Summer 2024 Studentships - Projects List

Supervisor: Prof. Nazif Alic, Institute of Healthy Ageing

https://profiles.ucl.ac.uk/195

Project Title: Transcriptional regulation of longevity in *Drosophila*

Project Outline: Transcriptional regulation of gene expression fundamentally underlies the plasticity of animal physiology, an animal's ability to adapt to changing internal and external conditions. We are interested in how regulation of transcription contributes to longevity, specifically downstream from endocrine pathways that maintain organismal homeostasis. We are studying transcriptional programmes triggered by sequence-specific transcription factors as well as the roles of the basic transcriptional machinery including RNA polymerases I and III in adult animal physiology and ageing. We use a combination of genetic, genomic, computational and physiological assays to uncover processes that drive ageing or those that promote longevity. The project could be in one of two areas: (1) molecular mechanisms of longevity downstream of RNA polymerase I or (2) the role of "fight-or-flight" monoamines in animal ageing. The exact project can be tailored based on the student's interest and current work in the laboratory. Examples of skills learned: fly genetics and physiology, ageing, molecular biology, computational analysis.

Eligibility: No specific prerequisites but an interest in the biology of ageing is a plus.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: n.alic@ucl.ac.uk

Supervisor: Dr. Florencia Camus, Centre for Life's Origins and Evolution

https://profiles.ucl.ac.uk/57803

Project Title (1): Understanding the role of metabolic genes in adaptation

Project Outline: Metabolism lies at the core of organismal survival and reproduction. Mitochondria are key to metabolic adaptation as they provide the hub that converts food into energy. This process is complicated by the fact that mitochondrial function relies on genes from two different genomes – nuclear and mitochondrial. We expect rapid coevolution between mitochondrial and nuclear encoded respiratory genes to occur within populations. Coevolution should also consider the environment these populations are adapting to, with rapid environmental change predicted to have massive impact on metabolism. Evidence suggests that matching could impact the phenotypic responses to dietary and temperature variations.

This project will aim to examine how mito-nuclear genotypes impact thermal tolerance traits in Drosophila melanogaster. We have source flies from the east coast of Australia, where we know that the north and south populations differ in thermal tolerance traits. Interestingly, there are also large genetic differences with populations from the north and south of Australia having different mtDNA genomes. We have created several new strains of fly that have either matched or mismatched mito-nuclear genomes. Using these genetic tools we will be able to fully understand the contribution of both these genomes, plus their interaction, to the process of thermal adaptation.

Project Title (2): Mito-nuclear cooperation and conflict

Project Outline: Mitochondria are key organelles involved in providing most of the cellular energy required for survival. Interestingly, mitochondria have retained a small genome, which encodes for crucial protein involved in the electron transport chain (ETC). These proteins must work tightly with nuclear protein, therefore harmonious interaction between both genomes is essential for life. Mismatches between these

two genomes can have drastic deleterious consequences, ranging from mild to severe phenotypes like mitochondrial disorders.

This project will aim to characterise Drosophila genotypes that present detrimental phenotypic symptoms due to a mitonuclear mismatch. We have two genotypes that suffer from these incompatibilities; one genotype is lethal at the larval stage, whist the other genotype produces sterile males. This project will involve both phenotypic characterisation of the incompatibility, and trying to find the genetic/physiological underpinnings. This will require some molecular biology skills, and consequently students with molecular genetics/ cell biology backgrounds are preferred.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: f.camus@ucl.ac.uk

Supervisors: Prof. Julia Day (UCL) and Dr. Rupert Collins (NHM)

https://profiles.ucl.ac.uk/1268

Project Title: Macroevolutionary dynamics of catfishes

Project Outline: Amazingly of the 60,000 living vertebrate species, one in every 16 is a catfish. Catfish diversity makes them the example par excellence for addressing some major questions in evolutionary biology – how has life become so diverse? did this happen in bursts or gradually? why are only some groups successful? are species equally distributed across the globe? Integrative studies, combining phylogenetic trees with functional trait data (i.e., morphological and ecological characteristics influencing organismal fitness) has proven a powerful tool for inferring large scale biodiversity patterns and processes on our planet, however, such data are especially sparse for freshwater organisms.

To help address these questions, we are building a global functional trait database of catfishes (Siluriformes). Catfishes are one of the most significant groups of freshwater fishes, with a truly global distribution, and therefore contrast with other animal global studies in being primary aquatic vertebrates (and therefore likely subjected to different selective pressures), with independent evolutionary origins.

