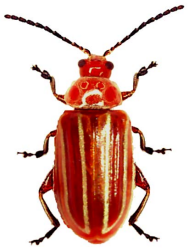

Peterhouse Biology Symposium 2025

Saturday 15th February 2025, Peterhouse Theatre

Justin Gerlach (Fellow) – **Reversing habitat degradation with giant tortoises or playing with nature?: 'Rewilding' in Madagascar**

Madagascar is famous for its extraordinary biota, with modern species descended from Gondwanan relicts and more recent colonists. A very high proportion of these species are threatened and its megafauna is almost completely extinct. Its ecosystems are also among the most threatened on earth, with forest areas reduced to fragments and extensive erosion in the central grasslands. There is a well established view that before human colonisation Madagascar was almost completely forested and the grasslands were created by deforestation, fire and the introduction of cattle. There are projects underway that hope to regenerate forests through the introduction of Aldabra giant tortoises *Aldabrachelys gigantea* as ecological replacements for the extinct Madagascan giants. These projects assume that the tortoises would have been significant seed dispersers of plants such as the baobab trees and that the Aldabra tortoises could restoring this function to the ecosystems. This is not a universal view however, and grazing by giant tortoises could maintain grass habitats instead. In order to understand this we need to compare the ecology of the living and extinct species. The diet of the megafaunal herbivores has been reconstructed using ^{12}C:^{13}C ratios to infer the proportions of C3 and C4 plants in the diet, with C4 being mainly grasses. These studies are complicated by lumping all the tortoises together as '*Aldabrachelys* sp.' and by an untested assumption that the ratios accurately reflect the plants consumed. I am planning to update our inadequate information on the historical distribution of the Madagascar giant tortoises and to review the dietary data with the aim of reviewing the potential role of the ecological surrogates.

In unrelated work on giant tortoises, I am also involved in a project looking at the genetics of ageing based on Jonathan, a giant tortoise on St Helena island who is believed to be the oldest living land animal at over 190 years. As well as genes associated with longevity, his genome shows evidence of 'epigenetic entropy' whereby epigenetic markers degrade over time, leading to deteriorating cellular function. This is thought to be one of the factors contributing to the ageing process.

Charlotte Wright (PhD) – **Out of the blue: bursts of chromosome diversity in the blue butterflies**

Chromosome rearrangements, such as fusions and fissions, are a ubiquitous feature of eukaryotic genome evolution. However, rates of chromosome rearrangement vary widely across eukaryotes and the reasons for this remain obscure. Around 20% of eukaryotes have holocentric chromosomes, where centromeric activity is dispersed along the length of the chromosome rather than at a single region as in monocentric chromosomes. Holocentric chromosomes have been hypothesised to help chromosomes resulting in fusion and fission events to be inherited, leading to higher rates of chromosome rearrangement in holocentric groups of species. However, the story is more complex as a wide range in chromosome number is seen in both holocentric and monocentric taxa. Lepidoptera, the butterflies and moths, is one of the largest groups of holocentric species. Within Lepidoptera, the greatest range in chromosome number is found in Polyommatina, a young subtribe of blue butterflies that evolved 23 million years ago. Polyommatina is characterised by two modes of chromosome evolution: extreme stability in chromosome number in the majority, with rapid chromosome number change in some clades of species. Chromosome-level genomes for 27 species of Polyommatina reveal a complex history of chromosome rearrangement in genus *Lysandra* and *Polyommatus* subgenera *Agrodiaetus* and *Plebicula*. Parallels between the histories of fission in each group are found, including the observation that fissions tend to

occur in the lightly-packed regions of the genome in each group. Additionally, fission has been shaped by chromosome length and tends to occur in the middle of chromosomes. We speculate that this may point towards the mechanism of fission and be related to the observation that species of Polyommatina can undergo two types of meiosis, known as conventional or inverted. This work deepens our understanding of chromosome fission, a fundamental process that shapes the evolution of genome structure across the diversity of eukaryotes.

James McCulloch (PhD) – **Reconstructing the ancestral genomes of sedges**

Organisms with holocentric chromosomes – chromosomes with kinetochore activity spread along the whole chromosome, rather than concentrated at a single centromere – have been hypothesised to experience higher rates of chromosome rearrangements. Sedges are an example of a holocentric clade and do exhibit exceptional variability in their chromosome number. It's necessary to reconstruct ancestral karyotypes to build a more accurate picture of the number of chromosomal fissions and fusions which have occurred throughout the sedges' evolutionary history, but the tools currently used for this have not yet been tested on a group with such extant variability. I found that the tool Agora performs best but may still require adjustment. Nevertheless, the Agora output reveals an even greater number of rearrangements than would be expected from the known karyotypes at the tips of the phylogeny. The results pave the way for investigations into the ecological correlates of rearrangement frequency and the genomic characteristics which promote fissions and fusions.

