Summer 2023 Studentships - Projects List

**Host Unit:** Alic lab, Institute of Healthy Ageing

**Supervisor:** Dr Nazif Alic

**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 the Xbp1 transcription factor or (2) the role of catecholamines in animal ageing. The exact project can be tailored based on the student’s interest and current work in the laboratory.

*Deadline for contact:*
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** n.alic@ucl.ac.uk
**Host Unit:** Florencia Camus Group, Centre for Life’s Origins and Evolution  
**Supervisor:** Dr. Florencia Camus

**Project Title:** Understanding the role of metabolic genes in adaptation

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. Their harmonious interaction is essential for organismal viability. 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. Indeed, evidence suggests that intergenomic 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. Using genetic tools specific to Drosophila, we can manipulate genomes, and have created several new strains of fly that have either matched (north-north, south-south) or mismatched (north-south, south-north) 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.

**Deadline for contact:**  
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** f.camus@ucl.ac.uk
**Host unit:** Gems lab, Institute of Healthy Ageing

**Supervisor:** Prof. David Gems

**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**

13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** david.gems@ucl.ac.uk
**Host unit:** Niccoli lab, Institute of Healthy Ageing  
**Supervisor:** Dr Teresa Niccoli

**Project Title:** The effect of lithium on Frontotemporal Dementia

**Project outline**
A hexanucleotide repeat expansion within the C9orf72 gene (C9) is the primary genetic cause of Amyotrophic lateral sclerosis and Frontotemporal dementia. Toxicity in neurons results from the production of dipeptide repeat proteins (DPR) which are translated via non canonical non-ATG initiated translation of the repeats. To understand the mechanisms leading to neuronal death we have developed a Drosophila melanogaster model expressing 36 hexanucleotide repeats (36R). This model displays neuronal toxicity and a shortened lifespan (Mizielinska et al., 2014).

Feeding lithium, a drug known to ameliorate A\(\beta\) toxicity in Alzheimer’s disease, to C9 expressing flies partially rescues the toxicity. This project will be looking at how this rescue is mediated.

The student will carry out lifespan and behavioral assays on C9 expressing flies down-regulating Gsk3 and Cdk5, proteins known to be inhibited by lithium, and characterise the expression levels and localization of DPR proteins.

The student will learn a variety of molecular biology techniques: Western blots, qPCR, as well as Drosophila genetics and husbandry, and how to set up and run lifespans and behavioral assays in flies.

**Special requirements**
The student needs to have a basic understanding of genetics, and be able to follow the information in the following training pack:

[https://academic.oup.com/g3journal/article/3/2/353/6025717](https://academic.oup.com/g3journal/article/3/2/353/6025717)

**Deadline for contact**
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** t.niccoli@ucl.ac.uk
Host unit: Nick Lane’s research group, Centre for Life’s Origins and Evolution
Supervisor: Prof. Nick Lane

**Project 1 title:** How energy flow structures metabolism and heredity at the origin of life.

**Project 1 outline**
How energy flow structures metabolism and heredity at the origin of life.

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 CO$_2$ reduction across inorganic barriers, the behaviour of fatty acid protocells, aspects of nucleotide synthesis, 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.

**Project 2 title:** How mitonuclear interactions shape mitochondrial function and fitness in *Drosophila*

**Project 2 outline**
This work would be in collaboration with Dr Flo Camus and uses a well-established fruit fly model to study mitonuclear incompatibilities. Several different projects would be available depending on the interest of the student and progress in the meantime, ranging from fluorespirometry using the Oroboros O2K to measure mitochondrial function, to analysis of metabolomic and proteomic datasets, to exploration of phenotypes in flies, ranging from male or female fitness to activity and lifespan. Projects could relate to the effects of diet, temperature and drug responses with a focus on overall physiology or brain-specific metabolism linked to dementia.

**Deadline for contact**
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: nick.lane@ucl.ac.uk
Host unit: Centre for Life’s Origins and Evolution

Supervisor: Prof Joel Dacks, Nick Lane and Andrew Pomiankowski

Project title: Evolution of sex at the origin of Eukaryotes.

Project outline
Cellular sexual reproduction allows for cell fusion and genetic exchange, both of which would have been critical for the evolution of complex life on Earth. However, the details of how this process evolved remain unclear. The student would choose among two computational projects, either delving into the origins of meiotic machinery in prokaryotic genomes (with particular focus on the ‘Asgard archaea’) or tracing the evolution of prokaryotic genetic transfer genes in eukaryotes. This project will be co-supervised by Profs Lane and Pomiankowski who have worked on many projects before, joined by Prof Dacks who has expertise in genome analysis. The student would join a dynamic group working on deep evolutionary questions using genomics and molecular evolutionary techniques.

Suggested Reading:

Colnaghi, M., Lane, N. and Pomiankowski, A. 2022 Repeat sequences limit the effectiveness of LGT and favoured the evolution of meiotic sex in early eukaryotes. Proc Natl Acad Sci USA, 119 (35), e2205041119.


**Deadline for contact:**
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** Andrew Pomiankowski: ucbhpom@ucl.ac.uk or Nick Lane: n.lane@ucl.ac.uk
**Host lab:** Stalk-eyed fly lab, Centre for Life’s Origins and Evolution  
**Supervisor:** Prof. Andrew Pomiankowski  
**PhD supervisor:** Sasha Bradshaw

**Project Title:** Investigating a selfish genetic element in wild populations of stalk-eyed flies.

**Project outline**
Selfish genetic elements are widely occurring and act to increase their own fitness at the detriment to the host organism. Meiotic drivers are a major class of SGEs. They disrupt normal gamete production during meiosis. We are interested in a sex-linked drive system on the X-chromosome (SR) in the stalk-eyed fly, *Teleopsis dalmanni*. In males, SR destroys all Y-bearing sperm to produce female offspring only. The two-fold advantage in transmission gained by drive is offset by a range of disadvantages.