To assemble a comprehensive global continuous morphological trait database we are harnessing the wealth of specimens from the world-class Natural History Museum fish collections, which has global representation of >8,000 registered catfish lots providing a major source for the acquisition of trait data.

Eligibility: This project will be particularly suitable for students who are interested in Zoology and Evolution.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: j.day@ucl.ac.uk

Supervisor: Prof. David Gems, Institute of Healthy Ageing

https://profiles.ucl.ac.uk/2485

Project Title: Biology of Ageing in *C. elegans*

Project outline: The project will involve some aspect of the biology of ageing in *C. elegans*, to be determined closer to the date of the project.

While developmental genetics has been an area of intensive study for many years, investigation of the role of genes in determining longevity and ageing only recently began. An ideal model organism in which to study ageing is the free-living nematode *Caenorhabditis elegans*. This species has well-developed genetics, its 97,000,000 base pair genome is fully sequenced, and its life span is a mere 2-3 weeks. Most importantly, numerous mutations have been identified in *C. elegans* which alter the rate of ageing, with some mutants living more than five times as long as wild-type worms. It is hoped that by understanding ageing in a simple animal like *C. elegans* we will be able to unravel the mystery of human ageing, which increases risk of a wide range of diseases, from cardiovascular disease and type II diabetes, to Alzheimer's disease and cancer.

A major focus of current work in this laboratory is understanding the genes and biochemical processes by which reduced insulin/IGF-1 signalling and dietary restriction increase lifespan. Other interests include sex differences in the biology of ageing, evolutionary conservation of mechanisms of ageing, and bioethical implications of ageing research.

Special requirements: These projects are suited for students who are considering a possible future career in scientific research. A good grounding in genetics is helpful.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: david.gems@ucl.ac.uk

Supervisor: Dr. John Labbadia, Institute of Healthy Ageing

Project Title: Enhancing protein homeostasis to promote healthy ageing

Project Outline: Generating and maintaining a functional proteome is central to the proper function of all cells. However, as cells age, their ability to maintain proteome integrity declines, leading to the appearance and persistence of misfolded, mislocalised and aggregated proteins. This phenomenon, often referred to as "Protein homeostasis collapse", leads to cell and tissue dysfunction, and the onset of age-associated diseases, such as Alzheimer's, Parkinson's and Motor neurone disease. Therefore, understanding how cells maintain protein homeostasis throughout life, and maintaining or activating these pathways in old age, has the potential to simultaneously suppress multiple age-associated diseases.

During the summer project, you will learn to use the small nematode worm *Caenorhabditis elegans* as a model system to monitor proteostasis capacity in ageing tissues (muscles, neurons, intestine), *in vivo*. You will then use small molecules and RNA interference to activate or suppress specific complexes/pathways and measure the effects on protein aggregation and tissue function throughout life.

It is expected that students will start in June/July and work for 10-12 weeks in the lab. However, the start date and duration of the project can be flexible.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: j.labbadia@ucl.ac.uk.

Supervisor: Prof. Nick Lane, Centre for Life's Origins and Evolution

https://profiles.ucl.ac.uk/11719

Project Title (1): How energy flow structures metabolism and heredity at the origin of life.

Project Title (2): How anaesthetics affect mitochondrial function in Drosophila

Project Information: We have several experimental and computational projects that address different aspects of the origin of life from an energetic perspective, specifically how the first cells came to be powered by proton gradients across membranes. The student would be able to choose, depending on their interests and progress in the meantime, between projects on CO2 reduction across inorganic barriers, the behaviour of fatty acid protocells, aspects of nucleotide synthesis, the impact of anaesthetics on mitochondrial function, and interactions between amino acids and nucleotides. Computational projects would focus on the origin of the genetic code in relation to the coevolution of metabolism and the code.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: nick.lane@ucl.ac.uk

Supervisor: Prof. Richard Mott, UCL Genetics Institute

https://profiles.ucl.ac.uk/53101

Project Title: Interplay of constitutive DNA methylation, sequence composition, mRNA and protein expression in Arabidopsis

Project Outline: This project is entirely computational. The objective is to analyse data our lab has collected on gene-body methylation, mRNA expression and protein expression in 19 accessions (inbred strains) of the model plant Arabidopsis thaliana. We have re-assembled these genomes using long read sequence data and re-annotated their protein-coding gene content. The questions to be addressed are (i) to what extent can gene body methylation (gbM) can be predicted from local sequence composition, such as codon usage? (ii) How does local sequence composition impact mRNA and protein expression (iii) how do gbM and mRNA expression impact protein expression?