Dylan Flicker (MPhil) – **What the cat dragged in: are bovid fauna lists a good proxy for Plio-Pleistocene hominin ecologies?**

South African hominin sites have yielded key discoveries that have shaped our understanding of hominin behaviour, culture, and evolution. Understanding the ecological context of South African Plio-Pleistocene hominin species is critical to reconstructing the selective pressures that drove their evolution. While broad climatic signatures can link these species on a regional scale, only detailed, site-specific ecological analyses can reveal their niche distinctions and true motivations for diversification. Taxon-free and taxon-dependent analyses of fossil bovids are often used to extrapolate the paleoenvironment, as different bovid clades are strongly associated with different ecological conditions. Many fossil-bearing cave sites in South Africa are suggested to have formed partly due to carnivore behaviour, with non-carnivoran fauna accumulating after being dragged in as prey. This presentation hopes to demonstrate the value of applying established taxon-free ecometric methods to test the core hypothesis that ecological reconstructions from fossil fauna are influenced by taphonomic biases inherent to carnivore accumulation sites, further clarifying the environment context of South African Plio-Pleistocene hominin evolution.

Harry Howard (II Zoology) – **Comparison of Moorean invertebrates based on presence of the little fire ant *Wasmannia auropunctata***

Wasmannia auropunctata, known also as the little fire ant or electric ant, is recognised as one of the top 100 invasive species according to the IUCN. Like many other invasives, it is particularly damaging on islands, with studies on little fire ants on islands generally finding that its presence is correlated with low diversity of other ant species. However, work seems to focus on ants while ignoring the impact of little fire ants on other invertebrate species that may be functionally important. I investigated whether the presence of *Wasmannia auropunctata* is a significant determinant of the invertebrate community. The French Polynesian island of Moorea provides a key site in which to test this as, unlike nearby Tahiti, it is only partially infested with *Wasmannia* allowing us to make comparisons of infested areas and nearby pristine rainforest. The impact of the ant was tested using pitfall trapping to sample the invertebrate community in each of three sites, with my results finding no significant difference in Simpson indices between the three sites (other than the difference caused by the high numbers of the little fire ant itself) but finding significant differences in community structure between the control and test sites. These results suggest that the presence of *Wasmannia auropunctata* is a key determinant of invertebrate community structure which could have significant implications globally as the little fire ant spreads.

Wes Robertson (Research Associate) – **Genome design and synthesis for non-model bacteria of the gut microbiome**

Synthetic biology enables us to control certain genetic programs and introduce novel phenotypes in model bacteria such as *E. coli,* though as a field we lack the ability to comprehensively engineer the bacteria we know significantly affect human health. The Robertson lab develops genome engineering tools for the de novo synthesis of non-model gut bacteria, with the ultimate aim of reprogramming the microbiome. These aims build on the key contributions I have made while at the LMB for the total synthesis of *E. coli* genomes as well as applications for the resultant recoded bacteria. In particular, the potential of sense codon reassignment to generate orthogonal genetic communication systems (e.g. viruses can't infect our cells) provides a powerful approach to address unmet needs for the stability and biosecurity of current gut bacterial models used to study the microbiome. Furthermore, we are developing genome design tools to enable recoding while maintaining high fitness levels in synthetic strains. To this end, as a synthetic genomics lab within PNAC we redesign, synthesize, and deploy bacterial species abundant in the microbiome.

Margaret Johncock (III Biochemistry) – **Histon B45: Function through disorder**

Andrzej Wolniewicz (Research Associate) – **Unearthing the dragon: new insights into the early evolution of reptiles from southern China**

Reptiles are an exceptionally diverse group of vertebrates, representing about one-third of modern vertebrate species. Living reptiles are divided into two major clades: Lepidosauria (tuatara, lizards and snakes) and Archelosauria (turtles, crocodiles and birds). However, understanding the origins of this diversity and the evolutionary assembly of the main reptilian body plans requires investigation of the reptile fossil record. The fossil record reveals key morphological transitions in reptiles and documents many extinct reptile lineages with no living descendants. Resolving the phylogenetic positions of these extinct groups is essential for a comprehensive understanding of reptile evolution. Sauropterygia were a diverse clade of Mesozoic marine reptiles that ranged from the Early Triassic to the Late Cretaceous. It is traditionally divided into two subgroups with distinct body plans: the short-necked placodonts with crushing dentition and the long-necked eosauropterygians with pointed teeth. Even though sauropterygians have an abundant fossil record, their early evolutionary history and position within reptiles remain incompletely understood. The discovery of a new Early Triassic saurosphargid from the Nanzhang-Yuan'an fauna in southern China provides new insights into the origins and early evolution of Sauropterygia. Phylogenetic analysis recovers saurosphargids as the sister group to eosauropterygians, suggesting they represent an intermediate morphology between placodonts and eosauropterygians. Furthermore, phylogenetic analysis recovers Sauropterygia within Archelosauria, indicating extreme morphological diversity of archelosaurians, in contrast to their lepidosaur sister group. The factors underlying this disparity in body plan evolution between the two major groups of reptiles remain unknown.

