

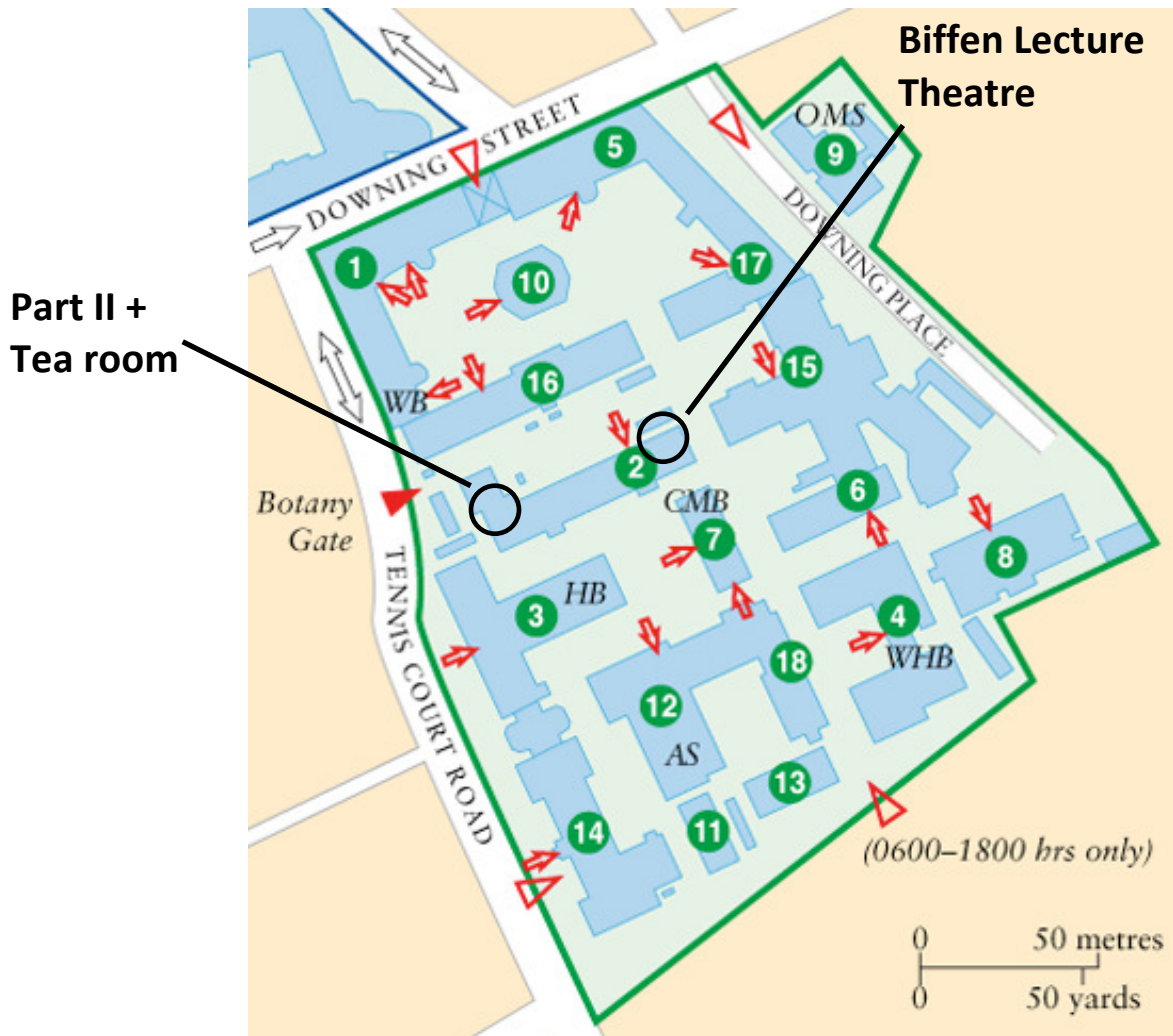
## 4<sup>th</sup> Cambridge Evolutionary Genetics Workshop