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: r.mott@ucl.ac.uk

Supervisors: Professor Andrew Pomiankowski and Professor Aida Andres
Host Unit: Stalk-eyed fly lab, CLOE, GEE

https://profiles.ucl.ac.uk/11067
https://profiles.ucl.ac.uk/64497

Project Title: Genomic evolution of a meiotic drive chromosome

Project Outline: Male stalk-eyed flies have highly exaggerated eyespan, caused by strong female mate preferences. These flies suffer from meiotic drive, a selfish genetic elements that disrupt normal gamete production. We are interested in an X-linked meiotic drive (SR), in the stalk-eyed fly, *Teleopsis dalmanni*. In males, SR drive causes Y-bearing sperm to degenerate, only the sperm with the SR chromosome are viable, resulting in all-female broods.

In this project, you will study the molecular evolution of the SR drive chromosome. We whole-genome sequenced the wildtype and drive males. The assembly shows that the drive X chromosome has 3 large inversions and a translocation which restrict recombination with the wildtype X. The lack of recombination is predicted to cause the accumulation of deleterious mutations. We also know that the SR chromosome has undergone adaptive evolution. Drive males invest in very large testes which allows them to maintain fertility under sperm competition. This trait has probably undergone an evolutionary trade-off with eyespan (the trait used to attract females) which is reduced in drive males.

We recently annotated the wildtype and X chromosomes and so know where the genes are located. In addition to the assembly, 100 flies (50 wildtype, 50 drive) were individually sequenced giving polymorphism data, and we also phenotyped these flies for eyespan, body size and reproductive traits. You will firstly use standard

metrics to date the origin and order in which the inversions and translocation arose. You will then compare drive and wildtype loci for evidence of the accumulation of deleterious mutations and adaptive evolution on the drive chromosome. There is also the possibility to look for genetic associations with the male phenotype – both in male eyespan the sexual trait males use to attract females and male reproductive traits that are known to vary in drive males.

Recent References from the lab:

Bates, S., Meade, L. and Pomiankowski, A. 2024 Meiotic drive does not impede success in sperm competition in the stalk-eyed fly, *Teleopsis dalmanni*. **Evolution** 77, 2326–2333.

Bradshaw, S.L., Meade, L., Tarlton-Weatherall, J. and Pomiankowski, A. 2022 Meiotic drive adaptive testes enlargement during early development in the stalk-eyed fly. **Biology Letters**, 18, 20220352.

Mackintosh, C., Pomiankowski, A. and Scott, M. F. 2021 X-linked meiotic drive boosts population size and persistence. **Genetics** 217(1) iyaa018.

Meade, L., Finnegan, S.R., Kad, R., Fowler, K. and Pomiankowski, A. 2020 Maintenance of fertility in the face of meiotic drive. **American Naturalist** 195(4), 743-751.

Finnegan, S.R., White, N.J., Koh, D., Camus, M.F., Fowler, K. and Pomiankowski, A. 2019 Meiotic drive reduces egg-to-adult viability in stalk-eyed flies. **Proceedings of the Royal Society London B** 286, 20191414.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: ucbhpom@ucl.ac.uk or a.andres@ucl.ac.uk

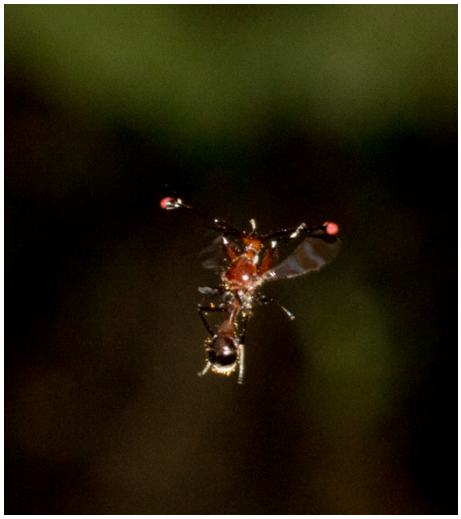
Supervisor: Professor Andrew Pomiankowski
Host Unit: Stalk-eyed fly lab, CLOE, GEE

https://profiles.ucl.ac.uk/11067

Project Title (1): Sexual selection and fertility

Project Outline (1): Male stalk-eyed flies have highly exaggerated eyespan, caused by strong female mate preferences. These flies suffer from meiotic drive, a selfish genetic elements that disrupt normal gamete production We are interested in an X-linked meiotic drive (SR), in the stalk-eyed fly, *Teleopsis dalmanni*. In males, SR drive causes Y-bearing sperm to degenerate, only the sperm with the SR chromosome are viable, resulting in all-female broods.

