealed high variability in spot cover on the surface of the seeds, where less fit plants produce “unspotted seeds” (see Fig. 1 in Introduction). Unspotted L. amplexicaule seeds showed higher variation in germination time and lower germination rate. Moreover, M. ebeninus ants preferably collected these unspotted seeds. Our results show that low fitness L. amplexicaule plants produce seeds with higher potential for dispersal, supporting the FAD hypothesis in a plant-animal system.

Evolutionary Ecology 2

Hydrodynamic constraints shape the performance landscape of the feeding mechanism of fish larvae during the critical period

Victor China

Eilat

Larval fishes experience extreme mortality rates, with up to 90% of a cohort perishing within days after starting to actively feed. Over a century ago, Hjort (1914) famously attributed this “critical period” of low survival to the larvae’s inability to obtain sufficient food. However, no consensus has emerged regarding the role of different mechanisms in determining larval mortality, and specifically in explaining the larvae’s inability to obtain food. In my study, I explored the role of hydrodynamics in structuring predator-prey interactions. Using feeding experiments and modeling, as well as high-speed video observations of larval feeding strikes, I found that successful feeding strikes were characterized by Reynolds numbers that were an order of magnitude higher than those of failed feeding strikes. I also found that the pattern of increasing strike success with increasing age was driven by the ontogeny of traits that facilitate the transition to higher Reynolds numbers. Modeling the performance landscape for larval feeding revealed that larvae climb towards a peak of higher performance as they mature, and that the landscape is not age-specific. Concomitantly, constraints on the kinematics that are associated with successful feeding strikes relax throughout ontogeny, resulting in older larvae displaying a wider kinematic repertoire. My study demonstrates how understanding an organism’s hydrodynamic environment promotes our understanding of ecological processes; and how large-scale ecological patterns can be governed by small-scale physics.

Evolutionary Ecology 2

Male effects on the evolution of monandrous mating strategy in moths

Ally Harari[1], Yarden Dodi, Yftach Golov, Hadass Steinitz

[1]Volcani

In most sexual breeding species females are polyandrous and thus most females mate more than once, whereas in the minority of species female are monandrous, whereby most females in the species mate once only. Males in both mating systems typically mate more than once. During mating, male moths transfer to females a spermatophore full with nutrients and two types of sperm, eupyrene, the fertilizing sperm that is produced in limited amounts, and apyrene, a non-fertilizing sperm, that is produced in high numbers and is assumed to have a role in sperm competition. Testing the costs and benefits of remating in the monandrous moth Lobesia botrana, we applied strong selection for polyandry, producing 70% of remating females, vs 10% of remating in the typically monandrous females in the wild type. After a few generations we measured the sperm content in testes of virgin and mated males and found that sons of polyandrous females have an increased amount of the apyrene sperm and they transferred to females more of the apyrene sperm than sons of monandrous females. Searching for a cost imposed on polyandrous females and males, we found that polyandrous females suffer reduced fecundity relative to monandrous females, and sons of polyandrous females die faster than sons of monandrous females. Testing male mate choice of “monandrous” and “polyandrous” males we found that the two male types do not differ in their mate choice, preferring virgin monandrous females over mated polyandrous females and mated polyandrous females over mated monandrous females.

Evolutionary Ecology 2

Using performance landscapes to understand adaptive diversification within fishes

Roi Holzman[1], Karin Olsson, Christopher Martin

[1]Tel Aviv University

The complex relationship between form and function provides the foundation for the generation of organismal diversity. Selection acts directly on performance, which is the product of interacting phenotypic components. Thus, the ability to predict how multiple phenotypic traits interact in determining performance is key to understanding the evolution of complex functional systems. Here, we demonstrate how performance landscapes, which map the performance consequences of different phenotypic combinations, can be used to understand adaptive evolution of suction feeding fishes. A hydrodynamic model of the suction forces exerted on the prey allows us to explore the complex performance space for aquatic predator-prey interactions, and enables us to predict prey capture performance for any given phenotype. Using this model, we generated performance landscapes for three prey types that pose different challenges to the predators, namely planktonic prey that senses the hydrodynamic disturbance generated by the predator, visually oriented prey that escapes the looming predator and attached prey that clings to its holdfast. We explored the topography of the multidimensional performance landscape and determined it to be rugged with multiple local performance peaks. We used the landscape to generate a-priori hypotheses regarding the position of extant species relative to the theoretical optima in this performance space, which we tested by mapping prey-capture kinematics of fishes from four radiations onto the three generated performance landscapes. Whereas previous research generally focused either on studying phenotypic diversification using morphological traits, or on the biomechanical basis of performance, we integrate these approaches using a detailed mechanistic model to explore how a highly nonlinear and multidimensional performance space shapes organismal diversity in suction feeding fishes.

Evolutionary Ecology 2

Social inheritance shapes spotted hyena social networks and influences offspring longevity

Amiyaal Ilany[1], Kay Holekamp, Erol Akcay

[1]Bar-Ilan University

The structure of animal social networks influences survival and reproductive success, as well as pathogen and information transmission. However, the general mechanisms determining social structure remain unclear. Using data on 73,767 social interactions among wild spotted hyenas over 27 years, we show that a process of social inheritance affects how offspring relationships are formed and maintained. The relationships of offspring with other hyenas are similar to those of their mothers, but the degree of similarity depends on maternal social rank. The strength of mother-offspring relationship affects both social inheritance and offspring longevity. These results confirm the hypothesis that social inheritance of relationships plays an important role structuring animal social networks.

Evolutionary Ecology 2

Testosterone is associated with male and female copulation success in opposite ways in wild rock hyrax

Koren, L.[1], Weissman, Y., Shnitzer, I., Beukboom, R., Bar Ziv, E., Demartsev, V., Barocas, A., Ilany, A. and Geffen, E.

[1]Tel Aviv University

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

Evolutionary Ecology 2

Stress as an adaptation: Does experimental cortisol supplementation affect predation risk assessment in foraging gerbils?

Franklin Sargunaraj[1], Burt P. Kotler, Justin R. St. Juliana and Nadja Wielebnowski.

[1]Ben-Gurion University of the Negev

Background: Organisms are well known for trading off food and safety. We have previously shown for Allenby's gerbil (Gerbillus andersoni allenbyi) that the intensity of this tradeoff changes with energetic state (Kotler et al., 2004) and the fecal levels of corticosteroid metabolites in desert rodents change in response food availability, competitor density, and moonlight (St. Juliana, 2005). This suggests that stress hormones play an adaptive role in managing foraging decisions. Hypothesis: In gerbils, we predicted that higher levels of the exogenous stress hormone cortisol would increase their marginal valuation of energy (MVE) and their vigilance. In general, it will mediate responses to slowly changing factors associated with food and safety, but not to rapidly changing ones. Methods: In order to test these hypotheses, we manipulated cortisol levels in a set of gerbils by injecting each subcutaneously with 21-day slow-release 0.01 mg cortisol pellets and compared their foraging behavior with a control group. The experiment was conducted in a large outdoor vivarium where we could simulate features of the gerbils' desert environment, manipulate the presence of an owl (i.e., a rapidly changing factor), and quantify patch use over the course of a lunar cycle from new moon to full moon (i.e., a slowly changing factor). Foraging behavior was quantified by giving-up densities (GUD; the amount of food left in a resource patch after foraging), time allocation, and harvest rate curves in artificial foraging patches (seed trays). Results: Supporting our notion, GUDs were affected by an interaction of cortisol treatment and moon phase, and not by the interaction of cortisol treatment and owl presence. Gerbils implanted with cortisol foraged longer, but harvested food more slowly (suggesting greater vigilance and apprehension) than placebo-treated gerbils. This reaffirms that glucocorticoids affect energy acquisition, and provides a physiological context to explain how foragers manage risk and the tradeoff between food and safety.

Evolutionary Ecology 2

The combined effect of host and food availability on optimized parasitoid life history traits based on a three-dimensional trade-off surface

Michal Segoli[1] and Eric Wajnberg

[1]Ben-Gurion University of the Negev

The reproductive success of many insects is considered to be limited by two main factors: the availability of mature eggs to lay (termed egg limitation) and the time to locate suitable hosts (termed time limitation). High host density in the environment is likely to enhance oviposition opportunities, thereby selecting for higher investment in egg supply. In contrast, a shortage of food (e.g., sugar sources) is likely to increase the risk of time limitation, thereby selecting for higher allocation to initial energy reserves. To our knowledge, the combined effect of host and food availability on these optimal life history allocations has never been investigated. We thus modeled their simultaneous effects on a three-dimensional trade-off between longevity, egg number, and egg size, while focusing on insect parasitoids. The model was based on Monte Carlo simulations coupled with genetic algorithms, in order to identify the optimal life history traits of a single simulated parasitoid female in an environment in which both hosts and food are present in varying densities. Our results reproduced the simple predictions described above. However, some novel predictions were also obtained, especially when specific interactions between the different factors were examined and their effects on the three-dimensional life history surface were considered. For example, investment in egg number increased with host density, but this was mostly pronounced when food sources were abundant. Similarly, investment in longevity was negatively affected by food availability, but this was only apparent when hosts were abundant. Egg size was the highest under conditions of low host availability and high food availability, where neither investment in eggs number or longevity was strongly needed. The work sheds light on a long-lasting debate regarding the relative importance of time vs. egg limitation in determining insect life history traits and highlights the complexity of life history evolution, where several environmental factors act simultaneously on multiple traits.

Experimental Evolution

Exploring the balance between mutations and horizontal gene transfer during bacterial adaptation.

Shai Slomka De Oliveira, Itamar Francoise, Tammy Biniashvili, Gil Hornung, Yitzhak Pilpel and Orna Dahan[1] These authors contributed equality

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Genetic variation is a driving force in evolution. Living organisms are equipped with various mechanisms to generate genetic diversity. Microbes evolve by mutations, and through acquisition of foreign DNA, a process known as horizontal gene transfer (HGT). Bioinformatic examinations of genomes reveal remnants of HGT events but they typically do not reveal the evolutionary processes that led to their acquisition and fixation. Here we aim to explore the dynamics of HGT and to compare its relative contribution to that of mutations, in bacterial evolution. We evolved several populations of naturally competent Bacillus subtilis, either with or without foreign DNA from diverse microbial species. Sequencing of evolved populations reveled extensive acquisition of foreign DNA. HGT occurred only from relatively close Bacilli but not from more remote microbes. HGT occurred in bursts, whereby a single bacterial cell appears to have acquired dozens of fragments at once. Acquired segments tend to be clustered in integration “hot spots”. In addition to HGT, genomes also acquired local mutations. Many of these local mutations occurred within, and seem to alter, the sequence of flagella proteins. As for dynamics of evolution, we found that clones that appear earlier in evolution contained only local mutations. Finally, we show that while some HGT fragments could be neutral, others are adaptive and accelerate evolution.

Experimental Evolution

Recovery from costs associated with adaptation will often lead to loss of adaptive alleles once selection in their favor stops

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Bacteria can rapidly adapt to almost any imaginable selective pressure. Many rapid adaptations display antagonistic pleiotropy, meaning that while they are adaptive to certain bacterial traits they harm others. Understanding whether such costly adaptations will tend to persist once selection in their favor stops is important for predicting the long term consequences of rapid adaptation. Bacteria can alleviate many of the harmful effects of adaptive alleles through the acquisition of compensatory mutations. Such compensatory mutations can occur at various different loci and therefore likely occur more frequently than reversion mutations. It is thus thought that costly adaptations will more likely persist, due to their deleterious effects being compensated for, rather than revert back to their original form. Here we provide evidence suggesting that this may often not be the case. First, we show that bacterial populations can maintain high levels of standing genetic variation, even as they adapt to strong and prolonged selective pressures. This leads to rapid loss of costly adaptations, once these are no longer favored, through fluctuations in genotype frequencies. Furthermore, during adaptation, mutators, defective in their mismatch repair often emerge. We show that in contrast to non-mutators that tend to recover from costs of adaptation through the acquisition of compensatory mutations, mutators tend to recover through reversion mutations. This leads to the loss of costly adaptive alleles, even when these are fixed across an entire population.

Experimental Evolution

EVOLUTION OF RECOMBINATION FEATURES: NUMERICAL MODELS AND EXPERIMENTS WITH DROSOPHILA

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Recombination's omnipresence in nature is hard to explain. Numerous hypotheses highlight its evolutionary advantages which may outbalance its drawbacks. The plausibility of these hypotheses is confirmed in theoretical models, although it remains unclear to what extent the model requirements hold in nature. Yet, recombination does not just exist – it displays a set of essential features, such as crossover interference, sex differences in recombination rates (RR), ecological plasticity, etc. Some of them (e.g., interference and sex differences) are well recognized, while others (e.g., condition-dependence) still lack empirical evidence. In our experiments with Drosophila, directional selection on an adaptive trait, desiccation tolerance, led to indirect selection on higher RRs and relaxation of positive crossover interference (up to the appearance of negative interference), thereby further increasing the number of crossover events. Additional tests on the same material showed ecological plasticity of both RRs and crossover interference with respect to desiccation stress. Moreover, desiccation-induced changes in both parameters were to some extent modulated by desiccation tolerance, a measure for genotype fitness: fitter genotypes showed lower, if any, reactivity of recombination. Our numerical models confirmed that condition-dependent (CD) recombination, dependence on either ecological stressors or genotype fitness, can be evolutionary advantageous in diploids. This holds for cyclical selection, mutation-selection balance, and Red Queen dynamics caused by antagonistic interspecific interactions. Under CD recombination, population mean RRs slightly departed from the state of independence, leading to an interference-like effect. However, in general, the revealed evolutionary advantage of CD recombination appeared robust to crossover interference. Not rarely, CD recombination was favored even when any non-zero constant RR was rejected, making condition dependence an "evolutionary rescue" for recombination. In our simulations, recombination-modifier allele for the favourable RR (at least in situations with constant recombination strategies) tended to become dominant along the trajectory. Sometimes, the selected system demonstrated two alternative stable states, differing both in favourable RR and in dominance of the corresponding recombination-modifier allele. At that, what affected the 'attraction' potential of these states was crossover interference.

Experimental Evolution

An ecological tragedy: The collection of pre-parasitized prey by a potter wasp

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Females of the solitary wasp Delta dimidiatipenne collect lepidopteran caterpillars from vegetation and place them inside a cell along with a freshly laid egg for their offspring to feed on. It has been observed that occasionally, D. dimidiatipenne collects caterpillars that are already parasitized by another parasitoid wasp of the genus Copidosoma. In these cases, Copidosoma larvae feed on the caterpillar host, depleting the food for the D. dimidiatipenne offspring. This raises the question why do D. dimidiatipenne wasps collect prey that appears to be sub-optimal for feeding their young? To address this question, we surveyed newly built nests of D. dimidiatipenne in the Negev Desert collecting their content, while also collecting caterpillars from the nearby vegetation. Under laboratory conditions, D. dimidiatipenne eggs were placed with a manipulated number of prey inside vials, in order to observe the development of the potter wasps in relation to the number of prey provided and their parasitism status. We found that the presence of parasitized caterpillars inside the vial reduced the chance of the potter wasp completing their development, as well as the weight of the emerging adults, suggesting a high cost for the collection of parasitized caterpillars in term of offspring survival and fitness. In the field we found that the proportion of parasitized caterpillars inside potter wasp nests (~52%) was higher than that of caterpillars on nearby vegetation (~29%), possibly indicating a biased collection of parasitized caterpillars by potter wasp females. One possible explanation may be that the potter wasps prefer parasitized caterpillars as they are larger. Indeed we found that parasitized caterpillars had a higher mass than non-parasitized ones, which could falsely advertise a good nutritional value. We will next conduct choice experiment to directly test the ability of potter-wasps to discriminate between parasitized and non-parasitized caterpillars.

