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Balancing selection and beyond: machine learning approaches for determining selection scenarios in a complex parameter space

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How important is balancing selection compared to other modes of selection acting on the genome? Despite recent attention to the role of selection in shaping genomic variation, this question has remained open, in part because most methods used to detect selection focus on a single mode of selection, and cannot compare multiple modes of selection at a given site. Previous work from our group (Sugden et al., Nature Communications, 2018) developed the SWIF(r) framework, which uses one-dependence estimation to learn the pairwise joint distributions of population parameters and calculate the per-site probability of different selection scenarios given the parameters observed. Here, we extend this supervised classification framework to detect balancing selection in both simulated data and human genomes, and compare the probabilities of different selection scenarios acting at a given site. In addition to increasing detection power over univariate statistics, the SWIF(r) framework allows us to define the statistical signature associated with a given mode of selection, and to compare statistical signatures across multiple selection modes. For example, during the first several generations after introduction, positive and balanced mutations will both increase in frequency for a number of generations, resulting in similar values for many statistical measures of selection. By identifying scenarios where statistical signatures of differing modes of selection overlap, we can (1) develop new statistical methods to distinguish between modes of selection, and (2) determine parameters that will result in confusion between two or more selective scenarios.

A Bayesian method to detect targets of selection in Evolve-and-Resequence experiments

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Selection is a key process in the evolutionary history of populations; however, while evidence for adaptive evolution is widespread in the literature, it is generally not trivial to measure signatures of selection in genome-wide data. New approaches combining experimental evolution with high-throughput sequencing techniques, allow testing for selection on populations that are subjected to a given selective pressure over time. These approaches are referred to as Evolve-and-Resequence experiments, allowing to disentangle the architecture of the adaptive process. Nevertheless, more efficient and statistically sound methods are needed to detect the true targets of selection. Here, we present a fully Bayesian approach based on the Moran model of allele evolution to estimate selection coefficients from such experiments. The model is characterized by overlapping generations, allowing to describe alternative experimental designs. We also propose a new hypothesis testing approach to detect selected alleles that avoids the computational burden of simulating the empirical null distribution. We tested our method for several demographic and experimental conditions to assess its accuracy and precision. Our method performs well in most of these scenarios, but some care must be taken with specific allele trajectories, i.e. small effective population size (where drift largely dominates) and low starting frequencies. We compare our method with existing ones and report that ours has generally higher accuracy even for such difficult trajectories. Furthermore, our approach outperforms available software in terms of computational time, which permits its use genome-wide.

Local adaptation to spatio-temporal variation in salinity in the halotolerant micro-algae *Dunaliella salina*

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How local adaptation works in microbes is still little understood. The common belief has long been that for microbes, "everything is everywere", such that no broad-scale biogeographic patterns should be expected. Yet at a smaller scale, some micro-organisms inhabit environments that vary drastically over space and/or time. And because their usually enormous effective and census sizes allow for very efficient natural selection and large mutational input (respectively), local adaptation should be favored as long as it is not entirely swamped by gene flow (in which case spatial heterogeneity can maintain variance overall, but does not increase the genetic structure). Searching for molecular signatures of local adaptation at specific loci is however challenging in microbes, because their reproduction system causes the dynamics of adaptation to be quite different from that in obligate sexuals. These dynamics are entirely driven by clonal interference in pure asexuals, while for facultative, and especially environmentally induced sexuals, the possibility for polygenic adaptation may depend on the environment, and covary with the strength of selection. Furthermore, if the environment also varies with time in each locality, then specific response mechanisms such as phenotypic plasticity may be favored by selection, or even undergo local adaptation themselves. To get a better understanding of these processes, we studied natural populations of *Dunaliella salina*, a halotolerant micro-algae that is the main primary producer in hypersaline environment. Its natural habit consists of shallow ponds whose salinity fluctuates with climate conditions (temperature, wind, precipitation) over days, weeks, and seasons. Their plastic traits involved in salinity tolerance are well characterized at the physiological level, and the genetic underpinnings of these traits are well understood. We collected *Dunaliella* from a saltern in Aigues-Mortes, where large ponds with extremely variable mean salinity (from seawater to salt saturation), and different fluctuations in salinity, occur over a few kilometers. We sampled populations from ponds with markedly different salinities, and used whole-genome pool sequencing to study their genomics characteristics. We also characterized their salinity tolerance and acclimation (involving phenotypic plasticity) in the laboratory. We found relatively strong differentiation between populations (Fst ~ 0.2), consistent with some variation in their tolerance curves, and are conducting genome-wide analyses to detect signals of adaptation to fluctuating selection in salinity. We compare these results with the outcome of experimental evolution of different strains from this species exposed to randomly fluctuating salinity.