In all cases of meiotic drive in *Drosophila*, males bearing drive have greatly reduced fertility. Drive males typically have less than half the number of sperm of wildtype males. Their success in gaining fertility is particularly bad under sperm competition. We expected the same in stalk-eyed flies, as females mate repeatedly, several times a day, over a lifespan of several months. However, this is not the case. Drive males deliver the same number of sperm per ejaculate as wildtype males. There is no evidence for differential paternity between the two types of males, regardless of the order of mating. Nor do drive males do worse after a single mating to a multiply mated females, again regardless of the order of mating. These surprising results reflect the greatly expanded size of the testes in drive males. Drive male testes expansion results from greater allocation of resources to the testes at pupation as well as a greater rate of growth post-eclosion. This secondary adaptation is possible in *T. dalmanni* because the driving X chromosome includes several inversions that collectively repress recombination across most of the X chromosome. This ensures co-inheritance of many genes with the driver itself in a “super-gene”, allowing adaptive changes at many loci.



We have recently started investigating a related stalk-eyed fly, *T. whitei.* It too has greatly exaggerated male eyespan and strong sexual selection. It also suffers from X-linked meiotic drive. But there is no evidence that the drive locus is embedded in inversions on the X chromosome – in fact, a scan between drive and wildtype males found no discernible genetic differences. This gives us a clear system in which to test our hypothesis that adaptation on the drive X chromosome is only possible when the drive locus is embedded in a "super-gene". You will discover whether testes expansion is absent from drive males in *T. whitei.* You will investigate whether drive males do poorly in sperm competition in *T. whitei*. You will also investigate whether *T. whitei* male eyespan, the sexual trait used by female in mate choice, is less exaggerated in drive males – which is another secondary adaptation in *T. dalmanni.* These simple investigations promise deep insight into adaptive change in this group of stalk-eyed flies.

Project Title (2): Sexual Selection in the wild

Project Outline (2): Male stalk-eyed flies have highly exaggerated eyespan, caused by strong female mate preferences. These flies suffer from meiotic drive, a selfish genetic elements that disrupt normal gamete production We are interested in an X-linked meiotic drive (SR), in the stalk-eyed fly, *Teleopsis dalmanni*. In males, SR drive causes Y-bearing sperm to degenerate, only the sperm with the SR chromosome are viable, resulting in all-female broods.

In December of this year, we collected ~400 flies from wild populations in Malaysia. They need to phenotyped for morphological traits (eyespan and body size) and male reproductive traits (testes & accessory glands). Female fecundity was estimated from dissections in the field (egg counts) where we also recorded "lek structure" – males and females aggregate in mating assemblies at dusk and then the dominant male mates with females at dawn. DNA extraction from samples is needed so that males and females can be genotyped for

meiotic drive. In this local population, the flies co-exist with a “cryptic species” which needs to be distinguished, again using genetic markers. You will work with a PhD student to learn all these laboratory techniques.

The data from 2024 will be added to our large dataset from 4 previous collections carried out over the last 15 years. Two main hypotheses will be investigated. (1) Is meiotic drive associated with extinction. Our theoretical work shows how X-linked drive skews the sex ratio to females and boosts population size. But if drive becomes too common, the lack of males causes local extinction. You will use the meta-population field data to study population size, population persistence and associations with the frequency of meiotic drive. (2) Does sexual selection through female choice discriminate against meiotic drive. There is no evidence that females can directly discriminate against meiotic drive males when making mate choice. But drive males have reduced eyespan, the predominant trait that females use in mate choice. You will use the field data on lek structure to examine whether drive males attract fewer females to their leks and whether females carrying the drive X chromosome are less choosy in the mate choice.

Recent References from the Lab:

Bates, S., Meade, L. and Pomiankowski, A. 2024 Meiotic drive does not impede success in sperm competition in the stalk-eyed fly, *Teleopsis dalmanni*. **Evolution** 77, 2326–2333.

Bradshaw, S.L., Meade, L., Tarlton-Weatherall, J. and Pomiankowski, A. 2022 Meiotic drive adaptive testes enlargement during early development in the stalk-eyed fly. **Biology Letters**, 18, 20220352.