Experimental Evolution

Establishing an experimental-evolution-based method for understanding an incomplete penetrance mechanism in a model of C. elegans.

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A wide range of diseases manifest a not-fully-penetrant phenotype; however, the mechanism of the phenomena is still not clear. Incomplete penetrance of mutation is characterized by variability of the phenotypes, despite identical mutant alleles. Understanding the mechanism of incomplete penetrance is important to the prediction of disease onset and adjustment of treatments for those carrying not-fully-penetrant mutations. We believe that evolution can abolish sick phenotypes. Furthermore, examination of evolved Vs un-evolved populations will reveal a compensatory mechanism. For in house examination we employed adaptive experimental evolution in order to establish it as tool for understanding mechanisms of not-fully-penetrant mutations. More specifically, I used Caenorhabditis elegans with a nonsense mutation in C- terminal of the daf-18 protein, leading to an incompletely penetrant phenotype of starvation non-durability. To reduce the mutation effect, daf-18 impaired populations were subjected to strong selection for starvation resistance. Phenotype screening showed a fluctuating penetrance rate over the first sixty generation with a subsequent stabilization of low penetrance rates. Genotyping revealed several possible compensatory mechanisms. To characterize these mechanisms, we plan to perform DNA sequencing, expression and methylation analysis with subsequent integration and validation of the results.

Experimental Evolution

Transgenerationally inherited information regulates reproductive strategies in *Caenorhabditis elegans.*

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Worms use heritable small RNAs to transfer information across generations, and epigenetic inheritance was hypothesized to be advantageous under environmental challenges. As most inherited responses following stress are transient, the ability of epigenetic inheritance to impact the course of long-term evolution is unclear. In the present study, using the androdiecious nematodes C.elegans, we found that inherited epigenetic information can directly affect the genetic composition of the population by influencing the worms' mode of reproduction (selfing Vs. outcrossing). We found that mutants impaired in epigenetic factors are more attractive to males. We show in a competitive scenario that attraction of males is translated into higher mating rates among "attractive" hermaphrodites. Enhanced attractiveness was induced also in the wild-type progeny of mutated animals, indicating that this process is regulated transgenerationally. Moreover, hermaphrodites grown under a stress, as well as their descendants grown under normal conditions for >3 generations, were more attractive, indicating that environmental challenges can affect this phenotype transgenerationally. Conditions that generated attractive hermaphrodites consistently increased the incidence of males in the population, boosting the opportunities for outcrossing. While it is established that sexual mating is adaptive in changing environments, our findings suggest that disturbances in inherited epigenetic information enhance the chances for outcrossing under stressful conditions, and highlight a direct influence of transient epigenetic processes on the genetic structure of the population.

Genome Evolution

The role of tRNAs in the cellular proliferation state regulation

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The dichotomous choice of metazoan cells between proliferation and differentiation states is critical for the formation of multicellular organisms. Regulation of proliferation and cell cycle arrest is crucial for development, tissue homeostasis, and malignancy prevention. In this work, we uncover tRNAs that have a regulatory role in governing the proliferative state of human cells. Using the CRISPR-Cas9 technique, we succeeded to knockout tRNA genes. We identified those that caused a significant reduction in the proliferation capability and fitness of fast-growing cells (i.e., "pro-proliferation" tRNAs). In comparison, slow-growing cells were sensitive to the knockout of a partially distinct set of tRNAs (i.e., "pro-differentiation" tRNAs). Moreover, we found that CRISPR editing of the "pro-proliferation" tRNA genes in fast-growing cells significantly changed the cellular tRNA pool, while manipulation of "pro-differentiation" tRNA genes in the same cell type resulted in only a mild change of the cellular tRNA pool. As tRNAs are known for their essentially in fast dividing cells, less is known about their role in non- dividing cells. We are currently intrigued to identify tRNAs that are crucial for the transition from proliferation to cell cycle arrest. In particular, we are interested in two types of cell cycle arrest states- quiescence and senescence. We will sequence the tRNA pool of arrested cells to point out the tRNAs that may promote the transition between the cell cycle states. Then, using our CRISPR-Cas9 methods for tRNA knockout, which we will apply on the arrested cells, we will investigate whether the expression explains the essentially of the tRNA candidates to the transition process. While we previously showed a correlation between the tRNA pool and codon usage biases in differentially expressed genes to the proliferative state of the cell (Gingold et al., 2014), this current project highlights the role of specific tRNAs in maintaining and determining the cellular state of human cells. We believe that these tRNAs may hold as a basis for new therapeutic strategies against tumorigenesis and aging-related diseases.

Genome Evolution

The evolution of short inverted repeats

Einat Hazkani-Covo

OpenU

Inverted repeats (IRs) are sequences with internal symmetry that form non-canonical DNA structures and can induce genome instability. Diverged IRs frequently undergo template switches, in which one arm of the repeat serves as a template for synthesis of the second arm resulting in erasing of variation between arms. In contrast to other mechanisms that resulted in correction of IR arms during evolution, the evolutionary impact of template switching was previously neglected. If template switching occurs in genomes, then we expect it to contribute to the correction of imperfect IRs to perfect ones, resulting in the conservation of IRs through evolution. In addition, Template switching is a non-conservative mutation mechanism that introduces multi nucleotide mutations at once. Thus, it has the potential to introduce functional changes into genomes. Our analysis shows that short IRs are conserved during evolution of Escherichia coli and Saccharomyces cerevisiae, supporting the model of IR arm corrections by template switching. Evolution of short IRs also introduces multiple changes into proteins.

Genome Evolution

Biased Evolution in RNA Viruses

Talia Kustin[1] and Adi Stern

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RNA viruses are among the most prevalent agents of diseases in animals and are extremely genetically diverse. Here we set out to test whether there are common evolutionary features that characterize RNA viruses and found that most RNA viruses bear a skew in their nucleotide composition, manifested as highly Adenine rich ("A-rich") coding sequences. This leads to two hypotheses: (a) A-rich coding sequences have some evolutionary advantage and thus selection acts to preserve A, (b) A-richness is merely a reflection of the mutation rate that is biased towards A. To answer this question, we constructed a dataset denoted as phyVirus, which contains ~50,000 sequences spanning a diverse set of RNA virus families, and phylogenetic trees of related sequences. Evolution along a phylogenetic tree reflects two processes: mutations that occur during viral replication, and selection operating on these mutations. Our main challenge was to separate these two processes and tease out the role of selection from mutations. To this end we devised a metric that contrasts between the rate of evolution at the tips of a phylogenetic tree, where selection is relaxed, versus the rate of evolution at the internal edges of the tree. Our results show that in the Picornaviridae, Coronaviridae and Paramyxoviridae viral families selection towards A manifests as A-richness in the coding sequence; in other families such as Orthomyxoviridae and Flaviviridae, lack of selection points at skewed mutation rates as the reason for the A-richness. Surprisingly, in HIV that displays the most profoundly A-rich genome (30-40%), we discovered selection against A throughout the phylogeny coupled with high mutation rate towards A. Our interpretation for these results is that HIV coding sequence has become over-saturated with A due to a strong bias of the HIV reverse transcriptase, to the point where any additional A is selected against. We further suggest that the mutational bias towards A may be related to the cellular abundance of ATP, a statement that merits further research. Our research sheds light on the processes that shape viral genomes and affect their long-term evolution.

Genome Evolution

Metabolic heterogeneity in pancreatic Beta cells: Single cells Mitochondrial transcript heterogeneity as a model

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Mitochondria plays a significant role in cellular metabolism and energy production via the oxidative phosphorylation system (OXPHOS), especially in pancreatic beta cells. Several distinct subpopulations of beta cells have been proposed, but only little is known about the metabolic heterogeneity across single beta cells in terms of mitochondrial DNA (mtDNA) gene expression. Here, we analysed single cell RNA-seq experimental data from four studies, containing 1952 alpha and beta cells from human type-2-diabetes mellitus (T2DM) and healthy individuals, as well as 718 beta cells from postnatal and adult mice. Unbiased cluster analysis revealed two distinct beta cells populations, divided according to their mtDNA gene expression in all studied individuals regardless of health status. Such sub clusters also notably differed in the mt-RNA mutational repertoire. Coexpression analysis uncovered consistent association of higher mtDNAgene expression with both insulin gene expression and with nuclear DNAencoded OXPHOS subunits. Finally, the distinct beta cells population divergence was also found in mice, thus supporting evolutionary conservation of the phenomenon. Our observations suggest new insight into the cellular mitochondrial regulatory heterogeneity of mammalian pancreatic beta islets.

Genome Evolution

A shift in tRNA modifications and abundance during T-cell activation

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The abundance of available transfer RNAs (tRNA) in a cell determines the efficiency, throughput, and accuracy of conversion of the protein-coding transcriptome into the proteome. We have previously identified a differential codon usage in proliferative cancerous cells and arrested/differentiated cells, which is coordinated with changes in the tRNA pool. Does normal programmed proliferation differs from cancerous proliferation? T-cells activation is a non-cancerous cell proliferation process, which is characterized with massive clonal expansion. We analyzed the transcriptome from naïve mice T-cells and during the activation process. We uncovered a striking difference in translation demand for certain codons. In parallel, we measured and analyzed tRNA expression changes in those cells using a tRNA deep sequencing approach. This method allow us to measure both the tRNA expression levels and certain post-transcriptional modification based on reverse transcription failures. We have found that changes in tRNA expression result in higher translation efficiency of the differentially expressed genes in the proliferative state. We further found that two types of tRNA modifications are reduced dramatically during T-cells activation. The two particular tRNA modifications, Wybutosine and ms26A, are known to encode highly slippery codons and to be involved in ribosome frameshift (FS) prevention. Governing the FS rate might play a role in HIV infection cycle due to programmed FS in the gag-pol protein. We used fluorescent FS reporter to validate the connection between the modification levels and FS rate. The changes in tRNA expression and modifications uncover a layer of translation regulation during the process of immune-cells clonal expansion.

Genome Evolution

Insights into the evolution of Myxozoa mitochondrial genomes

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The Myxozoa comprise a class of cnidarian parasites that encompasses over 2,400 species. The phylogenetic relationships among myzoxoans remain highly debated, due to both a lack of informative morphological characters and a shortage of molecular markers. The use of mitochondrial genomes has been proposed for the study of myxozoan relationships due to their richness of informative characters at the nucleotide, amino acid, and gene organization levels. However, only six myxozoan mitochondrial genomes have been sequenced to date, belonging to two closely-related genera: Enteromyxum and Kudoa. Here we present the complete mitochondrial genome sequence of five members of the genera Myxobolus, Theohanellus and Sphaeromyxa, assembled from Illumina and Nanopore reads. Unlike Kudoa and Enteromyxum, which possess partitioned mitochondrial genomes, the five mitochondrial genomes were encoded on a single circular chromosome. Only five protein-coding genes could be recognized in all the myxozoan genomes: cox1, cox2, cytb, nad1, and nad5. We also found that both the Myxobolus and Thelohanellus species share unknown open-reading frames. Our phylogenetic reconstructions based on conserved mitochondrial genes agree with previously published trees based on the 18S rRNA gene. Our findings confirm that mitochondrial sequences offer a useful tool for the identification of myxozoan species, and that they complement the phylogenetic inferences based on 18S rRNA. The results strengthen the view that the ancestral mitochondrial genome of myxozoan was encoded on a single circular chromosome; and, therefore, that its genome fragmentation is a derived state.

Human Evolution & Paleobiology

Human Social Evolution: Self-domestication or self-control?

Dor Shilton and Mati Breski[1]

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The human self-domestication (HSD) hypothesis suggests that since humans share several traits common to many other animal domesticates, they have gone through a similar process of selection against aggression. However, there are also significant differences between anatomically modern humans (AMH) and domesticates – most importantly, the human increase, rather than reduction, in brain size. Seeking to account for both similarities and differences, we suggest that selection for socially-mediated emotional control and plasticity underlies human social evolution. We highlight two more crucial differences between AMH and domesticates, besides brain size and controlled aggression: humans' co-dependency and their cumulative cultures. The former has made the social, gene-cultural evolution of humans more analogous to that of other ultra-social mammals than to the evolution of domesticates. The latter has led to the emergence of uniquely-human cultures that extended the emotional control of hominines and reshaped their social-cognitive emotional profile. We propose a staged account for the cultural evolution of emotional control and social motivation in humans. The first stage, which followed the emergence of mimetic communication, the beginnings of musical engagement, and mimesis-related cognition, required socially-mediated control of emotions and was accompanied by the new social emotions. The second stage followed the emergence of language and full-fledged musical engagement, when individuals began to instruct the imagination and engage the emotions of their interlocutors, and thus began to rely even more extensively on emotional plasticity and culturally learned emotional control.

Human Evolution & Paleobiology

Why did Moderns replace Neanderthals and not vice versa? And what took them so long?!?

Oren Kolodny[1] and Gili Greenbaum

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Great attention and heated debate have been directed towards the causes of the Neanderthals' rapid replacement across Europe by Modern humans between 50,000-40,000 years ago. Less attention has been directed towards an even more intriguing question: given that replacement across Europe could be so swift, what can explain the tens of thousands of years during which the two species' front of interaction was geographically localized to the Levant, and the sudden breakdown of this front? We propose that disease dynamics can explain the persistence of the interspecies boundary; in this view, each species carried pathogens to which it was largely immune and tolerant, but that could spread to the other, vulnerable, species, inducing a significant disease burden. Epidemics and endemic diseases along the inter-species boundary would have mitigated against bands of one species migrating into regions dominated by the other species. Together with decreased population densities and limited inter-group interactions due to disease burden, this mechanism could have resulted in a fixed and narrow contact-zone. We further propose that genetic introgression, including transmission of alleles related to the immune system, would have gradually allowed one or both species to overcome this barrier to pervasive inter-species interaction, leading to the eventual release of the inter-species boundary from its geographic localization. I will discuss these dynamics in the context of eco-cultural interactions between the two species and the transition from the Middle to Upper Paleolithic which occurred during this time period in western Eurasia.