Dan Nash (PhD) - **A virus in the brain: using proteomics to explore host-pathogen interactions of HSV-1 in human neurones**

Herpes simplex virus (HSV)-1 is a neuroinvasive human pathogen that persists in the sensory ganglia of infected hosts and can cause severe disease when it spreads to the central nervous system. Herpes simplex encephalitis, the most common viral encephalitis in the UK, can leave patients with severe neurological sequelae despite the availability of direct-acting antivirals. Furthermore, exposure to neurotropic viruses like HSV-1 is increasingly linked with the development of Alzheimer's disease and other associated dementias. Induced pluripotent stem cell (iPSC) technology allows culture of authentic CNS human neurones *in vitro*, facilitating the study of neuronal infection and providing an experimental platform for developing new prophylaxes and antiviral therapies. We have used this technology to perform quantitative temporal proteomic studies to assess how the cellular and plasma membrane proteomes are affected during infection, identifying significant changes in proteins involved in regulating microtube morphology, ubiquitination and antiviral restriction, alongside a surprising change in abundance of a cellular transcription factor. We therefore also employed Oxford Nanopore-based RNA sequencing to reveal marked transcriptional shifts in neuronal gene expression upon infection. This comprehensive -omics analysis of HSV-1 infection in neurones has revealed further host-pathogen interactions that are unique to neuronal infection and will lead on to studies investigating how HSV-1 modulates the abundance of these host factors.

Dhruval Soni (II Pathology) – **Exploring the interface between La Cross virus glycoproteins and Notch signalling**

La Crosse virus (LACV) is a mosquito-borne bunyavirus which has become the leading cause of paediatric encephalitis in North America. The disease currently has no effective treatment and limited methods of diagnostics. The cell surface receptor used by LACV to gain entry into host cells is unknown but previous work has found high affinity binding to JAG2, a ligand of the Notch signalling pathway. In this project, the molecular interface between the LACV spike and the JAG2 cell surface receptor has been further characterised by finding residues that are important to the protein-protein interaction. This could provide information for therapeutic targets which would enable development of treatment for the disease.

Reem Alhassan (II Plants) – **Novel analysis of cell-to-cell communication**
Machine learning and AI are often touted as a solution to some of the busywork of research. This talk covers the use of Ilastik, a machine learning program which uses a random forest image classification system, to count GFP-expressing *Arabidopsis thaliana* pavement cells in images. I discuss the training and testing process for the programme, and why — despite Ilastik's output not differing significantly from lab member's results when counting cells — I chose not to move forward with recommending Ilastik for use in the analysis of a plasmodesmal closure assay.

Flo Buckley (II Pathology) – **Characterisation of the receptor usage and host range of an alphacoronavirus with human-tropic potential**

Alex Tsompanidis (Honorary Research Associate) – **The role of the placenta in neurodevelopment**
Autism, ADHD and related neurodevelopmental conditions have high heritability and are often attributed to Genetics. Yet males are more likely to be diagnosed, even when the general spectrum of traits or alternative presentations are considered in females. Sex differences in the prenatal environment may then be interacting with genetic variance to ultimately affect neurodevelopment. Recent findings indicate that the placenta may be the key mediator of this interaction and an understudied source of neurodiversity in humans. This is supported by the following lines of evidence. First, steroid hormones such as estradiol are elevated in the fetal and maternal circulation of autistic males and correlate with the development of autistic traits. Second, subtle sex differences in placental function (e.g. in the levels of the placental growth factor) mediate sex differences in the future autistic traits of the offspring. Third, sex differences in placental gene expression are enriched for genes implicated in autism. Fourth, recent assessments of large population registries, such as the MBR in Sweden, show that males are more likely to have placental complications and complicated labour, compared to females, who, in turn, are more able to adjust their growth patterns prenatally. Finally, evolutionary adaptations in the primate lineage may show 'changes of degree' in humans, such as increased steroidogenesis, which may be linked to both cortical expansion and conditions such as autism. In conclusion, several lines of evidence indicate that placental function is a converging point, where genetic and environmental factors interact with sex, in order to increase neurodevelopmental liability in males more than in females.

Alia dos Santos (Research Associate) – **Integrative *in situ* structural biology studies reveal changes in nuclear architecture during human spermatogenesis**

During sperm development, cells undergo major morphological changes crucial for fertility. We are using an integrative approach combining cryo-electron tomography, optical microscopy, and biochemistry to explore these transformations, focusing on nuclear pore complexes (NPCs) and proteasome organisation.
NPCs are essential gatekeepers of the nucleus, regulating the exchange of molecules between the nucleus and cytoplasm, controlling gene expression, and maintaining cellular function. We show that in human sperm NPCs lack key structural components, forming a compact, highly constricted shape that limits molecular transport. These changes occur as sperm cells differentiate in testes, following meiotic division.
Concurrently, in post-meiotic spermatogenic cells, DNA undergoes extensive compaction through the replacement of histones with protamines. We identify large proteasome clusters in the nucleus of these cells, which persist throughout the final stages of differentiation and are still observable in mature gametes. We propose that these clusters are critical for efficient chromatin compaction and may play a role in fertilisation.
Overall, our findings highlight how nuclear architecture undergoes dynamic changes during sperm development, to ensure fertility and protect the physical and genomic integrity of the sperm cell.

Hugo Fleming (Research Associate) – **Metabolism and the mind: investigating the link between glucose control and reinforcement learning in humans**