The summer student will join our field trip to investigate the effects of SR in wild populations of stalk-eyed flies found in the Ulu Gombak, Peninsular Malaysia. This project involves fieldwork for a period of 4–6 weeks in Summer 2023. Our goal is to understand how SR (1) affects reproductive behaviour and (2) affects fitness by measuring morphological and reproductive traits, (3) to determine whether the frequency of drive influences population size and sex ratio, and (4) to investigate the diversity of SR in wild populations. A keen interest in evolutionary genetics and enthusiasm for working in the field.

**Suggested reading:**

**Deadline for contact:**
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** Prof. Andrew Pomiankowski: ucbhpom@ucl.ac.uk
Host lab: Max Reuter lab, Centre for Life’s Origins and Evolution  
Supervisor: Prof. Max Reuter

Project 1 title: Investigating adaptive conflicts over sex-specific phenotypes in *Drosophila*

Project 1 outline  
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 so-called 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 previous work, we have used quantitative and population genetic techniques to identify regions in the fruit fly genome that harbour such sexually antagonistic variation. Here we want to characterise fly lines with genomes that have been edited to carry putatively sexually antagonistic alleles. Specifically, we want to measure male and female fitness in such lines 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 2 title: Characterising mito-nuclear incompatibilities in *Drosophila*

Project 2 outline  
Mitochondria play a central role eukaryotic metabolism and energy production. Interestingly, key parts of their function are performed by complexes that incorporate proteins encoded in two different genomes, that of the mitochondria themselves and
that of the cell nucleus. Tight coevolution is therefore expected between the genes in different genomic compartments to ensure optimal function. And conversely, mitochondrial function is compromised if coevolution is disrupted, something that can occur due to the fact that the two genomes are inherited via different routes, maternally in the case of mitochondria and biparentally in the case of the nuclear genome, and show divergent rates of molecular evolution.

Understanding the dynamics of this coevolution requires some knowledge of the loci involved in mito-nuclear mismatches and their fitness consequences. To study this, we have assembled a panel of Drosophila lines that combine mitochondrial and nuclear genomes form different geographic origins. Two of these lines show clear deleterious phenotypes, larval lethality in one case and male sterility in another. In this project, we want to characterise these deficiencies in greater detail. This will involve the phenotypic investigation of individuals expressing incompatibilities (and matched controls).

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 3 title:** Detecting signatures of selection in global fruit fly populations

**Project 3 outline**
Samples of genome-wide sequencing data make it possible to identify the specific signatures that selection leaves in the gene pool of a population. Based on computational analysis of the data, we can detect regions of the genome where populations undergo directional selection, for example where they adapt to their local environment. Local adaptation leaves characteristic sweep patterns of reduced genetic variability and increased population differentiation. Alternatively, we can infer the presence of balancing selection, where regions of the genome show and excess of variation compared to the levels we would expect under neutrality. This is often the case around genes with immune functions, where have more diverse gene
variants can provide better protection against pathogens, or in genes that are subject to conflicting selection pressures that prevent the fixation of one or the other allele.

We propose to perform such analyses using sequences from different populations of the fruit fly *Drosophila melanogaster*. Data is available from a range of populations covering the species’ ancestral range in Southern Africa and various regions that have been colonised more recently (Northern Africa, Europe, North America) and standard methods can be applied to scan genomes for the presence of both directional and balancing selection.

This is a computational project that gives hands-on experience in the analysis of population genomic sequence data. It will involve running analyses of large datasets using command-line tools. As a consequence, it will require some levels of familiarity and interest in computational approaches.

**Project 4 title:** Using computer simulations to predict signatures of balancing selection in genetic data

**Project 4 outline**

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 computer programming and theoretical evolutionary biology is expected, but no previous experience is required.
**Project 5 title:** Investigating how interactions between different environmental stresses may influence sexual selection and ultimately population fitness

**Project 5 outline**

In the face of ongoing climate change, it is imperative to understand how animals are affected by modifications in their environmental conditions. Two common climatic stressors that animals must deal with are alterations in their thermal environment along with the quality/quantity of nutritional resources available to them. One key aspect to comprehend is how interactions between these environmental conditions can influence offspring sex ratios. Implications for such possible effects in sex ratios are vast, influencing population dynamics and eventually affecting population fitness and persistence under different environmental conditions.

Previous work from the lab has shown sex-specific dietary preferences in adults that affect their fitness-related life-history traits like female fecundity and male competitive ability. Furthermore, preliminary data suggest variation in the number of female offspring when their parents are reared across combinations of temperature and diet. This project will aim to integrate the two aspects, by a) quantifying the number of male and female offspring generated from parents developing in combinations of thermal and dietary regimes, and b) assessing fitness-related life-history traits of these offspring to subsequently inform overall population fitness dynamics.

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

**Deadline for contact:**

13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

**Contact:** m.reuter@ucl.ac.uk
Host Unit: Shou lab, Centre for Life’s Origins and Evolution
Supervisor: Prof Wenying Shou

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:
13 January 2023. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: w.shou@ucl.ac.uk