Human Evolution & Paleobiology

The Neandertal's Place in Nature

Yoel Rak

Tel Aviv University

Ever since its discovery, the Neandertal has been an enigma. Much of this stems from the clash between the eagerness to consider the Neandertal a link in the modern human evolutionary lineage and the evolutionary difficulties posed by the Neandertal skeleton's unique anatomy. The Neandertal's fundamental boney facial architecture and his mandibular morphology (and what is implied by them on the biomechanics of his masticatory system), all emerge as part of a complex, highly derived morphology. In light of these facts, we are faced with a puzzling question: how can we reconcile such a fundamental morphological difference between Neandertals and H. sapiens, one that goes far beyond the differences exhibited by any other two related mammal species, with the presence of traces of one species' autapomorphic DNA in the genome of the other species? One explanation lies in the differing times at which each of the two species appeared. According to geneticists own calculations, H. sapiens appeared 200,000 years ago, or even later, whereas H. neanderthalensis appeared 600,000 years ago, or perhaps earlier. The common ancestor of these two branches thus certainly existed more than 600,000 years ago—and probably much earlier. Ergo, we must be missing some more primitive players (species) that are unknown to us or that are perhaps known to us but not recognized as intermediate links in this scenario. Possible candidates for this role include the so-called "early H. sapiens" from the Skhul, Tabun, Qafzeh, and Zuttiyeh Caves.

Human Evolution & Paleobiology

Comparative genomics of 1600 species reveal new insights about “super-traits”, Breast cancer, and human diseases

Yuval Tabach

Hebrew University of Jerusalem

Various eukaryotes have developed extraordinary traits such as genetic resistance to cancer and hypoxia, increased life span, ability to hibernate, regeneration of lost tissue, and adaptation to severe environments. Comparing the genomes of these and other species can reveal genetic – phenotypic – environmental crosstalk and lead to genomic approaches to tackle fundamental bio-medical challenges. We have analyzed 1600 eukaryotic genomes, evaluating simultaneously the evolution of pathways, proteins and Amino acids across the tree of life. By mapping all human genes into clusters of genes, with distinct patterns of conservation across eukaryotic phylogeny, we demonstrated that sets of genes associated with cancer, metabolic diseases or disease phenotypes, and also those associated with most gene networks, have similar phylogenetic profiles. In my talk I will demonstrate how we use comparative genomics to predict gene function, identify disease and pathway genes – in particular in hereditary breast and ovarian cancer, “improve” tumor suppressors and develop drug-repositioning platforms.

Human Evolution & Paleobiology

Estimating relatedness in ancient DNA samples

Benjamin Yakir

Hebrew University of Jerusalem

Dense genotyping of genetic markers has revolutionized population genetics, enabling the investigation of historical population events via their reflection in the genomes of modern samples, as well as the detection and dissection of unreported relatedness between samples. A more direct window into the past was opened with the recent development of the ability to extract and read DNA from ancient human samples (aDNA). A variety of tools for the investigation of historical population events using aDNA are available. Tools for dissecting relatedness are much fewer. In the talk we will present a new system under development for inferring communality between ancient samples. The approach we use involves the detection of segments of the genome that are inherited in two samples from the same common parental source. Such segments are denoted Identical By Decent (IBD). A modern sample is measured with millions of reads over hundreds of thousands of genetic markers. In contrast, ancient samples, that are of much poorer quality, are measured with far fewer reads and are summarized only by random reads. Consequently, algorithms such as GERMLINE, for IBD detection in modern samples do not work in the aDNA context. Instead, our algorithm computes the likelihood of IBD in the available random. Intervals in which the likelihood of IBD accumulates and is above a threshold are detected as such. Simulations are used in order to tune the algorithm and statistical models are fit to the detected intervals, enabling inference of relatedness.

Microbial Evolution

Micro and macro diversity are both important for bloom-forming cyanobacteria interactions with their phages

Emanuelle Laloum, Eti Cattan-Tsaushu, Dikla Kolan, Sarit Avrani[1]

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Bloom-forming cyanobacteria are an increasing global phenomenon that negatively impact aquatic environments worldwide. These blooms are comprised of multicellular cyanobacteria that form filaments or colonies. One of the advantages of filamentous cyanobacteria of the order Nostocales over other phytoplankton, is their ability to fix atmospheric nitrogen, which enables them to form blooms even when other nitrogen sources are not available. Although phages have the potential to play a significant role in the top-down control of cyanobacteria, the role of phages in cyanobacteria bloom dynamics is poorly understood. In order to expand our knowledge of phages infecting bloom-forming cyanobacteria, we have isolated and characterized 14 cyanophages from Lake Kinneret (Israel), using the filamentous Cylindrospermopsis raciborskii as a host. Sequence analysis of the genomes of the isolated phages suggest that they belong to two distinct lineages. One of these lineages was previously described, while the other is a new linage of phages which is widespread within bacterial genomes (as prophages), however was not isolated previously. Significant differences in host ranges were found between phages with both totally different and nearly identical genomes, suggesting that both micro and macro diversity can have a significant effect on phage-host interactions. Micro diversity of the phages also influenced the ability of the host to become resistant to these phages, suggested from the significantly different time it took the host population to recover (by resistant strains growth) from infection by different phages. Interestingly, while the rate of recovery varied, all isolated strains had a cost of resistance manifested by reduced ability to induce heterocysts (specialized cells in which N2 fixation occurs). Such cost may prevent resistant strains from proliferating under nitrogen starvation. Altogether, our results suggest that cyanophages can affect bloom-forming cyanobacteria populations in at least three levels, which are tightly connected: infection, resistance and cost of resistance. These effects can be influenced by the diversity of the phage population. Additionally, the various host range and resistance patterns, sometimes in nearly identical strains suggest that micro diversity within phage populations can be a key factor affecting the host populations diversity and dynamics.

Microbial Evolution

How can holobionts evolve?

Ehud Lamm

Tel Aviv University

Holobiont is a term used to describe an individual host and its microbial community, including viruses and cellular microorganisms. Since the (re)introduction of the holobiont notion and the proposal of the hologenome by Eugene Rosenberg and Ilana Zilber-Rosenberg there have been extensive debates about their evolutionary implications and in particular about the claim that holobionts are units of selection. In contrast to much work in the field, this paper gives a sketch an evo-devo perspective on holobionts. The focus is on the mechanisms involved in acquisition and maintenance of the microbiome. I distinguish between /specific acquisition/expulsion mechanisms/ that evolved for particular symbionts and hosts; /general purpose mechanisms/ that may be involved in relations with microorganisms in general and other functions; and /goal-directed mechanisms/ that are sensitive to functional contribution of bacteria to the holobiont (and may be either specific or general purpose). The conjecture that goal-directed mechanisms play an significant role in holobionts is defended. This analysis is based on two fundamental properties of holobionts that are often neglected: that holobiont evolution involves the combination of multi-level selection and coevolution and what is known through mathematical modeling and phylogenetic analysis about the evolution of partner acquisition mechanisms. The analysis presented leads us to predict holobiont mechanisms that are based on preadaptations for coexistence with microorganisms and on goal directed mechanisms. This prediction matches what is found in paradigmatic holobionts. I conclude by contrasting my analysis with the song-not-singers model proposed by Doolittle and Booth.

Microbial Evolution

Vaccination affects selection for antibiotic resistance in Streptococcus pneumoniae

Uri Obolski

Tel Aviv University

The bacterial pathogen Streptococcus pneumoniae (the pneumococcus) is a major public health concern, causing more than 1.5 million deaths annually through pneumonia, meningitis, and septicemia. Vaccines against pneumococci are available but target only a subset pneumococcal serotypes. Hence, vaccination is often followed by substantial perturbations in the pneumococcal population dynamics. Non-vaccine serotypes are known to increase in frequency after vaccination, coupled by various genetic changes in the pneumococcal population. Interestingly, antibiotic resistance frequencies often increase in the non-vaccine pneumococcal serotypes, despite antibiotic consumption rates, and consequentially direct selection exerted to acquire antibiotic resistance, remaining constant or even slightly decreasing. We try to explain this phenomenon using a theoretical framework incorporating variation of serotypes and antibiotic resistances types to examine how their associations may be affected by vaccination. Using this framework, we find that vaccination can result in a rapid increase in the frequency of preexisting resistant variants of non-vaccine serotypes due to the removal of competition from vaccine serotypes. We identify such changes in pneumococci sampled 4-8 years after the introduction of the 13-valent polysaccharide conjugate vaccine (PCV-13) in Malawi. Using 1826 pneumococcal whole genome sequences sampled from children in Malawi, we find that certain pneumococcal strains exhibit an increase in frequency in the post-vaccine introduction period. These strains carry different metabolic and virulence genes, and some display increased antimicrobial resistance. We identify such strains and discuss how their increases in frequency are might be explained by our theoretical framework.

Microbial Evolution

Evolution of non-vertical social learning under fluctuating selection

Yoav Ram[1], Uri Liberman, Marc Feldman

[1]Interdisciplinary Center Herzliya

Individuals can learn a new trait or behavior from parents, other adults, or peers. These transmission modes are called vertical, oblique, and horizontal transmission, respectively. We have studied an evolutionary model in which both vertical and oblique transmission occur. Our results highlight scenarios in which a phenotypic polymorphism can be maintained, and in which oblique or vertical transmission are likely to evolve. Surprisingly, in some cases, vertical transmission evolves even though it is disadvantageous for the population — this is an example of the "prisoner's dilemma". This study exemplifies the complex dynamics that arise in gene-culture co-evolutionary theory.

Microbial Evolution

The Hologenome Concept of Evolution after 12 Years

Ilana Zilber-Rosenberg and Eugene Rosenberg[1]

[1]Tel Aviv University

In 2007, we published the hologenome concept of evolution, which posits that the holobionts with their hologenomes are a level of selection in evolution. The concept was based on four principles: (1) All animals and plants are holobionts, consisting of a host and abundant and diverse symbionts (the microbiome); (2) Fitness of holobionts is a product of the interactions between the host and microbiome; (3) Both the host genome and microbiome genome (the hologenome) is transferred between generations; (4) Changes in the hologenome (host or microbiome) constitute genetic variation and can lead to evolution. During the last decade, numerous experimental and theoretical studies have been published on the concept, which have supported, challenged and broadened the concept, leading to a better understanding of the holobiont system and how it evolves. These new understandings will be discussed, including the core microbiome, the special role of mothers, modes of genetic variation, and the subtle but important difference between microbe transmission and microbiome genome transmission.

Phylogeny

ModelTeller: machine-learning based model selection for optimal phylogenetic reconstruction

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Statistical criteria have long been the standard for selecting the optimal model for phylogenetic reconstruction and downstream statistical inference. These methods consist of evaluating the fit of every candidate substitution model for the data while accounting for the estimation of multiple parameters within each. While model selection is regarded as a mandatory step in phylogenetics, these calculations consume computational resources for long processing time, they are not always feasible, and sometimes depend on preliminary assumptions which do not hold for sequence data. Moreover, while these methods are dedicated to revealing the processes that underlie the sequence data, in most cases they do not produce the most accurate trees. Here, we present an alternative strategy that aims to identify the model that would result in the most accurate phylogeny. We present ModelTeller, a computational methodology for phylogenetic model selection, devised within the machine-learning framework. ModelTeller is optimized to predict the ranking of models with regard to the branch-length estimation accuracy. ModelTeller relies on rapid feature extraction and their assignment in a readily implemented model, thus results in decreased running time by a factor of 43 and 85 on the training and validation sets, respectively, on average. While on datasets simulated under homogenous substitution models ModelTeller is as accurate as AIC and BIC, it outperforms them when more intricate patterns – that aim at mimicking realistic processes – are considered.

Phylogeny

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

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The following two fields have never interacted before: reinforcement learning and molecular evolution. Here we propose to develop reinforcement-learning algorithms to solve a fundamental step in evolutionary studies; the reconstruction of phylogenetic trees, which are used to describe the evolutionary relationships among a set of organisms, genes or genomes. The current algorithms for phylogenetic tree reconstruction use various heuristics approaches to make tree inference feasible for problems involving more than a handful of sequences, thus all suffer from the known trade-off between accuracy and run-time. The novel methodology we propose here can greatly reduce the computing time without jeopardizing the likelihood of the obtained tree; considering the task of searching for the most-likely phylogenetic tree as a dynamic process, which can be viewed as a game in which the goal is to reach the maximum-likelihood tree in as few steps as possible, we aim to use reinforcement-learning techniques to learn an optimal strategy rather than only optimize the progress made in each single move. As a preliminary analysis we utilized a standard machine-learning algorithm (i.e., Random-Forest) to learn which phylogenetic tree moves are optimal for the next step. Our results clearly show that artificial-intelligence-based-learning can substantially improve our ability to accurately and efficiently reconstruct phylogenetic trees.

Phylogeny

Evolution of feeding modes and diversification rates in the megadiverse gall midges (Diptera: Cecidomyiidae)

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Gall midges (Cecidomyiidae) constitute one of the largest and most diverse families of Diptera, with close to 6600 described species and thousands of undescribed species worldwide. Fungivory is considered the ancestral state in the family but the greatest diversity is found in the herbivorous clades, and the family also includes predators and species associated with an obligatory fungal symbiont inside their galls. Until recently, the classification of the gall midges has been morphology-based, and the few phylogenetic inferences suggested for it have been based on fragmentary or limited datasets. Consequently, speculations about the evolution of feeding modes in this family have been unsubstantiated, as were hypotheses about the relation between life history attributes and diversification rates. In a first comprehensive phylogenetic analysis of the gall midges we recently analyzed sequences from 142 species representing 88 genera of 13 tribes from all feeding guilds and zoogeographic regions in order to gain insight into patterns of diversification and the evolution of feeding modes, and test the validity of the systematic division of the family. Our time-calibrated phylogenies corroborate to a great extent the morphology-based classification of the gall midges, supporting the establishment of all major clades in the Upper Cretaceous, concordant with the major radiation of angiosperms. The transition from fungus-feeding to plant-feeding occurred only once or twice in the evolution of the family and predation evolved only once, contrary to previous hypotheses. We show that all herbivorous clades of gall midges have diversified at a significantly greater rate than expected, but there is no support for the assertion that herbivorous clades associated with symbiotic fungi diversify faster than clades that do not have such associations. Currently available data also do not support the hypothesis that symbiotic clades have broader host ranges than non-symbiotic clades.

Phylogeny

A codon model for associating phenotypic traits with altered selective patterns of sequence evolution

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The last decade has witnessed an explosion of both sequencing data and character trait data. The combination of these two types of data provides means to examine possible associations between selective patterns exhibited at the molecular level with phenotypic traits. To date, such considerations are usually performed within the context of branch-site codon models that allow the identification of shifts in the selective patterns along specific branches of the phylogeny. However, the application of standard branch-site methods is based on an a-priori partitioning of the phylogeny that is, currently, performed in an ad-hoc manner, usually invoking reasoning based on the maximum-parsimony principle, thereby disregarding uncertainty in the evolutionary history of the organismal trait under study. Here, I present a probabilistic method for the association between binary phenotypes and selection intensity at the molecular level. The method, termed TraitRELAX, consists of two Markov processes that emulate the evolution of the phenotype and the coding sequences in a joint statistical framework. The first process is used to model the history of the trait, while the latter allows changes in the selection intensity at the codon level based on the probabilistic partitioning induced by the evolution of the character trait. With the combined model, one can detect changes in the selection intensity upon repeated character trait transitions. The performance of TraitRELAX was examined in simulations, where it demonstrated higher power and accuracy compared to existing branch-site codon models.