A clinal polymorphism at *foxo* contributes to life-history adaptation in *Drosophila*

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A fundamental aim of adaptation genomics is to identify polymorphisms that underpin variation in fitness traits. In *Drosophila melanogaster*, latitudinal life-history clines exist on multiple continents and thus make an excellent system for dissecting the genetics of adaptation. We have previously identified numerous clinal SNPs in insulin signaling, a pathway known from studies of mutants to affect multiple life-history traits. With few exceptions, however, effects of natural variants in this pathway have not yet been examined. Here we investigate how two strongly clinal alternative alleles at *foxo*, a major transcriptional effector of insulin signaling, affect fitness components. To evaluate this, we generated recombinant outbred populations in which the focal *foxo* allele was fixed for either the low- or high-latitude allele. Since both diet and temperature modulate insulin signaling, we phenotyped both alleles at two temperatures (18°C, 25°C) and on two commonly used diets that differ mainly in sugar source and content. Consistent with clinal expectations and *foxo* gene function, the high-latitude allele was associated with larger size and reduced wing loading. Furthermore, differences in size between *foxo* genotypes were equivalent to those observed between populations sampled from the latitudinal extremes. Although starvation resistance was typically greater in high-latitude populations, the low-latitude *foxo* allele conferred higher tolerance. The alleles also differed in the expression of *insulin-like receptor* (*InR*), a transcriptional target of FOXO. We observed few genotype-by-environment interactions; overall, allelic reaction norms were rather parallel. Together, our results suggest that allelic variation at *foxo* makes an important contribution to clinal life-history adaptation.

A quantitative framework for mechanisms of pleiotropic and genotype-by-environment interactions

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The effect of an allele depends on the context in which it is measured. In particular, an allele might have different effects on seprate traits, or affect the same trait differently in separate environments. Most work in this area has attempted to classify effects based on whether an allele has an effect in the same direction in each context ('positive pleiotropy'), in opposite directions ('antagonistic pleiotropy'), or significant effects on one trait only ('conditional neutrality'). However, this ignores useful quantitative information about the mechanisms of selection, and introduces a well known statistical bias towards conditional neutrality. I describe a simple method to quantify pleiotropic mechanisms, and apply it to reciprocal transplant experiments investigating the genetic basis of local adaptation. Results indicate that positive pleiotropy is much more common than previously realised, partly because it has been largely ignored.

Assessing the genetic contribution to complex behavioural traits in German Shepherd dogs

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The process of animal domestication involves numerous physiological changes, but possibly more importantly, encompasses important changes in temperament. During the process of dog domestication from ancestral wolves, genetic changes in behaviour have allowed a close bond with humans, thus there is great interest in identifying behaviour-associated genes. However, behavioural traits are complex phenotypes, which have been shown in to be influenced by numerous genetic and environmental factors, complicating their analysis. In this study, we investigated associations between genetic variants and environmental factors with behaviour traits of German Shepherd dogs (GSDs). We used principal components analysis to define thirteen complex behaviour traits for GSDs based on dog owner responses to questions of the established Canine Behavioral Assessment and Research Questionnaire (C-BARQ) and additional questions about playfulness. Linear models were applied to analyse the relationship between the behavioural traits and demographic factors of the dog, its living situation and its management. These environmental factors only explained a small proportion of the variance observed in the behavioural traits and thus, the genetic component of behaviour was also investigated by heritability estimation and genomic analyses. Several behavioural traits exhibited moderate pedigree- and genomic-based heritabilities, with the highest estimates identified for Playfulness and Non-social fear. We identified genomic regions distributed over 17 autosomes that showed at least chromosome-wide significant association with the analysed traits; for several traits, multiple regions were identified, supporting the hypothesis that behaviour traits are influenced by multiple genes. Further genomic analyses are being performed to identify signatures of behavioural selection.

Tracking signatures of response over 20 generations of selection for long leg length in mice

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Pedigreed selection experiments offer a powerful approach to directly observe how genomes evolve under selection. Here, we present genomic dissection of a detailed selection experiment to elucidate the impacts of genetic drift, directional selection, and varying genetic architecture on the response to selection. In this Longshanks experiment, mice in two replicate lines were bred over 20 generations for longer relative tibiae, resulting in 13-15% increase. We combined whole-genome sequencing and linked-read technology to capture changes in allele frequencies and haplotype segregation. We present results in two stages: 1) deep individual sequencing from the founders and generation F17, and 2) haplotype reconstruction through the pedigree. 1) Comparing allele frequency shifts between the founders and F17, we identified a broad polygenic response. By contrasting this against simulations of a pedigree-calibrated infinitesimal model, we found 8 discrete loci of major effect, 2 of which showed parallelism between replicates. Functional testing of enhancers at the major parallel locus *Nkx3-2* revealed that loss-of-function variants contribute to ~10% of the selection response. 2) We tested the feasibility of tracking haplotype segregation through each generation at high resolution by combining linked-read data and pedigree information. We also reconstructed locus-by-locus allele trajectories to contrast against estimates from selective sweeps. Finally, we assessed variation of local recombination rate through tracking the breakdown of haplotypes. We show here that despite small population sizes, selection response is rapid and robust. With nearly complete phenotypic, genomic, and pedigree datasets, the Longshanks experiment provides a comprehensively detailed system to study adaptive genomic evolution.