Jan 13<sup>th</sup>, 2012

Department of Genetics, Downing Site, Biffen lecture theatre/Part II room

- 10:15 Welcome and introduction
- Session 1**
- 10:20 **Chair: Chris Jiggins**  
Steve Russell, Department of Genetics  
*A meiotic drive system based on homing endonucleases (HEGs) with the aim of controlling the mosquito populations that transmit malaria*
- 10:40 Gianni Lo Iacono, Department of Veterinary Medicine/ Rothamsted Research  
*Epidemiological modelling; Evolution of plant pathogens in response to qualitative and quantitative resistance*
- 11:00 Eric Miska, Department of Biochemistry  
*Evolutionary viral sensitivity in small RNA in Caenorhabditae*
- 11:20 Rachel Walker, Department of Plant Sciences  
*Determining the regulators of petal spot development and the evolution of this specialised floral trait within the species complex *Gorteria diffusa**
- 11:40 Clare Baker, Department of Physiology, Development and Neuroscience  
*A "sixth sense"; the development and evolution of vertebrate electroreceptors*
- 12:00 – 13:00 Lunch
- Session 2**
- 13:00 **Chair: Frank Jiggins**  
Invited speaker: Judith Mank, University of Oxford/ University College London  
*Sex chromosomes, sex-specific selection and the genomic basis of sexual dimorphism*
- 13:45 Chris Illingworth, Wellcome Trust Sanger Institute  
*Quantifying selection acting on a complex trait using allele frequency time-series data*
- 14:05 Simon Martin, Department of Zoology  
*Species integrity of sympatric *Heliconius* butterflies is maintained despite pervasive introgression throughout the genome.*
- 14:25 Simon Frost, Department of Veterinary Medicine  
*Modeling associations between mutations with graphical models*
- 14:45 Paulo Amaral, The Gurdon Institute  
*The emerging roles of long noncoding RNAs in animal development and regulatory evolution*
- 15:05 – 15:40 Tea
- Session 3**
- 15: 40 **Chair: Fergal Waldron**  
Lucy Weinert, UCL Genetics Institute, University College London  
*The evolution of host shifts in *Staphylococcus aureus**
- 16:00 Peter Ellis, Department of Pathology  
*Gene amplification as a side-effect of genomic conflict*
- 16:20 Michaela de Clare, Department of Biochemistry  
*Evolution & conservation of growth control genes from yeast to humans*
- 16:40 Jason Tsai, Wellcome Trust Sanger Institute  
*Findings from the tapeworm genome project*
- 17:00 Hashem Koohy, Wellcome Trust Sanger Institute  
*Composure: an evolutionary approach for detection of regulatory sequences*

Followed by Happy Hour in the tea room at 17:20



More information can be found at

<http://heliconius.zoo.cam.ac.uk/comevolgen/2011/4th-cambridge-evolutionary-genetics-workshop/>

or contact Fergal Waldron ([fw272@cam.ac.uk](mailto:fw272@cam.ac.uk))

**Gianni Lo Iacono, Department of Veterinary Medicine/ Rothamsted Research**

**Epidemiological modelling; Evolution of plant pathogens in response to qualitative and quantitative resistance**

Theoretical studies on quantitative resistance are rather scarce. A general epidemiological model for plant diseases is formulated and applied to study the evolution of phenotypic traits of plant pathogens in response to both quantitative and qualitative host resistance. The model is built over fundamental biological processes occurring and measurable at the individual level (e.g. infection, spore production, genetic changes due to mutations in the offspring of the pathogen). The effects of such processes on the higher epidemiological and evolutionary scales are elucidated leading to a coherent, unified framework. The evolution of the phenotypic trait of the pathogen showing erosion of quantitative crop resistance naturally arises from the model. The model can be adapted to different patho-systems such as the study of vaccinations and the effect of antibiotics on humans and animals.

In particular:

- i) we highlight the differences between qualitative and quantitative resistance in the effect of key epidemiological and agronomic parameters on the durability of resistance.
- ii) we tested the hypothesis that the gain from quantitative host resistance could differ depending on the life-cycle component (sporulation rate or infection efficiency) constrained by the resistance

Rachel Walker, Department of Plant Sciences

**Determining the regulators of petal spot development and the evolution of this specialised floral trait within the species complex *Gorteria diffusa***

Walker, R. H.<sup>1</sup>, Rudall, P. J.<sup>2</sup> and Glover, B. J.<sup>1</sup>

<sup>1</sup>Department of Plant Sciences, University of Cambridge, Downing Street, CB2 3EA