Phylogeny

SEQUENCE-INDEPENDENT PHYLOGENY FOR RESOLVING THE NON-BILATERIAN ANIMALS RELATIONSHIPS

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The phylogenetic relationships among non-bilaterian animals are disputed. Understanding those relationships, however, is essential to understand the origin and evolution of key bilaterian traits, such as nervous systems, muscles, and guts. Conflicting non-bilaterian phylogenies have been published since more than a decade, specifically with respect to the placement of the Porifera and Ctenophora, which still is controversially discussed. Nonetheless, it has become clear that (amino acid) sequence based phylogenomic analyses alone are insufficient to resolve these phylogenetic uncertainties. This is due to the fact that such analyses are sensitive to methodological settings and changes. There is the urgent need to test conflicting hypotheses of non-bilaterian relationships using sequence-independent approaches. In this context, our goal here is to find new sequence-independent phylogenetic markers and increase non-bilaterian taxon sampling to obtain corroborative evidence and test existing hypotheses. To this end, we used bioinformatic approaches to create new, and supplement existing gene content data sets by supplementing those first with novel genomes from Porifera and Placozoa in an effort to increase taxon sampling. Later, we combined them with previously published data sets, some of which were re-assembled, to produce a large data set which includes 65 species from a total of 22 with 7829 presence/absence characters. To estimate a new phylogeny, we searched for homologous sequences, including protein sequences or domains, using a new homology-search tool. Finally, we applied a Markov Clustering (MCL) to define clusters of homologous genes as input for Bayesian phylogenetic tree reconstruction. Additionally, we investigated similarities and differences in the cluster patterns between included species in order to trace, if any, their evolutionary impact on non-bilaterian animal evolution. Our ongoing investigations promise to provide additional data to test the current controversial hypotheses about the phylogenetic relationships of non-bilaterian animals and hopefully end the long debate to finally arrive at a broadly accepted phylogeny.

Phylogeny

Probabilistic models for genome rearrangements

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A comprehensive characterization of sequence evolution is of great importance to a wide variety of questions in molecular evolution such as elucidating the dynamics of gene gains and losses, phylogenetic tree reconstruction, and the inference of selective forces shaping genes and genomes. Such characterization must accurately describe substitution and indel events as well as Macro Genomic Events (MGEs), such as gene gains and losses and changes in chromosome number. While probabilistic evolutionary models for substitutions and to a lesser extent indels are extensively studied, there is much less work regarding the inference of MGE dynamics, most probably due to the computational challenges associated with inferring parameters for such probabilistic models. With the aim to develop probabilistic models to infer and characterize MGEs, we utilized the Approximate Bayesian Computing (ABC) paradigm. Specifically, we built a series of increasingly richer models, which can potentially capture various aspects of genome evolutionary dynamics including gene inversions, translocations, duplications, losses, as well as changes in chromosome number. Based on extensive simulations we show that using this probabilistic approach we can accurately infer model parameters and confidence intervals around them.

Phylogeny

Model adequacy for likelihood models of chromosome-number evolution

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Chromosome number is an important feature of the eukaryote genome. Describing its evolution within a group of interest is of prime importance when trying to detect polyploidy and dysploidy events. Indeed, inferring taxa as diploids or polyploids is a fundamental step for various downstream comparative analyses. ChromEvol is a probabilistic inference tool that given a phylogeny and respective chromosome counts, infers ancestral chromosome numbers and detects probable shifts in chromosome numbers along each branch of the phylogeny, allowing the categorization of tip taxa into diploids or polyploids. A basic step in this process compares between possible models of chromosome-number change. However, fitting a model does not necessarily mean that the model truly describes the evolutionary pattern of the underlying data. This vulnerability may lead to incorrect conclusions when the assumptions of the model are not met. Using a model adequacy framework as part of the inference process will allow researchers to compare the absolute fit of alternative models and not only their relative one. To date, model adequacy approaches are established for sequence evolution and continuous valued organismal traits. However, these tools cannot be applied to chromosome-number evolution due to the unique nature of this trait. We have thus developed a model adequacy methodology that can be specifically applied to the analysis of chromosome-number evolution. Using this methodology, allows to pinpoint phylogenies whose underlying evolutionary patterns deviate substantially from current modelling assumptions (e.g., due to hybridizations). We will further discuss the circumstances in which such deviations impact the inference of polyploidy events.

Population Genetics

Bacterial adaptations – NOT what you thought

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Many different approaches were developed to detect the footprints that selection leaves on the genome. Among the most fruitful of which is the selective sweep detection approach. A selective sweep occurs when a beneficial mutation spreads rapidly throughout the population due to natural selection. In the last decade selective sweeps detection methods have emerged as a powerful tool for uncovering the genomic basis of adaption and the study of selective sweeps in eukaryotic systems is a well-established field of research. Nevertheless, selective sweeps in bacteria received little to no attention. In our work we demonstrate that selective sweeps can also be detected in bacteria. Studied on several different microbial genomic databases, we first study the performance of a commonly used method for selective sweep detection in eukaryotes over these data and we discuss its limitations. Subsequently, we devise a novel phylogeny-based method, for the detection of incomplete selective sweeps and apply it to different databases. We detect several interesting cases of incomplete selective sweeps. Using simulations, we demonstrate that most of the detected cases cannot be explained by neutral evolution under a model of no selection and no recombination, suggesting a bona fide signal for sweeps. Since this methodology is not strain-specific but rather general, it can be applied to any bacterial species, as long as they are able to share genes with their "neighbors". Thus, we expect our newly developed method should contribute to the effort of understanding bacterial phenotypic variation and adaptation at the genomic level.

Population Genetics

Impact of human-dominated sites on the fine-scale genetic structure of the Nubian Ibex in Israel

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Human-dominated sites, like cities and villages, offer abundant resources that attract wildlife and might affect their behavior. We suggest that these human-induced behavioral changes may affect wildlife fine-scale genetic structure. The Nubian ibex (Capra nubiana) is defined as 'vulnerable' (IUCN). The species biggest population resides in Israel, in which most ibex groups concentrate around desert oases along cliffy habitats in natural surroundings. Some groups, however, show affinity to human-dominated sites. These groups exhibit heightened tolerance to anthropogenic disturbance and utilize anthropogenic resources. We characterized the fine-scale genetic structure of the Nubian Ibex in order to assess the effect of human-dominated sites on population genetic structure. 238 samples were collected from 10 sites in two regions: Negev Highlands (NH) and the Judean Desert (JD). Sampling sites in each region included both natural and human-dominated sites. For each sample 12 microsatellite loci were genotyped, and a mitochondrial DNA segment was sequenced. Results revealed significant genetic structure (AMOVA Fst=0.073, p=0.001). The genetic structure was significantly affected by geographic distance in NH (Mantel, R2=0.5988, p=0.009), but not in JD. Pairwise Fst, between adjacent natural-anthropogenic sites (less than 15km apart) ranged between 0.023-0.048 (p=0.001), while values of pairwise Fst between pairs of adjacent natural sites were smaller, ranged between 0.002-0.02 and were mostly insignificant or marginally significant. Results indicate a possible indirect impact of human-dominated sites on fine-scale genetic structure that might have implications for species evolution. This possible phenomenon may be relevant to other species inhabiting human-dominated sites and should be of conservation concern.

Population Genetics

Demographic history of invasive fire ants

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Two closely related fire ant species Solenopsis richteri and Solenopsis invicta were introduced to Southern USA from their native range of South America early in the previous century. Here we use population genomic approach to reconstruct the demographic history of these species. Samples were collected from multiple introduced and native populations of both species. Restriction site associated DNA sequencing (RAD-seq), following by stringent filtering allowed for the genotyping of 10,272 single nucleotide polymorphic loci between the samples. The catalogue of polymorphic sites was used as the basis of a demographic history model of the fire ants species which details a timeline of demographic events in the ants' history including speciation, divergence and introduction. Using approximated Bayesian computations we estimated the effective USA founding population size of the invasive S. invicta ants to be 14-139, and the number of generations this population was bottled-necked to be 0-16. Analyzing the samples genomic sequences against a closely related ant species, Solenopsis fugax, we used another demographic inference algorithm based on maximum likelihood calculations. We found that there had been no genetic flow between the two species in their native range, in contrast to the admixture taking place in the introduced range. The time of S. invicta and S. richteri speciation was estimated to 0.95*105 - 2.82*105 generations ago. Our study of the demographic history of two related species that were independently introduced into the USA provides insights into the evolutionary and demographic processes underlying the genetics of invasive populations.

Population Genetics

Genetic variation of the distribution of various species of amphibians in Israel

Gad Degani

MIGAL

Abstract Climates in Israel change from Mediterranean in the north to desert in the south over a relatively small area. Seven amphibian species were found have the following limit of distribution from north to south of adapting to dry conditions: Salamandra infraimmaculata, Latzonia nigriventer, Pelobates syriacus, Hyla savignyi, Triturus vittatus followed by Bufo variabilis. The biological, ecological and physiological adaptions to two phases, aquatic and terrestrial, were compared among populations from various habitats. Different molecular methods were used in the amphibians' sequence analysis to study the variation: mitochondrial genes Cytochrome b (Cyt b), control region (Dloop), 12S, 16S–rRNA fragments, and AFLP. The hypothesis based on sequences belonging to the same species but in various populations in Israel that show higher variations in B. viridis and T. vittatus compared to other amphibian species might show adaptation to dry and unpredictable conditions.

Population Genetics

The Case for Genetic Genealogies in Population Genomics

Ilan Gronau

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Population genomics is a dramatically expanding field fueled by the increasing availability of population-level whole genome sequence date. Using increasingly sophisticated inference methods it is now possible use such data to uncover new insights about population history and natural selection. One of the most promising developments in this field in recent years has been the emergence of methods for inferring genetic genealogies from large sets of individual genomes. These genetic genealogies are represented by ancestral recombination graphs (ARGs). For decades the ARG has served as a fundamental modeling tool in population genetics, but its complex correlation structure and high level of uncertainty make ARG inference notoriously difficult. This is changing in the past few years with several effective methods developed to tackle this challenging task. In my talk I will introduce the problem of ARG inference and survey some of the recent methods developed for this purpose. I will conclude by presenting a couple of studies conducted by my research group that use inferred ARGs to investigate challenging questions in evolution. One study used ARGs to infer a complex network of genetic interactions between archaic human populations, and the other study uses them to examine selective forces that drive sequence divergence during the first stages of speciation.

Population Genetics

Inference of complex scenarios of adaptive evolution during rapid species radiation

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Species radiation provides us with a great opportunity to study the role of adaptation in shaping the landscape of genome sequence variation. However, the task of detecting genomic regions under positive selection is significantly complicated by population-specific selective forces as well as gene flow that takes place between emerging species. Conventional methods for detecting selective sweeps typically look for genomic regions with high levels of divergence from a closely related outgroup species and low levels of population diversity. This approach works well when studying a single speciation event, but it does not capture complex scenarios that occur in species radiation. Thus, we developed a method for analyzing complex scenarios of selective sweeps that makes use of computationally inferred genetic genealogies. Our approach takes advantage of recent progress in computational methods for genome-wide inference of ancestral recombination graphs (ARGs). As a case-study, we analyzed a data set of 60 whole genomes sequenced from five recently diverged bird species of southern capuchino seedeaters from the genus Sporophila (Campagna et al. 2017). These finch-like bird species live in sympatry, show low levels of overall genetic differentiation, but clear signs of differentiation in phenotypes such as male plumage coloration and song. We inferred genome-wide ARGs for this data set using ARGweaver (Rasmussen et al. 2014), and then used the inferred ARGs to examine the contribution of two scenarios that may contribute to divergence between species genomes: selection against gene flow and recent adaptive divergence. In the first scenario we expected interspecies coalescence times to be pushed back, which was not expected in the recent adaptive divergence scenario. On the other hand, recent adaptive divergence results in large clades that are relatively very young. We examined these genealogical signatures in 25 divergent genomic regions and found that recent partial population-specific sweeps contributed to most divergence regions, while cross coalescence times were not delayed. This implies that adaptation is an important force in shaping the regions of divergence and that selection mostly acted on newly occurring mutations rather than on standing variation. However, the few cases of ancient population-enriched clades indicate that there is probably a combination of the two scenarios underlying in the basis of the rapid Sporophila speciation.

Systems Biology & EvoDevo 1

Regulatory evolution: massive variations in gene abundances contrasts a largely invariant gene-regulatory network.

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Changes in gene expression drive novel phenotypes, raising much interest in how gene expression evolves. In contrast to the static genome, gene expression is highly dynamics. Comparative studies of gene related species revealed substantial variations in gene abundances. These studies, however, provided little information about variations in the gene regulatory network, since comparison was limited to few individual conditions. To close this gap, we profiled the transcription program of related yeast species under hundreds of conditions. Consistent with previous reports, we observe massive variations in orthologous gene expression in each individual condition. By contrast, gene regulatory dynamics, quantified by co-expression analysis, remained largely conserved. Allele-specific profiling of inter-specific hybrid revealed that while most variations in absolute expression result from gene-linked variations (cis effects), regulatory dynamics diverges mostly in trans. Our data suggests that gene expression diverges primarily by mutations that alter promoter strength, while maintaining dynamic regulatory properties largely invariant.

Hypoxic conditions distort sea urchin skeletal patterning through the BMP and VEGF signaling but not Hif1α, demonstrating divergent and convergent evolution modes

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Biomineralization, the process by which living organisms use minerals to form hard structures, is believed to have evolved rapidly and independently in different phyla utilizing pre-existing components. Sea urchin skeletogenesis is a prominent model for deciphering the biological control and the evolution of biomineralization. Previous works revealed remarkable similarities between the gene regulatory networks that drive sea urchin skeletogenesis and those that control vertebrates' vascularization, implying a common origin of these two functionally distinct tubular organs. Interestingly, growth in hypoxic conditions induces the ectopic growth of both blood vessels in vertebrates and skeletal rods in sea urchins, but the regulatory mechanisms that mediate this phenotype in the sea urchin embryo were not resolved. Here we study the molecular response to hypoxic conditions in the sea urchin embryo and discover both similarities and differences to the molecular pathways that control hypoxia-driven angiogenesis in vertebrates. We show that growth in hypoxic conditions at early developmental stages enhances skeletal growth through the removal of the dorsal skeletal repressor, BMP2/4 and the expansion of the expression of the skeletal activators, VEGF and VEGFR. These changes occur downstream of the ventral regulator, Nodal, that expands in hypoxic conditions, and independently of the hypoxia-inducible factor 1α (Hif1α), a key mediator of the transcriptional response to hypoxia in vertebrates. The interactions between BMP and VEGF pathways are common to sea urchin skeletogenesis and vertebrates' vascularization which supports divergent evolution. Nevertheless, the regulation of BMP and VEGF by hypoxic conditions in vertebrates lingers through life while in the sea urchin it occurs in a limited time window and through a sea urchin specific mediator (Nodal). We propose that the upstream regulation of sea urchin skeletal patterning is the result of both divergent and convergent evolution and this modularity is a signature of a rapidly evolving system, as predicted for a biomineralization control system.