Human adaptation in the last 10,000 years: new insights from ancient DNA

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Our understanding of human evolutionary history has advanced rapidly in the past decade, primarily due to explosive growth in ancient human genome-wide datasets, mainly from western Eurasia. However, only a handful of studies have used ancient genomes, exploring how humans adapted to the vast array of environments we currently inhabit. Consequently, present understanding of human adaptation is predominantly based on genome research from modern populations. We performed a detailed reconstruction of human adaptation in western Eurasia, combining >1,000 genome datasets ranging from the late Palaeolithic to the Bronze age. These were grouped into 25 populations according to archaeological metadata and compared against five modern human populations. Our analyses reveal that hard selective sweeps have played a much larger role in western Eurasian adaptive history than previously suspected. However, this history has seemingly become obscured in modern European genomes through subsequent bouts of admixture. We find that selective sweeps are aggregated in pathways specific to the immune response and the metabolism of carbohydrate byproducts (i.e. free radicals) and proteins, and that selection often targeted interacting gene cohorts directly involved in responding to stressful stimuli. Our results suggest that ancient Eurasian populations often utilised pre-existing reservoirs of genetic variation to counteract new selective pressures presented during the Neolithic transition. This study highlights the unique potential of ancient genomic datasets to unmask previously hidden evolutionary histories from a molecular biology and population genetics perspective.

Detecting adaptive differentiation in structured populations with genomic data and common gardens

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Adaptation in quantitative traits often occurs through subtle shifts in allele frequencies at many loci, a process called polygenic adaptation. While a number of methods have been developed to detect polygenic adaptation in human populations, we lack clear strategies for doing so in many other systems. In particular, there is an opportunity to develop new methods that leverage datasets with genomic data and common garden trait measurements to systematically detect the quantitative traits important for adaptation. In this talk, I discuss new methods that do just this, using principal components of the relatedness matrix to detect excess divergence consistent with polygenic adaptation and using a conditional test to control for confounding effects due to population structure. I apply these methods to inbred maize lines from the USDA germplasm pool and maize landraces from Europe. I also discuss applications to Arabidopsis traits measured in different environments to detect adaptation for GxE. Ultimately, these methods can be used with additional domesticated and wild species to give us a broader picture of the specific traits that contribute to adaptation and the overall importance of polygenic adaptation in shaping quantitative trait variation.

Genetic basis of flowering time variation within a Scandinavian population of *Arabis alpine*

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Understanding the molecular-genetic basis of adaptive processes is a major goal in modern evolutionary biology. In plants, flowering traits are often associated with fitness. We study the natural variation in flowering time and its genetic basis in the perennial plant species *Arabis alpina*. In previous field and greenhouse experiments, we have shown that the timing of flowering varies among and within European populations. Here we focus on a population growing in the Scandinavian Mountains in Norway. Particular variation in flowering time was observed within this population in the greenhouse experiments. To study the genetic basis of the observed variation, early and late flowering individuals from this population were crossed to obtain an F2 population for QTL (Quantitative Trait Locus) mapping. Flowering time segregated within the F2 population and QTL mapping identified one major and four minor QTL regions in different linkage groups. We now focus on the strongest-effect QTL and use a combination of high-resolution mapping and candidate gene analysis to identify the causal gene(s). Further field work will provide information about the adaptive significance of the observed phenotypic and genetic variation.

Optimizing the power to identify QTLs with Evolve and Resequence

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Evolve and Resequence studies are frequently used to dissect the genetic basis of quantitative traits. By subjecting a population to truncation selection for multiple generations and contrasting the allele frequencies between selected and non-selected populations, the causative SNPs may be identified. The role of different parameters, such as, the population size or the number of replicate populations have been examined in previous works. However, the influence of the selection regime, i.e. strength of truncation selection during the experiment, remains little explored. Using whole genome, individual based forward simulations of E&R, we found that the power to identify the causative alleles may be maximized by gradually increasing the strength of truncation selection during the experiment. Notably, such an optimal selection regime comes at no or little additional cost. Interestingly, we also found that the selection regime that optimizes the power to identify the causative loci is not necessarily identical to the selection regime that maximizes the phenotypic response. Finally, our simulations suggest that an E&R study with an optimized selection regime may have a higher power to identify the genetic basis of quantitative traits than GWAS.

The role of cryptic genetic variation in regulating the transcriptional response to new and stressful environments in flies

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The way organisms respond to new and/or stressful environments, as well as the role that standing vs *de novo* genetic variation play in such response have been the subject of extensive exploration in the field of evolutionary biology. However, a less explored topic is the amount of standing genetic variation that plays no role in regulating phenotypic variation under normal conditions but, under novel or stressful environments appears to affect/control such variation – this is known as cryptic genetic variation. Here we use an outbred population of *Drosophila melanogaster* to address the role of such cryptic genetic variation in modulating the transcriptional response of flies to high sugar diet. We sampled ~800 flies exposed to either control or high-sugar food over the course of their development, and generated transcriptional and SNP profiles for each individual fly. The fly population used here offers an extensive repertoire of genetic variation in as many genetic backgrounds as flies there are, allowing us to get a comprehensive overview not only of diet-specific eQTLs, but more importantly, of context-dependent eQTLs. Our results suggest that there is abundant cryptic genetic variation that only plays a role when flies are exposed to high-sugar diet, and that such variation is not only associated with disruption of coexpression patterns found under control conditions (decanalization), but also with possible gains of gene coregulation.

