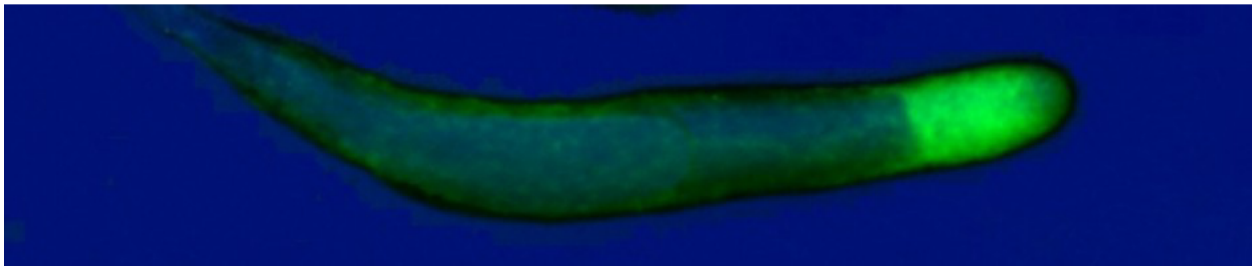


The role of genetic architecture and constraint in the maintenance of genetic diversity

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Introduction:



The Darwinian idea of ‘survival of the fittest’ is central to our understanding of the diversity of life on this planet. However, if only the fittest survive and reproduce, then why do we see so much variation among individuals in traits that are tied to fitness? Explaining the presence of genetic variation is thus one of the fundamental problems in evolutionary genetics. This is because different genetically variable traits often appear to have obvious fitness consequences, thus raising the question of what processes favour the existence of variation or allow for its persistence in the face of selection? One striking example of such variation is cooperative behaviour in which individuals perform costly acts that benefit others within groups. Cooperation is ubiquitous in nature, and is thought to underpin several major evolutionary transitions. However, the evolution and maintenance of cooperation is a paradox because it is potentially vulnerable to exploitation by ‘cheaters’ (or ‘defectors’) that gain the rewards of cooperation while paying less than their fair share of any associated costs. Cooperation can thus set the stage for conflict and competition between the self-interests of cooperating individuals. Consequently, to understand cooperative systems it is important to consider traits associated with cooperation in the context of conflict. Importantly, when cooperative traits are examined in diverse systems, one striking and unexpected feature is observed: individuals vary greatly in the *degree* to which they cooperate. For example, genetic polymorphism of defectors/cheaters and cooperators has been observed in the RNA phage phi6, the quorum sensing system of *Pseudomonas aeruginosa*, multicellular development in the social amoeba *Dictyostelium discoideum*, and production of queens in leaf-cutter ants. Importantly, although kin selection theory based on Hamilton’s rule can predict conditions under which selection favours cooperation and cheating, where individuals interact with relatives that gain the benefits of any costly cooperative acts and also bear the cost of exploitative cheating, it does not allow for polymorphism – i.e., it cannot explain variation in cooperation and cheating. The processes that favour the existence of such natural variation or allow for its persistence in the face of selection thus remain unknown.

Project Summary

We believe that a novel approach is needed to address the existence of such natural variation or allow for its persistence in the face of selection, where one considers both the nature of genetic variation in populations and the underlying genetic architecture of social traits, since these ultimately determines

how evolution can shape the system. We therefore propose to employ a uniquely powerful integration of computational, genomic and experimental approaches using the social amoeba *D. discoideum* to achieve the following goals:

1.1 Genome-wide identification of loci responsible for patterns of natural variation in social and non-social traits. You will integrate high throughput phenotyping (whole genome next generation sequencing) and large-scale genotyping of a panel of natural isolates to identify sequence variation associated with variation in fitness related traits. These data will provide unprecedented insights into the genetic architecture of *natural* variation in social and fitness related traits.

1.2. Understand the importance of pleiotropy in shaping variation. You will examine different fitness related traits to determine the degree to which variation in traits presumed to be under selection are controlled by the same loci. These results will provide insights into the genetic constraints (trade-offs) that potentially shape patterns of variation in social and non-social traits.

1.3. Validate the causal role of genes associated with natural variation in fitness related traits. You will generate gene knock-out and allelic replacement strains to experimentally confirm the causal influence and pleiotropic effects of genes putatively underlying natural genetic diversity.

1.4. Examine signatures of selection on social and non-social genes. You will model sequence evolution to understand the processes shaping diversity in genes identified by association analyses, as well as those predicted or previously confirmed to play a role in social and non-social traits by experimental approaches. Most importantly, we will apply tests to contrast predictions from a series of models to understand the evolutionary origins and maintenance of genetic variation.

Research training: Training in quantitative, computational and wet lab experimental skills is crucial to ensure UK scientists continue to remain world leading. This interdisciplinary project is therefore ideally suited to meet these professional development needs. The student will be trained in cutting edge quantitative skills related to genomic and phenotypic data manipulation, association mapping, maximum likelihood based mixed modelling, and computer simulation. The student will also develop analytical skills through the integration of mathematical theory with the analysis of experimental results. These skills will provide the student with a multifaceted toolkit that will prepare them for a research career.

References

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