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Evolution and recurrent subfunctionalization of Argonautes in Metazoa revealed by a functional study in sea anemones

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Argonautes (AGOs) are protein carriers of small RNAs (sRNAs) such as microRNAs (miRNAs), small-interfering RNAs (siRNAs) and piwi-interacting RNAs (piRNAs) that regulate levels of endogenous, viral and transposable element RNA levels in plants (excluding piRNAs) and animals. Base-pairing between these sRNAs and their targets enables AGOs to execute target downregulation and control essential processes such as development, viral defense and genome integrity in bilaterian animals. Frequent AGO duplications in arthropods and nematodes resulted in their sub-functionalization to carry either siRNAs or miRNAs. Here we identified and characterized the role of an independent AGO duplication that occurred ~500 million years ago in the last common ancestor of sea anemones and corals, members of the phylum Cnidaria, a sister phylum to most extant animals. We performed AGO-knockdowns followed by transcriptomic profiling, and AGO-immunoprecipitations followed by sRNA sequencing revealing that in the sea anemone Nematostella vectensis both AGO paralogs are essential for development, and are specialized in carrying distinct sRNAs. Like in insects and nematodes, one paralog (NveAGO2) carries siRNAs that target repetitive elements. Surprisingly, unlike other animals, the same AGO also carries miRNAs, which are different from the miRNAs that are sorted into NveAGO1. Moreover, our analysis suggest that cnidarian miRNAs are frequently born from their own targets, similarly to plants, which suggests a previously unknown evolutionary mechanism for miRNA birth in animals. Additionally, these results demonstrate unequivocally the functional importance of post-transcriptional regulation for the development of a non-bilaterian animal.

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Signaling via GABAB receptors regulates early development and neurogenesis in the basal metazoan Nematostella vectensis

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Cnidarians, dated to 700 million years ago, are among the first multicellular organisms to evolve a nervous system. Although simple and non-centralized, their nervous system shares many components and associated genes with those of higher organisms. Here, we show that in the basal sea anemone Nematostella vectensis, the GABAB signaling pathway plays important roles in the developmental transitions and specifically in neural development. We identified 8 homologs of GABAB receptors in Nematostella, and demonstrated using sequence and structure analysis that four of these homologs are tentative GABAB-R1 receptors with putative binding sites for GABA and the GABAB agonist baclofen. Application of baclofen inhibited the larva metamorphosis program, neurogenesis and ciliogenesis. This effect was reversible and after agonist removal larva development resumed. Using RNA-Seq, we further demonstrate that baclofen treatment resulted in downregulation of numerous neuronal-related genes, whereas soxB1, a negative regulator of neurogenesis in bilaterians, was upregulated. Additionally, we show that larva motility was affected by baclofen and that foxj1, a master regulator of motile cilia, was downregulated. Our findings suggest an ancestral role for GABAB signaling that is shared across divergent organisms, and that GABAB–dependent pathways function as negative regulators of neural development and differentiation in cnidarians.

Metabolic reconfiguration facilitates widespread sterol auxotrophy during the evolution of the animal kingdom

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Cholesterol is one of the hallmarks of animals. We analyzed fully-sequenced genomes across the animal kingdom and related unicellular organisms and identified a complete orthologues sets of the cholesterol-synthesis pathway (CSP) enzymes in unicellular Holozoa such as Capsaspora owczarzaki and in Porifera (sponges). This finding suggests that cholesterol synthesis is rooted to the base of the Holozoa taxa, among animals and their closely related unicellular ancestors. Nevertheless, the few invertebrates tested for cholesterol synthesis, including Caenorhabditis elegans (C. elegans) and Drosophila melanogaster (D. melanogaster), show an intriguing cholesterol auxotrophy. We identified the loss of the first three enzymes of the CSP to be an indicative signature of sterol auxotrophy. Analysis of available fully sequenced genomes of nematodes and arthropods predicts that these taxa are sterol auxotrophs, and given that these invertebrates are the vast majority of animals, we propose that most animals on Earth cannot synthesize sterols. These results raise the question of how do sterol auxotrophs thrive. Further analysis demonstrated that many sterol auxotrophs have proteins with sequence similarity to enzymes downstream to the first three enzymes of the sterol-synthesis pathway in humans. In C. elegans, we found that some of these enzymes play a role in the conversion of dietary available sterols, such as plant sterols (phytosterols) and fungal sterols, into cholesterol. Our work unveils a design principle that co-opts sterol-synthesis enzymes for the conversion of dietary sterols into cholesterol. This reconfiguration enables widespread sterol auxotrophy in the animal kingdom by interkingdom trophic interactions between sterol-auxotrophic animals and sterol producing fungi and plants.

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The draft genome of Actinia tenebrosa reveals insights into toxin evolution

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Venomous animals have evolved a wide array of toxic compounds with highly diverse and specialised pharmacological and biochemical properties. Toxin peptides found in venoms are often novel, lacking homology to other taxa. Cnidarians (sea anemones, corals, jellyfish and hydroids) are an ancient venomous phylum, delivering toxins using gland cells as well as novel stinging cells, called cnidocytes. These cnidarian-specific cells can be found across multiple morphological structures, some of which are unique to lineages within this phylum. Investigating venom and its delivery in cnidarians provides insights into the evolution and function of novel structures, cells, and genes. This project generated a draft genome for the sea anemone Actinia tenebrosa to examine the evolution of novel genes in cnidarian species using a comparative phylogenetic approach. Our results identified a highly conserved cnidarian core-gene set, but also a large proportion of gene families restricted to specific cnidarian orders. These novel gene families undergo pronounced expansion events compared to more conserved gene families. Moreover, genetic innovations restricted to sea anemones are found to be enriched for functions related to venom and its delivery. The suite of toxin genes identified in A. tenebrosa reveal an abundance of gene families evolving through lineage-specific duplications and, in some cases, concerted evolution. This study shows that gene duplication and divergent selective pressures have shaped the genetic variation in genes encoding toxins in actiniarians.

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Developing an integrated understanding of the evolution of arthropod segmentation using fossils and evo-devo

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Segmentation is fundamental to the arthropod body plan. Understanding the evolutionary steps by which arthropods became segmented is being transformed by the integration of data from evolutionary-developmental biology, Cambrian fossils that allow the stepwise acquisition of segmental characters to be traced in the arthropod stem group, and the incorporation of fossils into an increasingly well-supported phylogenetic framework for extant arthropods based on genomic-scale datasets. Evo-devo and palaeontology both make novel predictions about the evolution of segmentation that serve as testable hypotheses for the other, complementary data source. Fossils underpin such hypotheses as arthropodization originating in a frontal appendage and then being co-opted into other segments. Insights from development, such as tagmatization being associated with different modes of segment generation in different body regions, and a distinct patterning of the anterior head segments, are complemented by palaeontological evidence for the pattern of tagmatization during ontogeny of exceptionally preserved fossils. Fossil and developmental data together provide evidence for a short head in stem-group arthropods and the mechanism of its formation and retention. Future breakthroughs are expected from identification of molecular signatures of developmental innovations within a phylogenetic framework, and from a focus on later developmental stages to identify the differentiation of repeated units of different systems within segmental precursors.

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Evolution through reverse transcription: a potential means to employ Lamarckian-like adaptations

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Lamarck's theory of evolution predicts that mutations will arise in response to changes in environmental conditions. Retrotransposons could mediate a realistic manifestation of Lamarckian evolution since they can insert mutations following expression. We propose here that cells could hitchhike on retrotransposon systems to speed up the evolution of expressed genes. The Ty-retrotransposons in yeast are composed of genomic sequencesintegrated in the genome, which code for the machinery needed for duplication and genomic integration through reverse transcription. The translated proteins are assembled in a Viral Like particle (VLP). In the VLPs, Ty's mRNAsare reverse transcribed into cDNA, which can be integrated back into the genome. We hypothesize that transcribed mRNAs in a given environment may also be incorporated in the VLP compartments, and utilize the Ty system to undergo reverse transcription and genomic integration. This could result in the replacement of the original gene or integration into a different position in the genome and creation ofgene retro-duplication. The high mutation rate of the reverse transcription process can speed up the evolution of genes which facilitate growth in the present environment. We isolated VLP compartments from cells overexpressing the Ty system, and show that a selection of mRNAs of the host are found in the VLPs. We determine how exposure to different environmental conditions changes the potential of different mRNAs to be incorporated into the VLPs and undergo reverse transcription and genomic integration.

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Comparative analysis of yeast species reveals transcriptional rewiring in cis and in trans

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Divergence of gene expression plays a key role in the emergence of new phenotypes, and is dependent on mutations in either cis-regulatory DNA sequences or trans-regulatory factors and their interaction. Previous studies have systematically classified gene expression variation into cis and trans effects, however these have focused on a limited set of conditions, therefore overlooking dynamic aspects of gene expression and limited in distinguishing changes in the regulatory wiring from changes that affect only the mean expression level. To address this issue, we compared the transcription networks of the related yeast species S. cerevisiae, S. paradoxus and their inter-specific hybrid by measuring their expression profiles in hundreds of equivalent conditions. We report that a quarter of orthologous genes (≈1400) vary in expression levels but not in their co-expression pattern, being co-expressed with the same set of genes in both species. Differential co-expression was detected for only ≈200 genes, mostly resulting from switching of single genes between expression modules, for example being stress-induced in one species but stress-reduced in the other. For certain transcription factors, we observe that mutations in binding sites are more likely to cause loss of regulation, leading to differential co-expression in cis, rather than the expected reduction in expression levels. We further find evidence for a rewiring event of a whole module: phosphate responsive genes of the Pho4 regulon are tightly co-expressed in both species, but their position within the network diverged in trans. While in S. paradoxus Pho4 is part of the stress module, in S. cerevisiae it shows a distinct expression pattern, implying that phosphate utilization underwent different tracks in the evolution of the two species. Overall, we observe that core processes are regulated in a highly conserved manner, yet we find evidence for rewiring of modules that may indicate changes in phenotypic requirements. Our data and analysis provide the first comprehensive description of how the gene regulatory network is rewired between closely related species.

Systems Biology & EvoDevo 2

Anterior Segmentation in Arthropods

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Arthropod segmentation has been in the spotlight of Evo-Devo studies for many years, but the vast majority of these studies focused on trunk/abdominal segmentation and rarely on the head, specifically the brain segments. Arthropods have a tripartite brain, divided between the three anterior-most segments, which form earlier than all other segments. Studies done on distant arthropod clades such as spiders, centipedes and holometabolous insects showed that the segment polarity gene hedgehog is expressed during the formation of these anterior segments in all cases. This raises the hypothesis that anterior segmentation is a conserved arthropod developmental process, in contrast to trunk segmentation, which varies greatly in arthropods. However, not much else is known about hedgehog function in anterior segmentation, nor about the function of other segment polarity genes. To study anterior segmentation and its relation to the hedgehog pathway and the Wnt pathway, which is expressed in a similar spatial and temporal manner, I looked at the expression and knock down phenotypes of related genes in the hemipteran Oncopeltus fasciatus. hedgehog is expressed in the same manner in Oncopeltus as in other arthropods, further supporting the hypothesis that the anterior segmentation process is indeed conserved across arthropods. Knocking down hedgehog, the pathway activator, resulted in severe reduction of the anterior segments. knock down of shaggy, an important negative regulator in the Wnt pathway showed similar reduction. These results suggest that activation of hh and repression of the Wnt pathway in the anterior region is necessary for proper anterior segmentation in Oncopeltus.

Systems Biology & EvoDevo 2

Asymmetrical distribution of maternal nodal mRNA in amphioxus embryos by means of Arp2/3 complex

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Nodal signaling is a key player for establishing the zygotic expression domain of the nodal gene that is regulated by Lefty–Nodal interaction by having maternally supplied nodal mRNA in amphioxus embryos. Maternal mRNA of nodal is distributed evenly in unfertilized eggs of amphioxus. After sperm fusion, nodal mRNA concentrated into the animal hemisphere displaying an asymmetrical pattern. To elucidate the mechanism causing this pattern, possible interactions between maternal nodal mRNA and cortical cytoskeletons were examined. The active form of Arp (actin-related protein) 2/3 complex is a good candidate for analyzing the remodeling of the cortical actin filaments as it functions in nucleation and branching of actin filaments to activate cytoskeletal reorganization. Immunostainings for phosphorylated Arp2 (pArp2) in unfertilized and fertilized eggs displayed a movement of the immunopositive signals to one side of the egg in the cortical region. The asymmetrical distribution of the active Arp2/3 was co-localized with tubulin and F-actin signals in fertilized eggs and cleavage embryos. Fluorescent in situ hybridization with nodal probe and immunoreaction with an anti-pArp2 from fertilized eggs to blastulae demonstrated the asymmetrical distribution of maternal nodal mRNA which was co-localized with the active Arp2/3 complex. Although lack of evidence of direct interactions between cortical cytoskeletons and nodal mRNA exists, disturbance of the proper distribution of the Arp2/3 and of shaping the lefty-nodal expression domain by the perturbation with inhibitor CK666 suggests their intimate relationship. These results show that the activation of Arp2/3 complex affects the distribution of maternal nodal mRNA.

Systems Biology & EvoDevo 2

The evolution of extreme fertility in advanced eusocial bees and modifications in gonadotropic hormone signaling to reduce brain cost

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Gonadotropic hormones coordinate processes in diverse tissues regulating animal reproductive physiology and behavior. Juvenile hormone (JH) is the ancient and most common gonadotropin in insects, but not in advanced eusocial honey bees and ants. Here we combined JH removal and replacement with extensive transcriptomics and behavioral analyses to study JH function in the bumble bee Bombus terrestris which shows an intermediate level of sociality. We found that JH activates fertility pathways but this comes with a previously unknown cost to the brain. We identified thousands of JH regulated genes, which in the fat body were mostly upregulated and enriched for pathways involved in major metabolic and biosynthetic pathways. In the brain, more genes were downregulated with enrichment for genes encoding the ribosome, proteasome, and additional pathways involved protein turnover. In other species, similar downregulation of protein turnover is found in aging brains or under stress, and is associated with compromised long-term memory and health. Brain ribosomal protein expression is similarly downregulated in dominant orphan worker bees, which naturally have high JH titers compared to their subordinate group mates. The genes regulated by JH in the worker fat body overlap with genes differentially expressed between queens and gynes which naturally have high and low JH, respectively. We did not find a similar downregulation of ribosomal or proteosomal proteins in the brain of honey bees in which JH is not a gonadotropin but rather regulates division of labor. These findings are consistent with the hypothesis that the evolution of increased fertility, a hallmark of advanced sociality in insects, was associated with modifications in JH signaling pathways enabling extended high fertility while minimizing costs to the brain.