Next generation experimental evolution: expanding the evolutionary toolkit in pursuit of the molecular basis of phenotypic evolution

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Experimental evolution is a powerful approach for determining the identity and evolutionary dynamics of causal variants underlying the adaptation to new environments. While studies in single cell organisms starting from a fixed genotype have been frequently successful in this pursuit, results from multicellular organisms with large amounts of initial standing variation have revealed that the response to selection can be complex and multifaceted. The next step in understanding—and potentially simplifying—these dynamics is to bring precise control of additional evolutionary forces, such as migration, recombination, mutation, and outcrossing into the experimental evolution toolkit. We use replicated adaptation to high temperature within the nematode *Caenorhabditis remanei* at three different migration treatments (none, intermediate, and high) to illustrate the usefulness and potential impact of this approach. Evolutionary response was tracked both via changes in reproduction and via whole genome sequencing of several dozen replicate populations. In keeping with theory, high migration populations have far fewer sites that show evidence of positive selection. However, the resulting genetic architecture is still far from simple, moving from thousands of sites under selection to perhaps several hundred sites. Thus, divergence under migration can indeed influence the genetic architecture of adaptation, but whether not that architecture can be "simple" is likely to depend on migration-specific dynamics and the underlying functional biology of the traits themselves. We are developing additional genetic and genomic tools that allow the manipulation of even more evolutionary processes, with the long-term goal of creating a strong empirical platform for linking population genetic processes with quantitative genetic outcomes.

Genome-wide sexually antagonistic variants reveal longstanding constraints on sexual dimorphism in the fruitfly

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The evolution of sexual dimorphism is constrained by a shared genome, leading to 'sexual antagonism' where different alleles at given loci are favoured by selection in males and females. Despite its wide taxonomic incidence, we know little about the identity, genomic location and evolutionary dynamics of antagonistic genetic variants. To address these deficits, we used sex-specific fitness data from 202 fully sequenced hemiclonal Drosophila melanogaster fly lines to perform a genome-wide association study of sexual antagonism. We identified ~230 chromosomal clusters of candidate antagonistic SNPs. In contradiction to classic theory, we found no clear evidence that the X chromosome is a hotspot for sexually antagonistic variation. Characterising antagonistic SNPs functionally, we found a large excess of missense variants but little enrichment in terms of gene function. We also assessed the evolutionary persistence of antagonistic variants by examining extant polymorphism in wild D. melanogaster populations. Remarkably, antagonistic variants are associated with multiple signatures of balancing selection across the D. melanogaster distribution range, indicating widespread and evolutionarily persistent (>10,000 years) genomic constraints. Based on our results, we propose that antagonistic variation accumulates due to constraints on the resolution of sexual conflict over protein coding sequences, thus contributing to the long-term maintenance of heritable fitness variation.

Modeling introgression under linked, polygenic selection

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Highly polygenic architectures are often described using the infinitesimal model which assumes an infinite number of unlinked loci of infinitesimal effects, and has been remarkably successful in predicting short-term advance of quantitative traits under selection. We explore an extension of the infinitesimal model that incorporates linkage, by assuming a large number of loci of weak effect, spread over a linear genome. We analyse the introgression of a block of genome under directional selection into a population that lacks genetic variation, and clarify how the resultant dynamics is shaped by the interplay between recombination and polygenic selection. Our analysis touches upon various questions that have a bearing on the interpretation of genomic data: Is the introgression of a genomic block that contains many weakly selected loci qualitatively different from introgression in the absence of selection? Is a block with a large number of weakly selected loci less likely or slower to introgress than a single strongly selected locus? Do the same genomic fragments introgress across replicates, i.e., is adaptive introgression predictable even when selection on individual loci is weak?

Tracing the genomic footprints of fisheries-induced adaptation in Lake Malawi cichlids

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Besides their role as a model system for biological diversity and speciation, cichlids of the Lake Malawi radiation are the most important source of animal protein for millions of people and subject to intensive fisheries. This is particularly in Lake Malombe, a shallow, intensively fished water body at the out-flow of Lake Malawi. A striking reduction in adult size has been reported for the same species caught in Lake Malombe compared to Lake Malawi. Theory predicts that heavy fishing pressure induces selection for faster life histories and early maturation. Hence, besides direct demographic and environmental effects, local genetic adaptation could contribute to observed differences in adult size. To characterise the evolutionary and adaptive history of these populations, we sequenced for two species 24 individuals each from populations from Lake Malombe and Lake Malawi, corresponding to weak and heavy fishing intensity, respectively, and looked for signals of differential selection. While we found that populations are extremely closely related overall, narrow genomic regions of high population divergence suggest differential adaptation between the populations. Using sequencing data from a third population, we identified allele frequency changes specific to heavily fished populations. Thereby identified candidate genes include loci previously implicated in fisheries-induced early maturation. Furthermore, we identified cross-species gene flow specific to Lake Malombe, allowing us to test the hypothesis whether recent gene flow contributed to adaptation in this system.

How do *Arabidopsis lyrata* ssp. *petreae* populations at the edge of the distribution adapt, while coping with decreased genetic variation?