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Meade, L., Finnegan, S.R., Kad, R., Fowler, K. and Pomiankowski, A. 2020 Maintenance of fertility in the face of meiotic drive. **American Naturalist** 195(4), 743-751.

Finnegan, S.R., White, N.J., Koh, D., Camus, M.F., Fowler, K. and Pomiankowski, A. 2019 Meiotic drive reduces egg-to-adult viability in stalk-eyed flies. **Proceedings of the Royal Society London B** 286, 20191414.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: ucbhpom@ucl.ac.uk

Supervisor: Prof. Max Reuter, Centre for Life's Origins and Evolution

https://profiles.ucl.ac.uk/10749

Project Title (1): Experimentally characterising adaptive conflicts over sex-specific phenotypes in *Drosophila melanogaster*

Project Outline (1): Males and females of the same species often differ in their morphology, physiology and behaviour, reflecting the sexes' reproductive roles. But while sexual dimorphism is ubiquitous, recent work has highlighted that the divergence between the sexes is incomplete and adaptive conflicts are ongoing between males and females of many species. Divergent selection on male and female phenotypes, in combination with genetic coupling between their traits, can lead to sexual antagonism, where populations are polymorphic for genetic variants that are beneficial to one sex but detrimental to the other. Neither variant can easily get fixed, due to the advantage it provides to one or the other sex.

In our lab, we have experimentally evolved flies under sex-limited selection for 30 generations, by imposing competition among members of one sex while eliminating selection in the other sex. Here we want to phenotypically characterise the evolved populations. Specifically, we want to measure male and female fitness across these populations to verify the opposing fitness effects of the variants they carry, and measure other phenotypes where relevant.

The project involves the breeding and manipulation of flies to perform replicated experiments under tightly controlled conditions. Apart from attention to detail and an interest in evolutionary genetics, no previous knowledge is required.

Project Title (2): Comparing population genetic methods to infer selection from genomic data

Project Outline (2): Adaptive evolution leaves characteristic signatures in the genomes of populations. These marks can be used to detect loci that have been under selection and make inferences about the adaptive history from genomic

samples taken in wild or laboratory populations. A number of methods exist to perform this task. Some are based on explicit population genetic models that make it possible to calculate the probability (or 'likelihood') of observing the genetic data given a set of parameters. Others compare metrics calculated from the observed data to those derived from large numbers of equivalent samples generated by simulations. And finally, recent approaches use machine learning and artificial intelligence to detect indicative patterns in the data that do not correspond to common metrics and are not obvious to the human eye.

In this project, we will test and compare a range of methods for detecting selection in sequencing data generated in laboratory experiments. We will use simulation to generate datasets equivalent to those that will be obtained in experiments and subject these to different inference methods. The results of this work will be of immediate relevance to ongoing work in our research group.

This is a computational project. An interest in theoretical evolutionary biology is expected, and some computational skills (R, programming) are required.

Project Title (3): Using computer simulations to predict signatures of balancing selection in genetic data

Project Outline (3): Events that happen in the evolutionary history of species can leave marks on the genomes of individuals. These marks give us an opportunity to infer what happened in the past from a sample of present-day individuals. However, decoding the big story book recorded in genomes is complicated. Computer simulations can be helpful because they allow us to simulate various histories and learn what marks they leave in the genomes of a population. These marks are variations in the DNA sequences that are present in different numbers of individuals in a population. The rationale of this project involves simulating genetic data to understand the signatures left by natural selection acting to maintain genetic variation. Specifically, we are interested in comparing two modes of such 'balancing selection', one relying on a fitness benefit of being heterozygote at specific loci (so-called overdominance or heterosis) and another where balancing selection derives from different alleles being favoured in males and females.

This is a computational project. An interest in theoretical evolutionary biology is expected, and some experience in computer programming is required.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: m.reuter@ucl.ac.uk

Supervisor: Prof. Wenying Shou, Centre for Life's Origins and Evolution

Project Title: Artificial selection of microbial communities

Project Outline: Microbial communities often carry out biochemical functions that individual member species cannot. How might we improve community functions? One possibility is to perform artificial selection of communities: we grow many communities to allow mutations to occur, and only allow high-functioning communities to reproduce by splitting each into multiple offspring communities. We will use computer simulations to compare different selection strategies. An alternative project would be to programme our liquid handling robot to perform community selection experiments.

Deadline for contact

15 January 2024. Applicants should send a cover letter and a brief CV.

Contact: w.shou@ucl.ac.uk