Systems Biology & EvoDevo 2

Hemimetabolous insects elucidate the origin of sexual development via alternative splicing

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Insects are the only animals whose sexual differentiation pathway revolves around a cascade of sex-specific, alternatively spliced transcripts. Central to this pathway is the transcription factor doublesex, which binds to the same targets in males and females but has different effects on those targets depending on the the transcript's alternatively spliced 3' end. In most major holometabolous insect orders, control of the female-specific dsx isoform depends on the alternatively, sex-specifically spliced gene transformer. The form and function of these genes has been investigated in all major holometabolous orders, but how the tra-dsx axis arose from a system in which dsx is solely a male determiner lacking sex-specific spliceforms, and tra plays no role in sexual differentiation, is unclear. To resolve this evolutionary mystery, we examined the expression of tra and dsx in three basally branching insect lineages: Blattodea, Phthiraptera, and Hemiptera. We also used RNAi to investigate the role these genes play in the German cockroach. In the hemipteran Rhodnius prolixus, dsx and tra sex-specific spliceforms resemble those previously studied in holometabolous insects. In the more basally branching cockroach, we found that although dsx sex-specific spliceforms are conserved, dsx directs male, but not female differentiation. Surprisingly, we found that tra controls female differentiation in the German cockroach despite splicing patterns that differ from the familiar holometabolous mode. Together, our results suggest that the canonical sex-specific splicing of dsx and tra is decoupled from these genes' function in basally branching insects, and that the tra-dsx pathway gradually evolved in early insects.

Virus & Mobile Elements

Caught between pathogens and autoimmunity: The evolution of the mammalian immune system

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The immune system is under constant pressure from pathogens to evolve and mount a sufficiently strong response. At the same time, an overresponsive immune system can lead to autoimmunity and tissue damage. How these conflicting demands have shaped human immunity is not well understood. Here, we characterize transcriptional divergence in the innate immune response across primates and rodents using bulk and single-cell transcriptomics, combined with chromatin analysis. We discover that genes that diverge in transcriptional response across species vary in cell-to-cell expression within each species. These divergent genes are evolutionarily younger, experience rapid coding sequence evolution and display a distinct promoter architecture. They have exclusive immune functions, such as cellular defence and inflammation, while pleiotropic genes involved in immunity and other pathways are more conserved. Analysis of viral interactions and mimicry shows that viruses target conserved elements of the innate immune response, suggesting that regulatory constraints imposed on the host are exploited by viruses. Importantly, innate immune genes implicated in autoimmune diseases show high levels of transcriptional divergence but also more interactions with viruses. This reveals a conflict between pathogens and regulatory constraints, which has likely contributed to genetic architectures driving the pathogenesis of immune disorders.

Virus & Mobile Elements

Purifying selection of long dsRNA bounds the layout of mobile elements in metazoan genomes

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Background: Mobile elements comprise a large fraction of metazoan genomes. Accumulation of mobile elements is bound to produce multiple putative dsRNA structures within the transcriptome. These endogenous dsRNA structures resemble viral RNA, and may trigger false activation of innate immune response, leading to a severe damage to the host cell. A-to-I RNA editing is a common post-transcriptional modification, abundant within repetitive elements of all metazoans. It was recently shown that a key function of A-to-I RNA editing by ADAR1 is to suppress the immunogenic response by endogenous dsRNAs. Results: Here we analyze the transcriptome of dozens of species across metazoa and identify a strong genomic selection against endogenous dsRNAs, resulting in their purification from the canonical transcriptome. This purifying selection is especially strong for long and tight dsRNAs. These are almost absent from mRNAs, but not pre-mRNAs, supporting the notion of selection due to cytoplasmic processes. The few long and tight structures found in human transcripts are weakly expressed and often heavily edited. Conclusion: Purifying selection of long dsRNA is an important defense mechanism against false activation of innate immunity. This newly identified principle govern the integration of mobile elements into the genome, a major driving force of genome evolution. Furthermore, we find that most of ADAR1 activity is not required to prevent an immune response to endogenous dsRNAs. The critical targets of ADAR1 editing are, likely, to be found mostly in non-canonical transcript.

Virus & Mobile Elements

dsRNA sensing and antiviral immune response in a non-bilaterian model animal *Nematostella vectensis*

Magda Lewandowska[1], Ton Sharoni, Yehu Moran

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Antiviral immunity is present in every living organism, but the strategies for recognition and defence against viruses differ between kingdoms and species, reflecting major transitions in evolution and high evolutionary rates due to host-virus "arms-race". While vertebrates developed a sequence-nonspecific interferon response to cytoplasmic double-stranded RNA (dsRNA), a hallmark of infection by RNA viruses, both invertebrates and plants are known to harness targeted RNA interference (RNAi) to silence viral genomes. However, our understanding of the ancestral state of antiviral immunity in animals is severely impeded by the fact that the diversity of defence mechanisms within early-branching metazoans remains poorly explored. In order to reveal antiviral response mechanisms to RNA viruses in non-bilaterian animals, we performed zygotic microinjections of two potent viral dsRNA mimics to the sea anemone Nematostella vectensis, a model organism representing Cnidaria, a sister group of Bilateria. Microinjections were followed by monitoring dynamics of changes in transcriptomic response. Upon long dsRNA challenge, we observed significant upregulation of 1521 genes including two that encode putative cnidarian retinoic acid inducible gene I like receptors (RLRs), homologs of the major cytoplasmic dsRNA sensing receptors in Bilateria, suggesting their conserved function in long dsRNA recognition. These results are further supported by a positive response of our Nematostella RLRs fluorescent reporter lines to injections of long dsRNA mimics. Surprisingly, injection of short dsRNA with 5' triphosphate – a potent trigger of vertebrate antiviral immunity – revealed no specific antiviral response in Nematostella. Furthermore, cytoplasmic presence of long dsRNA mimic resulted in overexpression of genes coding for major RNAi proteins, although their roles in exogenous RNA degradation and post-transcriptional host gene silencing during the antiviral response are yet to be explored. The lack of recognition of one of canonical vertebrates' viral ligand and putative functional non-redundancy of anthozoan RLRs suggested by our previous phylogenetic analysis raises an interesting question about unknown functions of these dsRNA sensors in non-bilaterian animals.

Virus & Mobile Elements

Network structure of CRISPR immunity shapes the co-evolutionary dynamics between hosts and viruses

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As a heritable sequence-specific adaptive immune system, CRISPR-Cas is a powerful molecular mechanism shaping strain diversity in host-virus systems. Nevertheless, host-virus coevolution and interaction structure associated with diversification remain largely unexplored. We quantified the network structures of infection ('who infects whom') and immunity ('who is protected from whom') in a stochastic Lotka-Volterra model of host and viral populations that includes their evolution. The coevolutionary dynamics exhibit an alternation between periods of virus and host diversification and host control, in which viruses do not diversify. In periods of diversification, infection networks are partitioned into modules of hosts and viruses, reflecting the emergence of niches within which viruses can grow as the result of negative frequency-dependent selection. Acquisition of immunity closes available niches and builds a weighted-nested immunity network, representing redundant protection and causing a shift in the coevolutionary dynamics to a host-controlled regime. The nested structure enforces an orderly virus extinction, which in turn increases the potential for an escape mutation in viruses and another transition to a virus-diversification regime. These dynamics and structures are not obtained under neutral scenarios which retain all the evolutionary dynamics but lack specific immunity. FInally, the immunity networks in three empirical systems also exhibit weighted nestedness, a pattern our theory shows is indicative of host control. Our findings emphasize the role that network structure plays in CRISPR-induced host-virus coevolution, providing one explanation for existing host/viral diversity in natural and empirical systems.

Virus & Mobile Elements

Mechanistic insights into the evolutionary dynamics of competing cheater RNA viruses

Adi Stern

Tel Aviv University

Cheater viruses are defined as mutant viruses that cannot replicate on their own but effectively steal resources from wild-type (WT) viruses during co-infection. While the presence of cheaters may be inferred indirectly, a mechanistic understanding of how viruses cheat and how cheaters interact with each other is mostly lacking. During experimental evolution of MS2 phage, we observed the emergence of a point deletion mutation. We showed that this deletion mutant is a cheater virus that steals the viral polymerase from WT during co-infection, and further deciphered the mechanistic advantage of the cheater, which is its preferential packaging by coat products. Intriguingly, our results revealed the existence of an additional synonymous mutation cheater. Continued evolution of the experiment revealed the demise of the deletion cheater and rise of the second cheater. We developed a mathematical model for a three-way interaction between WT and the two cheaters. The model showed that a single cheater is expected to reach an equilibrium with WT, yet inferred that the two cheaters interact antagonistically, leading to the rise/demise pattern as observed in our experiments. While there is growing interest in using defective virus particles as anti-viral therapeutics, our findings highlight the inherently unpredictable nature of cheating RNA viruses.

Poster

Communication among lysogens and its implications

Nitzan Aframian[1], Shira Omer, Kholod Msaeed,Valeria Lipsman, Polina Shnayderov, Alaa Mahagna, Avigdor Eldar

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Temperate phages undergo two developmental switches during their life-cycle; a lysis-lysogeny decision upon first invasion of their host, and the decision whether to persist in the genome or undergo lytic induction from the lysogenic phase. Several instances of phage communication influencing the lysis-lysogeny decision have been previously demonstrated. Mechanisms of communication wherein the phage particle itself functions as the signal have been known for some time, and more recently SPbeta-like phages were shown to utilize a small peptide as the signal of communication. Similar to previous mechanism, this newly found system, termed the arbitrium system, was also found to influence the lysis–lysogeny decision. In this work we focus on the lysogenic state, and explore the possibility of communication among lysogens – that is whether prophages can send a signal (a possibility opened up by the discovery of a peptide signal), and whether they can respond to this same signal. Specifically, we examine whether the switch to lytic induction may also be influenced by communication.

Poster

Understanding the evolution of the DEG/ENaC ion channels in animals by their functional analysis in the cnidarian Nematostella vectensis

Jose Maria Aguilar-Camacho, Reuven Aharoni, Stefan Gründer and Yehu Moran

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The Degenerin/Epithelial Na+ channel superfamily (DEG/ENaC) includes ion channels with highly diverse activating stimuli and physiological functions (i.e. synaptic transmission, homeostasis and epithelogenesis). Most of these channels are gated either by cations (H+) or bile acids in different vertebrate and invertebrate species. However, two distantly related animals, the cnidarian Hydra and the mollusk Helix, possess DEG/ENaC channels that are gated by neuropeptides (RFamides). This unusual diversity in gating mechanisms results in lack of understanding of the ancestral mechanism of action and function of this channel superfamily. To further understand the evolution and ancestral state of this family of ion channels, a total of 15 DEG/ENaC (NeNaCs) genes were identified in the genome and transcriptomic datasets from the cnidarian Nematostella vectensis. These ion channels were cloned for performing elecrophysiological conductivity measurements and whole mount in situ hybridization (ISH) for the localization of the transcripts in the tissue of this species at four different developmental stages (gastrula, planula, metamorphic phase and primary polyp). Molecular phylogenetic analysis of the sequences from N. vectensis revealed a highly complex evolutionary pattern because they are dispersed in distinct phylogenetic clades (not monophyletic) within the DEG/ENaC superfamily that includes members from many other vertebrate and invertebrate species. The localization of the transcripts from the ISH experiment at different developmental stages suggested uncertain diverse functions. For example, NeNaC1 is expressed in endodermal and few ectodermal cells of the planula stage and in the tentacles and pharynx of the primary polyp. In contrast, NeNaC2 is expressed in the ectoderm of the aboral part of the planula stage and in the tentacle cnidocytes of the primary polyp. Further immunohistochemistry, electrophysiological and transgenic analyses will be carried out to understand the functions of these elusive ion channels in this model organism.

Poster

Population genomics of a reintroduced hybrid population – the Asiatic wild ass Equus hemionus in Israel

Lilith Zecherle, Richard Brown, Hazel Nichols and Shirli Bar-David[1]

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Species reintroductions are a powerful conservation tool, yet they are often characterised by low success rates and a populations long-term persistence strongly depends on its genetic makeup. Few founding individuals and population bottlenecks during reintroduction can cause low genetic diversity and high levels of inbreeding in the established population, ultimately increasing its risk of extinction. This can be counteracted by maximising the genetic diversity in the founder individuals. In Israel, hybrid individuals of two different subspecies of Asiatic wild ass Equus hemionus ssp. were reintroduced in the 1980s and 1990s, after the endemic subspecies had become extinct.
The population has since expanded its range and currently counts approximately 300 individuals. We used ddRADseq to analyse DNA samples from Israeli individuals and the original subspecies. We analysed admixture levels of the hybrids and investigated the population genomics of the reintroduction by comparing the Israeli population prior and post release with samples of the two subspecies from zoo populations. The Israeli population showed high levels of subspecies admixture (Mean hybrid index =0.44, SD=0.06). Despite the severe bottleneck (11 individuals) we find only a small decrease in heterozygosity in the reintroduced population. Overall more heterozygosity was retained in the Israeli population than in the managed captive populations. Deliberate admixture of distinct populations or subspecies is a highly controversial topic in conservation biology. Yet, our study suggests that the reintroduced population may have benefitted genetically from prior admixture. These results add to a growing debate on the value of hybrids for species conservation programmes.

Poster

Bottlenecked populations may be sustainable, until challenged by more genetically-diverse waves of migration

Yotam Ben-Oren[1], Oren Kolodny

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Many pioneer waves of migration go through severe demographic bottlenecks. Although genetic diversity is considered crucial for population survival, many of these highly bottlenecked populations seem to thrive. We suggest that when inter- and intraspecific competition is limited, such populations may be sustainable. However, an organism's fiercest competition comes from its own conspecifics, as these compete for an identical ecological niche; thus, later waves of migration which had proceeded at a slower pace and experienced less bottlenecks may threaten the "veteran" inhabitants and eventually genetically replace them. We outline a population genetics' model that tracks these dynamics and allows their exploration, considering jointly demographic, genetic, and environmental factors. The proposed perspective offers a possible explanation for population replacement by secondary waves of migration, such as has been recorded in humans and non-human organisms.

Poster

Evolution and ecology of hosts and their microbiome: a computational framework for hypothesis testing

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The host-associated microbiome may significantly influence its host's ecology and evolutionary dynamics, and recent developments in sequencing technologies provide an unprecedented view of these complex communities. However, for historical reasons and due to the complexity of the multi-level dynamics that are involved, there are few generative computational frameworks in this field. We will implement a simple modular framework, which will support the exploration of eco-evolutionary dynamics and will allow explicit hypothesis testing regarding microbiome assembly at the level of the host population, microbiome transmission dynamics, and possible influence of microbes on their host's fitness. Here, we present the planned framework and demonstrate its utility with results from a preliminary implementation, exploring a number of fundamental questions: (1) What is the ratio between acquisition of microbes from the environment to transmission from other host individuals that is necessary in order to preserve microbial diversity? (2) How would contribution of microbes to their host fitness interact with population dynamics of the host? (3) How would seemingly arbitrary assumptions about microbiome assembly dynamics at the level of the individual influence microbiome composition over host generations? The non-intuitive results of these simple explorations highlight the potential of theoretical frameworks for improved understanding of host-microbiome dynamics.

Poster

Below or above-ground? Where are the closest relatives of troglobite *Tegenaria* species?