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The accumulation of deleterious mutations at the range edge of expanding species may interact with their ability to adapt locally. We investigate the morphological and genetic differentiation of two *Arabidopsis lyrata* spp *petreae*, populations growing at the range edge and in the likely refugium of the species. Common garden experiments revealed that the two populations differ in their response to frost, while showing distinct patterns of vegetative and inflorescence growth in summer, confirming previous evidence for local adaptation. Furthermore, we used whole genome sequences to investigate the divergent signatures of positive and negative selection in the genome. In the Northern population, we find signs of a stronger bottleneck and increased proportion of heterozygotes. The latter pattern is in agreement with both a fast restoration of S-allele diversity and an increased flower pollination rate. We propose that the maintenance of self-incompatibility allowed the expression of heterozygote advantages and may have helped the population cope with the eroding effects of the severe bottleneck.

Polygenic adaptation and patterns of hitch-hiking

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Integrating evolutionary quantitative genetics with population genetics requires understanding how polygenic adaptation of quantitative traits impacts variation at linked neutral sites ("linked selection"). Thus, we need both analytical theory and efficient simulation schemes allowing for partial linkage amongst mutations affecting traits. I will show how "succinct tree sequences" allow for chromosome-scale forward-time simulations of polygenic traits in very large populations with arbitrary demography. Such simulations retain the entire recombination graph for the simulation while decreasing run times by several orders of magnitude. Using simulations of a single polygenic trait subject to Gaussian stabilizing selection, I show that the time to adapt to a sudden "optimum shift" and the patterns of variability flanking adaptive mutations depend on several factors, including the magnitude of the optimum shift, the mutational variance, the fraction of new mutations with a large effect on the genetic load (*sensu* DeVladar and Barton 2014, Genetics), and the details of the distribution of effect sizes of new mutations. For this classic model of an additive trait, detectable sweeps from both new mutations and those from standing variation have "hard sweep"-like effects on linked neutral variation. The reason for this is that standing variants are drawn from the mutation-selection equilibrium of this model where effect size and frequency are inversely-related. Thus, large-effect sweeps from standing variation are rare at the time of the optimum shift, resulting in few haplotypes sweeping to high frequency.

Efficiency of outlier methods for detecting loci involved in a polygenic trait under divergent selection: a simulation study

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As populations of the same species live in different environments, phenotypic optima differ for many traits among these populations. These traits are thus under divergent selection. Traits can be monogenic or polygenic, but most commonly-used methods aiming at detecting divergent selection were developed under a framework assuming monogenic selection. Using the quantiNEMO program, we simulated populations connected by gene flow and submitted to divergent selection on a given polygenic trait. We showed that, in many cases, the loci involved in the polygenic trait did not show a strong increase in their level of among-population differentiation. This can affect the efficiency of the methods aiming at detecting divergent selection, which look for outlier loci presenting an excess of differentiation as compared to loci assumed to be neutral. We benchmarked three of these methods (FDIST, OutFLANK and PCAdapt) under different selection schemes. Under all conditions, none of them was very efficient at detecting genes involved in polygenic traits under selection, but some were more powerful and/or more conservative than others depending on the conditions.

Distance to trait optimum strongly affects the selection signature of polygenic adaptation – implications for natural laboratory selection studies

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The genetic basis of polygenic adaptive traits is becoming a highly topical research theme. While polygenic adaptation of a quantitative trait after a shift in trait optimum is frequently associated with small allele frequency changes of many loci, recent work suggests that also large allele frequency changes can be expected. Laboratory natural selection (LNS) experiments provide an excellent experimental framework to study the genetic architecture of adaptation under controlled laboratory conditions: time series data in replicate populations evolving independently to the same trait optimum can be used to study selected loci. Nevertheless, the choice of the new trait optimum in the laboratory is typically an ad hoc decision without consideration of the distance of the starting population to the new optimum. Here, we study how the choice of the new trait optimum in the laboratory affects the inferred genetic architecture of adaptation. We used forward-simulations and simulated scenarios in which a population evolved to different trait optima. Allele frequencies and fitness of 100 beneficial alleles contributing to the trait were recorded at multiple time points mimicking an 'Evolve & Resequence' study. We show that the inferred genetic architecture of a trait in LNS studies highly depends on the distance of the ancestral population to the experimentally chosen trait optimum. Furthermore, the significance cut-off used for identification of loci in a genomic scan also has a major impact on the results. Our results have not only a major impact on the design of future E&R studies, but also on the interpretation of current E&R data sets.

Studying complex trait architecture of rosette growth adaptation to different temperatures in *Arabidopsis thaliana*

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Climate variation exerts significant evolutionary pressure on plants. *Arabidopsis thaliana* has a large geographic range and local varieties have acquired specific adaptations to their local environment. As a winter-annual, *A. thaliana* grows during autumn under decreasing temperatures that are usually considerably lower than standard lab conditions. Northern varieties may never experience temperatures above 10ºC until they are about to flower in spring. Although we expect northern strains (natural inbred lines, or "accessions") to be adapted to lower temperatures, the importance of temperature adaptation and the mechanisms involved are not known. To investigate the importance of adapting growth to lower temperatures we exposed a global set of *A. thaliana* accessions to simulated Swedish autumn temperatures. Over three months we gradually let the temperature decrease from 16 to 0ºC. Growth was phenotyped by daily taking pictures of the rosettes. At 16ºC the accessions originating from warmer regions clearly grew better than accessions from colder climates. When colder temperatures were reached, by the end of the simulated Swedish autumn, accessions from colder climates showed improved growth. We further confirmed this by characterising growth at constant temperatures. We saw that accessions from colder regions were less reduced in growth rates in colder temperatures, relative to their growth in warm conditions. Phenotypically we have indications that growth may be adapted to local temperatures. Currently, we further investigate what the genetics are behind the temperature adaptation of this highly complex trait and whether there are signs of polygenic adaptation.