<sup>2</sup>Jodrell Laboratory, Royal Botanic Gardens, Kew, TW9 3AB

Petal spots have evolved across a phylogenetically broad range of angiosperms and – in at least some cases – function in the attraction of pollinators. Spots develop through the accumulation of a contrasting pigment in a group of cells of the petal epidermis; in a few species the spots also exhibit elaborated epidermal cell morphologies. To study the evolution and development of petal spots, we have chosen a species that displays both elaborated epidermal cells and variation in overall petal spot morphology – the South African daisy *Gorteria diffusa* Thunb. (Asteraceae). The morphology of the *Gorteria* petal spot is complex, being composed of distinct cell types and a concentrated deposition of anthocyanin arranged across a structure (ray floret) that consists of several congenitally fused petals. *Gorteria diffusa* exists as several sympatric but geographically identifiable groups of populations that occur within a narrow range in the Namaqualand region of South Africa. We term these populations “morphotypes”. The morphotypes have distinct phenotypes in terms of spot morphology, including pigment content, cell shape and number and position of spots on the capitulum. These morphotypes therefore provide natural variation with which to compare the expression patterns and function of key regulators of petal spot morphology. We have utilised next-generation sequencing to generate comparative transcriptomic datasets to identify putative regulators of petal spot development. This has identified several differentially expressed candidate genes, including MYB and bHLH transcription factors that are known to regulate epidermal cellular processes. Further characterisation of these regulators are allowing us to formulate a model for the pathway of petal-spot development, ultimately defining the molecular events that have led to the evolution of this floral feature.

Keywords: *Gorteria diffusa*, petal-spot development, comparative transcriptomics, 454 sequencing.

**Clare V. H. Baker, Department of Physiology, Development and Neuroscience**

**A "sixth sense": the development and evolution of vertebrate electroreceptors**

**Authors: Melinda S. Modrell, J. Andrew Gillis and Clare V. H. Baker**

Electrosensory ampullary organs containing modified 'hair cells' that detect changes in weak electric fields in water (primarily used for detecting live prey) are found in all major groups of jawed vertebrates. These hair cells are innervated by neurons in lateral line ganglia that project centrally to specific electrosensory nuclei in the hindbrain. Despite their similarities, the embryonic origin of ampullary organs in different vertebrate groups has been controversial. Using a vital dye lineage-labelling approach for the first time in embryos of a basal ray-finned bony fish, the North American paddlefish (*Polyodon spathula*)\*, and a cartilaginous fish, the little skate (*Leucoraja erinacea*), we show that ampullary organs are derived from lateral line placodes, i.e., patches of thickened neurogenic cranial ectoderm that elongate in characteristic lines over the head, and that also give rise to neuromasts containing mechanosensory hair cells. Taken together with previous work on the axolotl (a representative of the lobe-finned clade of bony fishes), our data confirm experimentally that the ancestor of all jawed vertebrates had a lateral line placode-derived system of electrosensory ampullary organs and mechanosensory neuromasts. We have also used next-generation sequencing and a bioinformatic approach in paddlefish, validated by in situ hybridisation, to identify the first molecular markers (including ion channels) expressed in ampullary organs but not neuromasts. Using these approaches, we are beginning to reveal the developmental and evolutionary basis of electroreception.

\*Modrell, M. S., Bemis, W. E., Northcutt, R. G., Davis, M. C. and Baker, C. V. H.\* (2011) Electrosensory ampullary organs are derived from lateral line placodes in bony fishes. *Nature Communications* 2: 496 (<http://dx.doi.org/10.1038/ncomms1502>)

**Chris Illingworth, Wellcome Trust Sanger Institute**

**Quantifying selection acting on a complex trait using allele frequency time-series data**

When selection is acting on a large, genetically diverse population, beneficial alleles increase in frequency. This fact can be used to map quantitative trait loci by sequencing the pooled DNA from the population at consecutive time points, and observing allele frequency changes. Here we present a population genetic method to analyse time-series data of allele frequencies from such an experiment. Beginning with a range of proposed evolutionary scenarios, the method measures the consistency of each with the observed frequency changes. Evolutionary theory is utilized to formulate equations of motion for the allele frequencies, following which likelihoods for having observed the sequencing data under each scenario are derived. Comparison of these likelihoods gives an insight into the prevailing dynamics of the system under study. We illustrate the method by quantifying selective effects from an experiment in which two phenotypically different yeast strains were first crossed and then propagated under heat stress (Parks et al., *Genome Res.* 2011). From these data we discover that about 6% of polymorphic sites evolve non-neutrally under heat stress conditions, either because of their linkage to beneficial (driver) alleles or because they are drivers themselves. We further identify 44 genomic regions containing one or more candidate driver alleles, quantify their apparent selective advantage, obtain estimates of recombination rates within the regions, and show that the dynamics of the drivers display a strong signature of selection going beyond additive models. Our approach is applicable to study adaptation in a range of systems under different evolutionary pressures.