Efrat Gavish-Regev

Scientific Collection Manager, Arachnida & other terrestrial arthropods,

Caves are excellent systems to study evolution and speciation due to their unique conditions. Limitation of light may act as a filter and promote speciation. The Mediterranean genus *Tegenaria* Latreille, 1804 (Agelenidae) includes 105 species with many cave-dwellers. While European *Tegenaria* were recently revised, many Levantine and southwest Asian species remain poorly understood, particularly troglobites. Here we report several undescribed morphospecies of *Tegenaria* from Israeli caves with troglobitic characters (reduced eyes and depigmented). To address how troglobitic *Tegenaria* morphospecies are related to each other and to epigean species, we undertook a combined morphological and phylogenomic approach to resolving this species complex. Our work tests the hypothesis of single vs. multiple origins of the trolobitic morphology in the Israeli morphospecies using detailed descriptions and a RAD-Seq approach as complementary datasets. Here we show that at least two morphologically distinct troglobitic morphospecies occur in the caves, as well as two distinct non-troglobitic epigean morphospecies. We present the suggested relationships of the troglobite and non-troglobite species, and discuss the implications for understanding the main drivers of cave adaptation in habitats masked from the effects of the Quaternary glacial cycles.

Poster

Positive interactions increase the risk of extinction in changing environments

Yaron Goldberg[1] and Jonathan Friedman

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Positive interactions play crucial roles in shaping the structure and function of many ecological systems. Despite the importance of these interactions, their influence on species' evolution and adaptation to new environments is still poorly understood. The scenario in which adaptation is perhaps the most crucial is when an environment changes into an inhospitable one, causing a population to head towards extinction. In this scenario, survival requires a quick adaptation to the new environment via the rise of new mutants - a situation termed evolutionary rescue. Here, we elucidate how different types of positive interactions influence the likelihood of evolutionary rescue by conducting numerical and theoretical analyses. We find that the probability of evolutionary rescue is greatly reduced in the case of interspecies mutualism. This is primarily due to the fact that rescue requires the rise of rescuing mutations in both of the mutualistic species, thus necessitating two independent rare mutation events. These results indicate that while positive interactions may be beneficial in steady environments, they can hinder adaptation to changing environments. The results of this research highlight situations in which mutualistic systems have an elevated risk of collapsing. Furthermore, they may hint at the selective pressures that drove co-dependent unicellular species to form more adaptable organisms able to differentiate into multiple phenotypes, including multicellular life.

Poster

miRNA and siRNA Target Recognition in Cnidaria - Merging Experimental and Computational Approaches

Yael Hazan[1], Michal Linial, Yehu Moran

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Micro RNAs (miRNAs) and short interfering RNAs (siRNAs) are two classes of small RNA (sRNA) that play vital roles in many eukaryotic organisms including animals and plants. miRNAs take part in physiological and developmental processes by downregulating gene expression at the posttranscriptional level. siRNAs on the other hand, act as anti-viral and anti-transposon agents by promoting the cleavage of their targets in a process called RNA interference (RNAi). Both miRNAs and siRNAs function via base pairing to their targets. However, binding characteristics differ between and among these players and a growing body of evidence suggests large variation in target complementarity patterns of sRNAs. These patterns are pivotal to the function of sRNAs. Therefore, deciphering the features characterizing the binding of sRNAs has great significance in revealing sRNA targets and understanding their regulatory roles. Small RNAs in early branching metazoans such as the cnidarians are far less studied than in bilaterians and plants. However, as these early linages diverged from Bilateria more than 600 million years ago, revealing their sRNA mechanisms is of great importance to the understanding of these systems in the ancient ancestor of these groups. Here I propose a 3-steps research plan to shed some light on this understudied topic by merging experimental and computational approaches. In the main project, I plan to apply a novel method called CLEAR (covalent ligation of endogenous Argonaute-bound RNAs)-CLIP (Crosslinking Immunoprecipitation) on the cnidarian Nematostella vectensis. The goal is to unravel for the first time the direct interactions between miRNAs and siRNAs and their targets under native conditions in this organism. The procedure will include immunoprecipitation of the two Argonaute proteins of N. vectensis bound to the sRNAs and their targets. Stabilizing this transient interaction is achieved through use of ultraviolet cross-linking and ligation. This will be followed by high-throughput sequencing of the extracted RNAs. The other two complementary projects are the compilation of an endo-siRNA library for N. vectensis and the characterization N. vectensis viruses. This will be achieved by computational analyses of Nematostella sRNA-sequencing and transcriptomic data. Combined, these three projects will help closing the gap of knowledge in miRNAs and siRNAs – target interactions in cnidarians and shed light on their evolutionary pathways.

Poster

C. Elegans Lifecycle Compression via Experimental Evolution

Meanchem Isseroff, Anna Mellul

[1]Hebrew University, Dr. Yuval Tabach

In biology there currently exists a dualism regarding two key facets of life, lifecycle and lifespan. On the one hand these factors are easily observable in many organisms, and much is known regarding many minute details of a large variety of species. We know that throughout nature we see differences, orders of magnitude big, within these two factors. Some organisms live hundreds of years, some hours, some develop within days, and others take decades. We also know that there is a strong correlation between size, development time, and lifespan. Concurrently, we don't know why all this variation exists, and, moreover, what mechanisms are involved in this phenomenon, though many theories exist. There are many examples where trade-offs are used to describe a phenomenon. In economics it's referred to as "cost-benefit", in physics it's "newtons third law", and in aging genetics it's "antagonistic pleiotropy" (AP), or the idea that genes beneficial to an organism's reproductive success can have adverse impacts on longevity. AP is one of the more commonly accepted theories of aging. Utilizing c. elegans and experimental evolution we hope to elucidate the connection between time to sexual maturity and lifespan. By strongly selecting those worms that reproduce quickly, we have developed, and are continuing to develop c. elegans strains with "compressed" lifecycles. Our current strains show an average reduction in time-to-sexual-maturity of ~7%, following 7 months of selection. Recently, we have also begun utilizing EMS phenotype screens in conjunction with our evolutionary methods to develop additional strains. We hope to utilize these compressed strains to assist us in our goal of understanding the expansive interplay of genes involved in lifespan, as well as in our understanding of the processes involved in the evolution of complex traits such as lifespan and lifecycle.

Poster

The role of aneuploidy in adaptation - evolutionary simulations

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Aneuploidy is a widespread condition of an abnormal number of chromosomes in the cell. It occurs in animals, plants, and microorganisms. In humans, cancer cells are frequently characterised by aneuploidy, and common genetic disorders, like Down's syndrome and Edwards syndrome, are caused by aneuploidy. Therefore, it is critical to understand the impact of aneuploidy on adaptation and evolutionary dynamics. Though aneuploidy is usually deleterious, experiments with microbes show it can be advantageous under some environmental conditions. Specifically, Yona et al. (2012) have shown that aneuploidy can be a transient adaptive solution to heat or pH stress: aneuploidy can appear for a period of time and subsequently be substituted by focal and refined gene mutations. Thus, is seems like aneuploidy can help cells adapt to stress. To explore the effect of aneuploidy on adaptation, we implemented evolutionary simulations of populations undergoing both mutation and aneuploidy. We fitted the model to experimental results using Approximate Bayesian computation. We then analysed how changing the evolutionary parameters, e.g. selection, population size, and the rates of mutation and aneuploidy, affects the evolutionary dynamics: for example, when is adaptation accelerated or decelerated due to aneuploidy. Our results shed new light on the adaptive role of an often disregarded process for generation of genetic variation.

Poster

ADAR-like mutations observed during experimental evolution of Rhinovirus

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The last resort of host cells against viral infections is intracellular defense mechanisms. One intriguing mode of defense is to edit the viral genome, mainly via cellular deamineases. This mechanism of editing has been shown to result in hypermutated and hence non-viable viral genomes. However, it has also been suggested that editing of viral genomes may also promote viral growth. Here, we studied the mutation rates of Rhinovirus (RV), the predominant cause of the common cold and one of the most infectious human viral pathogens. We applied a highly accurate next generation sequencing protocol (AccuNGS), which allowed us to detect mutations as rare as 1 in 10,000 in the RV genome, and to infer the mutation rate of the virus. Intriguingly, we observed a significant abundance of low-frequency WA>WG mutations throughout the entire viral genome across twelve passages, which represent the editing contexts of the cellular deaminase known as ADAR. These data suggest that RV undergoes host editing in cell culture. Conversely, we did not find ADAR-like mutations at all in natural populations, both when analyzing intra-host diversity and when analyzing inter-host diversity. Our preliminary results thus suggest that ADAR-like mutations are deleterious for RV during long-term evolution. We hope this study will provide a deeper understanding of the causes of the rapid evolution of RV.

Poster

Approximate Bayesian computation algorithm for the inference on indel parameters

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A large body of research has been devoted to developing probabilistic substitution models and to infer their parameters using likelihood and Bayesian approaches. In contrast, relatively little has been done to model indel dynamics, probably due to the difficulty in writing explicit likelihood functions. We propose indel models that explicitly distinguish the insertion rate from the deletion rate, making the model more realistic. SpartaABC, an Approximate Bayesian Computation (ABC) reject algorithm to infer indel parameters from sequence data.

Poster

Co-Evolutionary Dynamics of Bacterial Communities

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Microbes function as part of diverse communities that play key roles in determining the health of virtually all living organisms, as well as that of the entire planet. In order to manage and design communities, it is crucial to be able to predict their structure - that is, to predict which species will coexist stably, and which will be driven extinct. While there are recent advances in predicting the structure of bacterial communities over short time scales, little is known about the stability community structure over hundreds of generations, where evolution plays a significant role. The goals of this research are to study the stability of community structure over evolutionary time scales; to study the repeatability of changes in community structure across replicates, and to identify factors that influence those features. For these purposes, we propagate 121 unique combinations of 16 bacterial species for ~400 generations and track their community structure, measure their interspecies interactions, and sequence their genomes. Our data reveal significant variation in stability across communities, with some communities changing significantly after as little as ~60 generations, while others remain stable for hundreds of generations. These changes were different when species evolved separately or together, suggesting that they are influenced by coevolution, rather than solely adapting to the experimental conditions. This study will reveal the time scales over which microbial community structure is predictable, and the factors that influence this predictability. This knowledge is crucial for engineering communities that function stably over hundreds of generations.

Poster

Limited DNA repair gene repertoire in Ascomycete yeast revealed by comparative genomics

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Ascomycota is the largest phylogenetic group of fungi that includes species important to human health and wellbeing. DNA repair is important for fungal survival and genome evolution. Here, we describe a detailed comparative genomic analysis of DNA repair genes in Ascomycota. We determined the DNA repair gene repertoire in Taphrinomycotina, Saccharomycotina, Leotiomycetes, Sordariomycetes, Dothideomycetes and Eurotiomycetes. The classes of yeasts, Saccharomycotina and Taphrinomycotina, have a smaller DNA repair gene repertoire comparing to Pezizomycotina. Some genes were absent from most, if not all, yeast species. To study the conservation of these genes in Pezizomycotina, we used the GLOOME algorithm that provides the expectations of gain or loss of genes given the tree topology. Genes that were absent from most of the species of Taphrinomycotina or Saccharomycotina showed lower conservation in Pezizomycotina. This suggests that the absence of some DNA repair in yeasts is not random; genes with a tendency to be lost in other classes are missing. We ranked the conservation of DNA repair genes in Ascomycota. We found that Rad51 and its paralogs were less conserved than other recombinational proteins. This suggests that there is a redundancy between Rad51 and its paralogs, at least in some species. Finally, based on the repertoire of UV repair genes, we found conditions that differentially kill the wine pathogen Brettanomyces bruxellensis and not Saccharomyces cerevisiae. In summary, our analysis provides testable hypotheses to the role of DNA repair proteins in the genome evolution of Ascomycota.

Poster

How natural selection drives and maintains floral colour variation: irises, pollinators and beyond

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Close your eyes and think of your favorite flower. What is its colour? Chances are that immediately you thought on one specific colour. Indeed, most flower populations have monomorphic uniform flower colour, believed to be the outcome of pollinator-mediated directional selection, but some species exhibit colour dimorphism or polymorphism, and in rare cases even a continuous scale of colours. Flower colour serves as a visual signal for the pollinators, which learn to associate it with reward, and in turn, exert selection on it. Pollinator-mediated selection can drive fixation of one colour, but other selection agents, such as pathogens or climate, as well as disassortative behavior of the pollinators, can increase fitness of multiple colours and maintain colour polymorphism. We studied selection on flower colour in four taxa of irises: in the colour dimorphic Iris lutescens selection on flower colour was not pollinator-mediated, while in the polymorphic I. pumila selection on one colour morph only was mediated by pollinators. Selection on flower colour in two species of the Royal Irises (section Oncocyclus) was found to be either weak or not pollinator-mediated. Possible mechanisms other than pollinator-mediated selection may drive and maintain flower colour variation, for example, spatio-temporal variation in selection, multiple selection agents act in opposite directions, and biased mutation-selection balance. We suggest that simultaneous mechanisms act to maintain flower colour polymorphism, and one need to take multidisciplinary approach in order to understand the evolution of flower colour variation or its lack.

Poster

Determinants of splicing efficiency in yeast and their effect on cellular function

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Pre-mRNA splicing is a crucial step during gene expression regulation in eukaryotic cells. However, the control and regulation of the splicing process itself is complex and not yet fully understood. In addition, to its effect on gene expression regulation in-cis, we hypothesize that the efficiency of splicing on one transcript might affect cellular functions in-trans as it influences the cellular supply and demand economy of the splicing machinery. In this work, we set out to map the effect of different features on splicing efficiency using a large library of synthetic intron-containing non-coding RNAs expressed in Saccharomyces Cerevisiae. We measured the splicing efficiency and the total RNA abundance of each variant in the library using specific RNA sequencing of the library. Moreover, we measured the global cellular effects of the library by measuring the cellular fitness of cells carrying each strain in the library using a pooled competition assay, and by measuring splicing efficiency in-trans using an intron-containing fluorescent reporter. Splicing is considered to be regulated through three functional sites, 5' donor, branch site, and 3' acceptor. Using our designed library, we explored the contribution of variations on motifs in these different splice site sequences to splicing efficiency and demonstrate that the different sites have different tolerance to perturbations. We also demonstrate that intronic and exonic sequences have a major effect on splicing efficiency. Moreover, we successfully designed sequence elements that are alternatively spliced to up to four different isoforms, which is intriguing since there are almost no evidence for alternative splicing in S. Cerevisiae. Hence, introduction of synthetic alternatively spliced introns might help to reveal the mechanisms of alternative splicing regulation. Finally, using our two phenotypic assays we show that certain design features disrupt the splicing machinery in a manner that influences other intron containing genes, and the cellular fitness, which demonstrates how changes to one transcript might affect the wellbeing of the cell by non-optimal usage of a common resource such as the splicing machinery.