Sex-specific adaptation to higher temperatures in *Drosophila*

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Sexual conflict occurs when natural selection favors opposing trait values in females and males. Pervasive sexual dimorphism in common traits implies the resolution of the conflict. Despite decades of intensive research, the molecular mechanism resolving the conflict has still not been conclusively documented. In this study, we exposed replicated *Drosophila* populations to a novel temperature regime. After more than 100 generations of adaptation, we discovered clear evidence of sexually dimorphic evolution in gene expression, metabolic and behavioral phenotypes. Male flies accelerated the turnover of their fatty acid metabolism while females slowed down the synthesis of fatty acid. In contrast, male flies deactivated the neuronal transcription activity and increased their reproductive activity at higher temperature while none of the involved genes showed significant changes in females. These results indicate that males and females have different functional requirements in the new temperature environment, but this potential genetic conflict was quickly (at least partly) resolved. Remarkably, this is the first study focusing on a resolving sexual conflict in an evolution experiment, which provides the unique opportunity to address the questions of the underlying mechanisms and phenotypic requirements empirically, rather than by indirect observation. With a regulatory network analysis, we aim to test the hypothesis that genetic conflict can be resolved quickly by the existing sex-specific regulatory architectures. Furthermore, we plan to demonstrate the antagonistic fitness effect of several sex-specifically or antagonistically evolving genes by experimental manipulation of their expression levels.

Comparative and population genomics of *Gyrodactylus bullatarudis* reveals rapid adaptive evolution of genes modulating host immune response

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A monogenea fluke *Gyrodactylus bullatarudis* is a common ectoparasite of the guppy fish (*Poecilia reticulata*), providing a good system for studding host-pathogen coevolution. To get insight into the molecular basis of this process we explored *G. bullatarudis* genome. The reference genome was sequenced and assembled from an inbred line. The genome assembly (genome size = 84.5Mb, scaffold N50 = 308kb, L50 = 75) and annotation (10749 genes, 15035 proteins, 40% genes functionally annotated) was then used for comparative analyses with other flatworms genomes and for population analyses with resequenced local populations originated from 3 Trinidadian rivers. We found high rate of molecular evolution in monogenea linage. The 522 gene families that experienced duplications in the monogenean linage were enriched in many coevolution related Gene Ontology terms, including G-protein coupled receptor signaling pathway, cell differentiation and response to stimulus. The gene family that experienced the largest number of duplications was the family of serine proteases with deep homology to cercarial elastase genes in *Schisostoma mansoni* – an enzyme that plays pivotal role in penetrating skin during infection. Interestingly, a single gene member of this family (Gbulla1a000092) was also identified as the most diverged between local populations gene. The rapid diversification of this gene was likely initialized by local chromosomal rearrangement. Other genes differentiated between local populations were associated with such processes as regulation of eating behavior or vacuolar protein processing. These results suggest rapid molecular evolution of *Gyrodactylus* species in genes likely involved in hosts-pathogen coevolution.

Investigating adaptation within populations of Swedish sand lizards

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Swedish sand lizards (*Lacerta agilis*) occur at the northern edge of the species' European distribution. The Swedish population was established while a land bridge to Europe was available, between 9,000-10,000 years ago, expanding as far north as 61st parallel. The modern population, however, has faced habitat fragmentation and exist in varying degrees of isolation and population size. Genetic markers have shown lower genetic diversity within Swedish populations compared to the European core, but nevertheless, sand lizards have adapted and populations persist across the Swedish landscape. We aim to investigate the signatures of adaptation within populations of Swedish sand lizards, taking advantage of the long-term monitoring and sampling from over 30 years research in focal Swedish populations. This will be complemented by a new study that will survey sand lizards from across the whole geographic distribution in 2019.

SRPK* and *Trf2* contribute to the expression of dormancy in *Drosophila

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Genetic adaptations facilitating survival have been of long-standing interest to evolutionary biologists. Dormancy is a well-studied adaptation to facilitate overwintering and has often been considered to have a polygenic basis due to its complex nature. In *Drosophila*, dormancy is studied as a state of suppressed oogenesis in the ovaries. Although few studies have dived into the genetics of dormancy in *Drosophila*, a genome-wide scan for the genetic basis of this ecologically extremely important trait has not been done. We screened a South African *D. simulans* population for dormancy incidence at two temperature regimes (10°C and 12°C, LD 10:14) and performed a Pool-GWAS to identify the genetic variation that contributes to the expression of the syndrome in this population. We sequenced pools of isofemale lines that are either dormant or non-dormant at both temperatures, or shift from dormancy to non-dormancy between these two temperatures (plasticity). In the SNP level, we identified many polymorphic positions, which is in accord with the expected polygenic nature of the trait. However, when we searched for structural polymorphisms, we identified two prominent associations with the genes *SRPK* and *Trf2*. In the case of *SRPK*, we are probably dealing with an associated retrogene present in the plastic pool. In the case of *Trf2*, a tandem duplication in a 5' UTR intron is present in the non-dormant and plastic pool. Both genes are highly expressed in the ovaries. Our results suggest that even complex traits can be underpinned by few loci with large effects.