**Simon Frost, Department of Veterinary Medicine**

**Modelling associations between mutations with graphical models**

In the case of highly variable RNA viruses, such as HIV-1, we are often interested in whether individual mutations interact functionally, but even when it is straightforward to assess the effect of mutations, the sheer number of genetic differences between any two viruses make it infeasible to test experimentally all pairwise differences. As a screen for such experiments, it is possible to examine all pairwise associations between mutations, but this can often result in a long 'laundry list' of mutations that is difficult to interpret. I will discuss our work on the use of efficient implementations of Bayesian graphical models to identify the joint distribution of associations between mutations, and our approaches to overcome false positive associations due to shared phylogenetic history.

**Paulo Amaral, The Gurdon Institute**

**The emerging roles of long noncoding RNAs in animal development and regulatory evolution**

**Paulo P. Amaral<sup>1,2</sup>, Marcel E. Dinger<sup>2</sup>, Tim R. Mercer<sup>2</sup>, Ryan J. Taft<sup>2</sup>, John S. Mattick<sup>2</sup>**

**1The Wellcome Trust/ CRUK Gurdon Institute, University of Cambridge, Cambridge, UK; 2Institute for Molecular Bioscience, The University of Queensland, Brisbane, Australia.**

A protein-centric perspective has dominated our understanding of the molecular basis of evolution for the past century. However, genome sequencing has shown that the protein-coding content of genomes has remained relatively static throughout the evolution of animals and that differences in protein-coding sequences between distantly related organisms are insufficient to explain their phenotypic variation. It is also now evident that the majority of morphological evolution is enabled by alterations to the expression programs of conserved developmental genes. We argue that a large fraction of genomes of higher eukaryotes is dedicated to body plan development via RNA regulatory networks that have changed and expanded over evolutionary time, based on the following observations: (i) Unlike protein-coding genes, non-protein-coding sequences progressively dominate metazoan genomes as organism complexity increases. (ii) Metazoan genomes are almost entirely transcribed, generating tens of thousands of long noncoding RNAs (lncRNAs). (iii) Different classes of ncRNAs play diverse regulatory roles utilising RNA-RNA, RNA-DNA and RNA-protein interactions, and affect gene expression at all levels. (iv) lncRNAs are dynamically expressed during development and many cis- and trans-acting RNAs are involved in the regulation of conserved developmental genes. (v) Hundreds of lncRNAs are under purifying/positive selection, indicating that they have an important impact on fitness. Experimental data from our laboratory supporting key roles for lncRNAs in vertebrate development will be presented. We propose that changes in the complement, properties and expression of RNA genes that control conserved developmental genes are central mechanisms of regulatory evolution in complex organisms.

**Peter Ellis, Department of Pathology**

**Gene amplification as a side-effect of genomic conflict**

**Authors: Peter Ellis, Julie Cocquet, Joanne Bacon, Shantha Mahadevaiah, Paul Burgoyne, Nabeel Affara.**

Deletions on the long arm of the mouse Y chromosome lead to sperm head shape abnormalities, reduced fertility and sex ratio skewing. These phenotypes are accompanied by gross disruption of sex chromosome transcriptional activity in spermatids. Specifically, Sly (a multi-copy gene on Yq) acts to globally repress sex chromatin transcription in spermatids, while its X-linked counterpart Slx has the opposite effect. These opposing effects on sex chromatin, together with the sex ratio skew, imply the presence of a genomic conflict driven by distorter genes on the X that favour a female-biased sex ratio, and genes on Yq (including Sly) that repress transcription of the distorter genes.

Another feature of the mouse sex chromosomes is the presence of massive ampliconic gene tracts with no direct structural parallel in the human genome. We show that expansion of these mouse-specific amplicons occurred subsequent to the appearance of Sly on mouse Yq, and that the expansion in X gene copy number during mouse evolution is not in general accompanied by an equivalent change in transcript levels. This suggests that many of the ampliconic genes on the mouse X have become amplified in order to maintain adequate transcript levels in the face of Sly-mediated transcriptional repression, and in effect constitute "collateral damage" from the ongoing genomic conflict.