Poster

Identifying new photosynthesis genes by massive comparative genomics

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Photosynthesis is a highly conserved process, by which plants and other photosynthetic organisms turn solar energy, water, and carbon dioxide into yield and oxygen. This highly conserved process is a key interest for increasing yield production globally, mark improving photosynthesis efficiency as a promising target. Here, we are using Phylogenetic profiling (PP) method to point new potential genes, being involved in photosynthesis. PP is based on correlated occurrence and absence pattern of genes along evolution, which tend to reflect their mutual function in biological processes or complexes. The proteome of the well studied model plant Arabidopsis thaliana was clustered according to its evolutionary pattern in ~1150 eukaryotes, out of 115 plants. The main components of photosynthesis ("Light" and "Dark" reaction) were found in genes clusters with a specific evolutionary pattern, represented mostly by photosynthetic organisms. These clusters significantly enriched with the main components, regulation and assembly of the photosystem machinery, the components of carbon fixation process and other known photosynthesis-related processes. Importantly these clustered also contained ~90 unannotated genes, that also highly co-expressed correlated with the photosynthetic genes. Overall all our computational- evolutionary analysis suggest additional genes in the photosynthesis-related processes. The identification of these genes might open a new ways to improve photosynthesis efficiency for global yield increasement.

Poster

Illuminating the Specificity-Determinants of RNase-Based Self-Incompatibility

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Many hermaphroditic plants have evolved sophisticated mechanisms to prevent self-fertilization, a property generally termed “self-incompatibility” (SI). In recent years, a particular type of RNase-based SI mechanism, which follows a unique mode of non-self-recognition, was found in several distant families (Solanaceae, Maloideae of Rosaceae, Plantaginaceae). In this mechanism, the female determinant is a cytotoxic ribonuclease (denoted as SRNase), which arrests self pollen growth. The male determinant is an F-box protein (denoted as SLF), which may interact with non-self SRNase proteins, and thus allow for fertilization. A unique evolutionary hallmark of this system is large allelic variability of both SRNase and SLF genes, where the distinction between self and non-self is based on specific molecular recognition between particular SRNase-SLF protein pairs, but not by others. While this phenotypic behavior was characterized in fertilization experiments, the molecular underpinnings of protein interaction specificity are still not understood. Nevertheless, genetic manipulation studies shown that, in both genes, substitution of very few amino acids may alter phenotype. To elucidate the evolution of this protein network, we aim to reveal which protein residues are located in proximity to the interaction interface and to characterize the impact of amino-acid composition on interaction intensities. This would enable a better understanding of the biophysical constraints on the evolution of these proteins and in particular how novel alleles emerge. Our main challenges are: 1) SLF structure is yet to be solved experimentally, limiting the quality of computational docking simulations; 2) the available data of SLF-SRNase interactions is not sufficient for statistical evaluation of inter-protein covariation. We performed phylogenetic analyses and applied various structural modeling tools. Our preliminary results identified strong evolutionary evidence supporting the structure of SLF’s C-terminus domain: a six-blades beta-sheet propeller. This finding highlights the residues at the top of the propeller as good candidates for SLF’s specificity-determinants, since they are less likely to affect protein stability and function. These residues indeed appear less conserved. These results should be further validated in future experiments or by computational models, once additional sequences and interaction data become available.

Poster

Population genomics of Drosophila reveals extensive latitudinal clinal variation in clock genes

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Environmental fluctuations such as temperature, light intensity, food availability, or predation risk are major drivers of adaptation. Because temperature and photoperiod change systematically with the latitude, any genetic variation that follows a latitudinal cline is likely to represent a molecular adaptation, driven by natural selection. Examples of latitudinal cline have been previously demonstrated in circadian clock genes, such as period (per) in Drosophila, or Clock (Clk) in salmons and blue tits. Recently, an extensive Drosophila genomic dataset has been made available by the European Drosophila Population Genomics Consortium (DrosEu), which is aimed at studying the population genomics of D. melanogaster. The data were derived from 48 different populations across Europe and their genomes were sequenced using pool sequencing approach (Pool-Seq). We analyzed allele frequencies of SNPs in core circadian clock genes, including Clk, clockwork orange (cwo), cycle (cyc), cryptochrome (cry), doubletime (dbt), Pigment-dispersing factor (Pdf), Pigment-dispersing factor receptor (Pdfr), per, shaggy (sgg), timeless (tim) and vrille (vri). We used general linear models and identified SNPs that show significant latitudinal clines. Out of 9776 SNPs that were present in these genes, 276 SNPs exhibited a significant latitudinal cline (FDR < 0.05). Importantly, the ls-tim polymorphism that previously was shown to be clinal, is among those significant loci. Of special interest are a missense (non-synonymous) SNP in Clk, three SNPs in dbt that showed extreme clinality (comprising a missense, 5' UTR and an intron variants), and two intronic SNP in Pdfr. The functional role of these SNPs is currently being tested by generating transgenic flies that express the various alleles.

Poster

The mechanism and role of phenotypic plasticity in adaptation of the generalist insect Bemisia tabaci to less-suitable host plants

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Bemisia tabaci (Hemiptera: Aleyrodidae), is a phloem-feeding insect, that utilizes numerous plants as hosts. Still, some plants are considered less-suitable for the insects' development than others. Nevertheless, B. tabaci populations can show a significant increase in their performance on less-suitable host plants within several generations. The mechanisms underlying these generational host adaptation processes are still poorly understood. We aims to explore the possibility that adaptation to less-suitable host plants in B. tabaci involves a plastic change in expression, that results from selection of specific alleles or epigenomic changes in DNA methylation. For this, we established a colony of B. tabaci on habanero-pepper, a less-suitable host plant on which the insect's initial survival is only 5%. Within 10 generations, survival increased to 60% and also the development time was shortened by 2 days. The experiments were conducted in two temperatures (24 ○C and 30 ○C) which suggested that the two stressors (habanero-pepper and 24 ○C) interact, potentially in an antagonistic way. RNASeq data suggest that the samples are arranged according to the host plant on which the whiteflies evolved throughout the experiment, regardless of the original host of the population, and in the population that underwent adaptation to the habanero-pepper there is a higher expression of the proteins associated with the insect's cuticle. In contrast, in order to be able to develop successfully on cotton, B.tabaci should be able to overexpress peptides such as the cathepsin gene family. This data raises the possibility that changes in gene expression are resulting from alteration of the methylation model in these genes.

Poster

The regulatory role of Pitx1 in the skeletal development of sea urchin embryo

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Understanding of structure and function of the gene regulatory networks (GRNs) that drive embryonic development is key to a mechanistic understanding of developmental processes. The GRN that drives skeletogenic cell specification in the sea urchin embryo is one of the most elaborate models of developmental GRNs. We previously studied the downstream targets of the vascular endothelial growth factor (VEGF) pathway, a key factor in sea urchin skeletogenesis, and discovered hundreds of genes affected by VEGFR inhibition. One of the genes that are activated by VEGF signaling is the transcription factor Pitx1, a sea urchin homolog of vertebrates' Pitx1, 2 and 3. The vertebrates' Pitx transcription factors regulate various morphogenetic processes, such as hind-limb development and left-right symmetry. The function of Pitx1 in sea urchin skeletogenesis was not studied before. Here we study the spatiotemporal expression and role of Pitx1 during sea urchin embryogenesis. We show that Pitx1 expression in the sea urchin is highly dependent on VEGF signaling throughout skeletogenesis. Pitx1 is first expressed in the skeletogenic cell clusters where the calcite skeletal rods are initiated, and later its expression is localised to the growing tips of the post-oral rods. Nevertheless, Pitx1 downregulation results in malformations of various degree at all skeletogenic rods of the sea urchin embryo. We propose that Pitx1 has a role in regulating the differentiation of subsets of cells within the skeletogenic lineage, which could explain how skeletal growth is restricted to specific cells within this lineage.

Poster

Characterizing the function and evolution of the HYL1-Like protein (a plant protein) in Nematostella vectensis

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MicroRNAs (miRNAs) are 21 to 24 nucleotide long small RNAs, known to be involved in post-transcriptional gene regulation and play important roles in both plant and animal development. Previously, different components of miRNA biogenesis machinery were identified in the cnidarian Nematostella vectensis, which represents a sister group to the vast majority of extant animals, and most of them were found to be homologous to bilaterian components. However, Nematostella lacked homologues of classical bilaterian Dicer protein partners such as PACT or TRBP. Interestingly, two HYL1 homologues called, HYL1-Like a (Nvhyl1la) and HYL-Like b (HYL1Lb) were identified in Nematostella. Phylogeny reconstruction using the double-stranded RNA-binding motif (DSRBM) of these proteins supported the notion that they are indeed HYL1 homologues, as they cluster with Arabidopsis and rice HYL1. In plants, HYL1 is a partner of the Dicer homolog DCL1 and aids in the precise processing of miRNA primary and precursor transcripts. In this study we have functionally validated the Nvhyl1la by using gene knockdown approach. We injected splicing morpholino antisense oligo into the zygote of Nematostella and found that the development was hindered as more than 95% animals did not proceed into the polyp stage. Further to check the effect of Nvhyl1la on miRNA synthesis, the miRNA expression was quantified by using stem loop quantitative PCR. We observed significantly reduced expression of all the miRNAs in the morpholino-injected animals. This study suggests that the common ancestor of plants and animals might have already employed a HYL1-Like protein in miRNA biogenesis.

Poster

Phylogenetic relationships of Aplousobranchia (Tunicata) based on mitochondrial genomes

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With approximately 1,500 species, the order Aplousobranchia is the largest within tunicates. Although aplousobranchians include several harmful invasive-species, very little is known about their phylogenetic relationships. Our lack of knowledge can be explained by the fact that tiny distinguishing characteristics are used for morphological identification. Until now aplousobranchian relationships have been investigated with only two molecular markers: the nuclear 18S rDNA and mitochondrial (mt) COI gene. However, many relationships were not resolved with these markers. Complete mt sequences have been shown to be highly efficient for solving difficult phylogenetic relationships within tunicates. We sequenced twenty new complete mt genomes using Illumina from representatives of 9 or 12 Aplousobranchia families. Phylogenetic relationships were reconstructed, based on the 13 proteins encoded by mt sequences. Our results provide some unexpected insights regarding Aplousobranchia relationships: Aplousobranchia is divided into six clades: Clavelinidae (clade I); Diazonidae (clade II); Polyclinidae+ Ritterellidae (Clade III); Euherdmaniidae + Polycitor (clade IV); Eudistoma+Pseudodistoma+Sigillina (Clade V); Didemindae+Cystodytes (Clave VI). The family Polycitoridae is found to be polyphyletic, and Polyclinidae is found to be paraphyletic as it encompasses Ritterellidae. Clades V and VI can be characterized by the number of stigmata rows present on the branchial sac: 3 and 4, respectively. Our findings also confirm the sister-clade relationship of Cionidae and Aplousobranchia, the early divergence of Clavelinidae among aplousobranchians, and the nested position of Diazonidae within Aplousobranchia. These results provide a novel view of Aplousobranchia relationships and confirm that sequencing mt genomes is a powerful phylogenetic tool.

Poster

The power of randomization by sex in multilocus haploid and diploid models

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Many hypotheses have been proposed for how and under what conditions sexual reproduction may facilitate an increase in the population mean fitness; these include the Fisher-Muller theory, Muller's ratchet, and others. More recently, a different approach has been proposed, called mixability theory, which argues that sexual recombination shifts the focus of natural selection away from favoring specific genetic combinations of particularly high fitness and toward favoring alleles that perform well across a wide variety of different genetic combinations, or ``mixable alleles.'' Recently it has been shown that, in finite populations, by essentially randomizing the genetic partners for each allele, sex makes selection for mixability analogous to a proper statistical test from which an inference can be drawn. Because of this randomization by sex in a finite population, if one allele performs better than another across the different combinations of alleles with which it interacts, that allele will likely also perform better overall across a vast space of potential combinations of interacting alleles that have not yet been tested. Thus, the interaction of natural selection and sex acts as though an inference is made about the mixability of alleles in future potential interactions. So far, however, this surprising effect has been established only for a single-locus diploid model with interacting pairs of alleles. Here we show that this effect also occurs in the multilocus case, for both the haploids and diploids, and that it becomes substantially stronger with increasing numbers of loci.

Poster

Predicting the Pathogenicity of Variants in BRCA1 by Cross-Species Evolutionary Patterns Using Machine Learning

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A major challenge in clinical diagnostics is estimating the pathogenicity of detected variants of uncertain significance (VUSs). This challenge entails major clinical implications, for example the pathogenicity of VUSs in BRCA1 directly translate into the risk to develop hereditary breast and ovarian cancer, which for high risk cases requires preemptive-surgical or chemotherapeutic treatments. Therefore, accurate estimation of the pathogenicity of VUSs is necessary to improve patient outcomes. One successful approach to predicting VUS pathogenicity is to estimate the functionality of variants based on their conservation-rate across species. Here we present a novel approach for the assessment of VUSs by analyzing nucleotide evolutionary-patterns (EvoPatterns). We hypothesized that additional knowledge can be extracted, not only by inspecting the rate of conservation, but also by identifying informative conservation-patterns of nucleotides across species. To generate EvoPatterns, we profiled the conservation-patterns of BRCA1 nucleotides across 100 vertebrates, which we denoted evolutionary-patterns. We then used machine-learning to uncover relationships between these evolutionary-patterns and the pathogenicity of known variants in BRCA1. EvoPatterns is the first to incorporate complex evolutionary-patterns into prediction tools. We show that EvoPatterns successfully captures associations between distinct evolutionary-patterns of known variants in BRCA1 gene and their pathogenicity, suggesting that the complex nature of the evolution of nucleotides in BRCA1 is affected by the functionality of variants and is reflected in these patterns. Moreover, it correctly predicts the clinical implications of known BRCA1 mutations better than established conservation methods. As the genomic data of patients, disease models and species continue to grow exponentially, we expect EvoPatterns to further improve in prediction accuracy, enabling better association of evolutionary-patterns and phenotypes.

Poster

Vocal communication of the White Spectacled Bulbul (*Pycnonotus xanthopygos*)

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The White Spectacled Bulbul (Pycnonotus xanthopygos) is a common and widespread species, that has not been extensively studied. It is characterized by tight social bonds between individuals and a large repertoire of vocalizations ("words" and songs). We suggest that study of Bulbul vocal communication, particularly of communication outside of a mating context, may lead to insights about the purpose and meaning of the calls and about the ecological impact of such communication. In a preliminary study conducted over the years 2016-2017, at 3 sites in the Upper Galilee region, we have found that the White Spectacled Bulbul has a wide range of complex vocalizations which repeat themselves; that different Bulbul populations have different dialects; and that the "words" are comprised of base units (syllables) which are repeatedly found in different words and dialects. Further, based on our observations, the variation in syllable order seems to follow certain regularities, suggesting possible importance to syllable order. In the poster I will present some preliminary findings about the apparent regularities in Bulbul vocalizations from the Hula valley and will outline an experimental scheme designed to link vocalizations to other dimensions of Bulbul behavior. The study will leverage the species' widespread distribution and the relative fearlessness of Bulbuls to allow high-resolution recording of behavior, coupled with vocalizations, to be compared across sites in different geographical regions. These comparisons will help to elucidate the ways in which vocalizations in general, and dialect differences in particular, influence and relate to the species' ecology and behavior.