Population genetics of speciation

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While ecological/competitive/adaptive speciation received significant empirical support recently, its theory is not considered, as well established. Such process is impossible on a fixed (frequency-independent) adaptive landscape. Adaptive dynamics provides theory of evolutionary branching for clonal evolution; the key point is that evolution feeds back on the landscape. On this basis Dieckmann & Doebeli (1999) provided numerical support for adaptive speciation with two diploid multilocus traits (an ecological one and a mating one) in a Lotka-Volterra-type ecological context. Here I report an analytic approximation for this model. Frequency-dependent selection against intermediate ecological trait values drives evolution of assortativity. However, assortativity based on ecological phenotype alone cannot ensure reproductive isolation in presence of segregation variance. Fortunately, the selection regime operates also to selectively eliminate allelic (and segregation) variance. This process is arrested in the infinitesimal limit, i.e. for infinite number of loci, and is slow for high, but not infinite locus number. The two process together can result in significant reproductive isolation. The counterintuitive aspect is that the two processes, selection for assortativity and for decreasing variance, are usually attributed to disruptive and stabilizing selection, respectively. Natural origin of this double personality of the selection regime will be explained. The emerging picture is that speciation is an adaptation to an environment with multiple niches.

Inheritance of rapidly evolved morphometric traits in Italian wall lizard

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Evolution is generally accepted to be gradual and slow, but there is evidence of evolutionary events on ecological time scales from both natural and experimental studies. In 1971 five pairs of Italian wall lizard *Podarcis sicula* native from the island of Pod Kopište were introduced on the nearby islet Pod Mrčaru (Adriatic Sea). Follow up study showed that in only 35 years distinctive changes in ecology, morphometry and gut structure occurred in transplanted population, probably linked to the adaptation to omnivory. Until this date it is unknown if this phenotypic shift is due to genetic changes or phenotypic plasticity, to unravel this question we conducted lab crosses in a common garden experiment. This experiment encompasses reciprocal crossing between and within ancestral and the transplanted population raised on the same insect-based diet, and phenotyping of all parents and offspring. Nine morphometric traits were measured in the parental and F1 generations through the year time-line of development and here we present the preliminary results of this experiment. This approach will allow us to estimate the mode of inheritance and heritability of these traits. In addition, using GBS sequencing we defined more than 58.000 SNPs for the two populations from the transplant experiment and 18 other natural populations of *P. sicula* and *Podarcis melisellensis from the region. We identified* candidate loci for evolution that were significantly different between the transplanted population and others. These results will be combined with genotype-environment-phenotype associations to tackle the mechanism underlying rapid evolution of *P. sicula*.

Ecological insights to the identification of adaptive scenarios

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A major difference between studies of selection and adaption lies in the need of providing evidence for the correspondence of the potential targets and agents of selection in case of adaptation studies. While the methodological problems of detecting genomic signatures of selection, which are related to population structure, dispersal and allele surfing, are addressed, less attention is paid to the accurate identification of the ecological situation driving the selection processes. Ecotypes usually differ in several traits in response to several differences in the local communities. Besides climatic variables, associated changes in population density, in population regulation, in the food web may all impose selection that ought to be considered systematically in genome–environment association studies. Theoretical considerations as well as many empirical results confirm that the target of selection may change with the quality and quantity of the available resources and with the presence or absence of natural enemies. Thus, the more knowledge one has about the ecological differences between the locations compared, the higher the chance that all the corresponding targets and agents of selection are revealed instead of artefacts. A list of the defining characteristics of an ecological situation will be given based on the framework of Darwinian ecology.

Using ultra low-coverage whole-genome sequencing to reconstruct founder-line mosaic genotypes in intercross pedigrees bred from outbred founders

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Experimental intercrosses between outbred founder populations are powerful resources for mapping loci contributing to complex traits (Quantitative Trait Loci or QTL). Here, we present a method to, with high-resolution, infer founder-line mosaics in such populations using whole-genome high coverage sequence data on the outbred (heterozygous) founder individuals (~30x) and ultra low coverage sequence data on intercross individuals (<0.5x). The method is illustrated in a large advanced intercross pedigree (~4,000 individuals) between lines of chickens that have been divergently selected for 40 generations for the same trait (body weight at 8 weeks of age). We describe how the individuals were whole-genome sequenced in a cost- and time-efficient manner using a Tn5-based library preparation protocol optimized for this application. In total, 7.6M markers segregated in this pedigree and 10.0 to 13.7% were informative for inferring the founder line mosaic genotypes in the intercross individuals within individual F_0-F_2 families. The genotypes inferred from the ultra low coverage sequence data were highly consistent with genotypes obtained for individual SNP markers across the genome using a GoldenGate assay (95%). The resolution of the recombination breakpoints was high with 50% being resolved within <10kb, facilitating QTL mapping and linkage map construction in such pedigrees. The proposed method thus provides high quality, high-resolution genome-wide genotypes in a cost-efficient manner to help pinpoint QTL with highest possible resolution in intercross populations bred from outbred (heterozygous) founders.

References:

Preprint describing method: https://www.biorxiv.org/content/early/2018/09/20/421768

Link to software pipeline: https://github.com/CarlborgGenomics/Stripes

Understanding methylation variation in *Arabidopsis thaliana*

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Epigenetics is fascinating as it can make Lamarckian adaptation possible with the inheritance of acquired characteristics. In *Arabidopsis thaliana*, a model plant system, experiments suggest DNA methylation marks are faithfully inherited over generations and they affect important traits. Genome wide association studies in natural populations suggests that most of the epigenetic variation has a genetic basis. We try to determine different sources of variation for global pattern of methylation. We are performing coalescent simulations and analysing intercross populations to determine genetic or epigenetic nature of methylation patterns.

Selection pressure in wild and domestic pigs

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Domestic animal histories are evolutionary experiments that have often lasted for millennia with the result of dramatic phenotypic changes to suit human needs. This history can be quite complex; many events remain unknown or poorly documented. They, therefore, offer a material of utmost interest to study the interplay of demography and accelerated adaptation. The pig (*Sus scrofa*) is a particularly interesting species and one in which there is abundant genetic tools and sequence data available. It originated in the Southeast Asian region ca. 4 MYA and migrated towards the west, colonizing all climates in Eurasia except the driest. Subsequently, the pig was domesticated out of local wild boars independently in both Asia and Europe ~9,000 years ago. The main purpose of this work is to detect the selective effect of the domestication. Domestication is an intense selection process that occurred in a short evolutive time and, as a result, it is expected that new mutations have been accumulated in a small proportion in relation to the mutations segregating at the whole genome. In all, a genome-wide appraisal of the relevance of protein coding changes associated with domestication is largely incomplete in animal species. To fill this gap, here we have investigated the patterns of selection genome-wide in domestic and wild pigs via the McDonald-Kreitman test (MKT), which exploits the fact that the ratio between non-synonymous and synonymous/silent mutations within a population is distorted under selection when compared to the same ratio in terms of divergence. Thus, we have analyzed the differential ratio of polymorphism-divergence of wild and domestic pigs at genomic, metabolic pathway and gene scale, in order to evaluate the effect of selection and of demographic patterns during the domestication process.

Connectivity and adaptation capacity of common octopus and red shrimp populations across the Mediterranean

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In this era of fast global change, defining connectivity and adaptive potential of marine stocks is critical for assessing their resilience to the selective pressures exerted by climate change or fisheries. However, management of exploited marine species is often limited to the geopolitical boundaries and stocks are perceived as static, non-evolving units. Though the use of genetics tools is not pervasive in fisheries management, evolutionary concepts that derive from its use provide much needed information regarding stock structure and its adaptation capacity. In our study, we examine the integration of evolutionary-based knowledge in fisheries conservation of two target species: common octopus, *Octopus vulgaris* and red shrimp *Aristeus antennatus*. To that end, we sampled 19 octopus and 12 red shrimp populations across the Mediterranean and collected data on their distribution, status, and fisheries. Populations were genotyped using genotyping-by-sequencing (GBS) approach and a number of polymorphic genetic markers (SNPs) were validated for each species and population. In order to assess stock structure, genetic differentiation among populations was estimated with F-statistics and patterns of genomic variation across spatial scales were obtained, providing evidence of connectivity. The dataset was tested for correlation with the differences in environmental factors between sampled sites, and for evolution under selection in order to investigate occurrences of local adaptation. Here we provide high resolution perspective on structure, connectivity, and local adaptation of octopus and red shrimp populations in the Mediterranean and indicate fishery areas that are critical to preserve, contributing directly to the sustainable management of Mediterranean fishery populations.

Evolve and Resequencing (E&R) studies allow us to monitor adaptation at the genomic level

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By sequencing evolving populations at regular time intervals, E&R studies promise to shed light on some of the major open questions in evolutionary biology such as the repeatability of evolution and the molecular basis of adaptation. However, data interpretation, statistical analysis and the experimental design of E&R studies increasingly require simulations of evolving populations, a task that is difficult to accomplish with existing tools, which may i) be too slow, ii) require substantial reformatting of data, iii) not support an adaptive scenario of interest or iv) not sufficiently capture the biology of the used model organism. Therefore, we developed MimicrEE2, a multi-threaded Java program for genome-wide forward simulations of evolving populations. MimicrEE2 enables the convenient usage of available genomic resources, supports biological particulars of model organism frequently used in E&R studies and offers a wide range of different adaptive models (selective sweeps, polygenic adaptation, epistasis). Due to its user-friendly and efficient design MimicrEE2 will facilitate simulations of E&R studies even for small labs with limited bioinformatics expertise or computational resources. Additionally, the scripts provided for executing MimicrEE2 on a computer cluster permit the coverage even of a large parameter space. MimicrEE2 runs on any computer with Java installed.