

Lecture series: “All about *Drosophila*”

A series of genomes of the *Drosophila* species have been sequenced and projects are under way to determining genomic variation in some of these species on a large scale. The lecture series will have its own home page at <http://www.stats.ox.ac.uk/~hein/Drosophila/> closer to the term. If the individual lecturers agree, their slides will be made available at this www-site before the lecture.

This lecture series is inspired by the success of previous lecture series – “The Human Genome” – “Beyond the Human Genome” – “Bioinformatics, Systems Biology and the Omics” and is a natural follow up to this. Most of the lectures can be found at: <http://www.stats.ox.ac.uk/people/hein/index.htm> The lecture series will be in Hilary Term 2007 and take place 2-4 pm Tuesdays in Seminar Room, Oxford Centre for Gene Function 3rd floor, Oxford. Each lecture is 2 times 45 minutes or 90 minutes dependent on the lecturer. If you plan to attend the lectures, please email mitchell@stats.ox.ac.uk.

The place of *Drosophila* among Metazoans – Peter Holland - 16th January

The first part of this lecture will outline the evolutionary relationships between all animal groups, explaining how the body plan has been modified in the major animal lineages. The position of *Drosophila* within flies, within insects, within arthropods, within Ecdysozoa, within Bilateria and within Metazoa will be explained. It will also be explained why prior knowledge of evolutionary relationships is vital for any study in comparative genomics.

The second part of this lecture will explain how strategies are set for sequencing the genomes of animal species, which genomes are currently completed, which are underway, and which projects are approved but not yet started. These projects will provide the key data for the science of comparative genomics. Homeobox genes will then be used as an example to show how comparisons between genomes from very divergent animal groups give insight into the pathways of diversification of genes and genomes. Since many homeobox genes play roles in patterning the body plan, such analyses will eventually give insight into how changes in the genome are reflected in changes to the organisation of animal body plans.

Comparative Genomics of *Drosophila* – Lior Pachter – 23rd January

We present a detailed analysis of the multiple alignment of 12 *Drosophila* genomes. Starting at the nucleotide level, we identify conserved elements, including ultra-conserved elements, that differ considerably in nature from those in vertebrate genomes. In the case of genes, our alignment is able to reveal structural changes in specific lineages, allowing us to substantially refine models of gene evolution. We also examine transposable elements and their impact on genome evolution, and finally, we address the nature of large scale rearrangements and duplications in *Drosophila*. These analyses provide an overview of the dynamic forces that are shaping the genomes of the Drosophilids. Joint work with Anat Caspi, Sourav Chatterji, Colin Dewey, Jotun Hein, Dan Levy and Rahul Satija.

Neuroscience of *Drosophila* - Guy Tear – 30th January

Drosophila has been a model organism for the study of the nervous system for many years. This work spans neuroscience from initial neurogenesis in the embryo to studies on adult behaviour. In the first part of my lecture I will discuss the formation of the nervous system and the screens that have been performed to identify the genes that regulate this process and the extent to which these genes have been conserved through to the vertebrate. In the second part I will present how *Drosophila* has been used to study neuronal function at the level of single neurons, simple circuits and finally to identify the genetics of behaviour.

The *Drosophila* Species – Mike Ashburner - February 6th

Drosophila melanogaster is just one species in a family of Diptera with nearly 4,000 known members. I will highlight some of the aspects of the biology of members of this family, with an emphasis on comparative studies and of opportunities of 'exploiting' our considerable knowledge of the biology, especially development, and genome of *D. melanogaster*. I will also discuss some of the early conclusions from the study of the genomes of 11 species of *Drosophila* that have recently been released. Finally, I will talk about our own recent analyses of chromosome evolution in *Drosophila*.

Population Genetics of *Drosophila* - Brian Charlesworth - February 13th

Charles Darwin was the first person to recognize that evolutionary change over time is the result of processes acting on genetically controlled variability among individuals within a population, which eventually cause differences between ancestral and descendant populations. Knowledge of the nature and causes of this variability is crucial for an understanding of the mechanisms of evolution, animal and plant breeding, and human genetic diseases. *Drosophila* has long played a leading and pioneering role in the study of natural variation. This will be reviewed in the first half of the lecture; the second half concerns how we can use information on patterns of variation and evolutionary divergence in species of *Drosophila*, to make inferences concerning the causes of evolution.

Genetic screens in *Drosophila* – Daniel St Johnston - February 20th

Genetic screens provide a very powerful and unbiased way to identify the genes required for any biological process, and have played an important role in the history of *Drosophila melanogaster*. Indeed, the two Nobel prizes in *Drosophila* have been awarded for the discovery of the mutagenicity of X-rays and the first genome-wide saturation screens for embryonic patterning mutants, and the power of these forward genetic approaches is one of the main reasons why *Drosophila* has become one of the major model organisms. In this lecture, I will describe the evolution of genetic screens in *Drosophila* from the classic Weischaus and Nüsslein-Volhard screens, through enhancer and suppressor screens, to the more recent FRT/FLP clonal screens, and will discuss the advantages and major discoveries that have emerged from each type of approach. Finally, I will consider the recent creation of UAS-RNAi lines for every gene in the genome, and how these may be used to perform new types of screen in the future.

Gene regulation and evolution in *Drosophila* - Casey Bergman - February 27th

The wealth of genetic and genomic resources in *Drosophila melanogaster* have allowed rapid progress in decoding the functional and evolutionary consequences of gene regulation in metazoan species. The first half of this lecture will review model systems in transcriptional regulation in *Drosophila* and bioinformatic methods to predict cis-regulatory sequences in genomic DNA. The second half of this lecture will cover inferences about the mechanisms of gene expression evolution derived from microarray and molecular evolutionary studies. Open questions concerning the relationship of gene expression, sequence evolution and genome organisation will be discussed in the context of the 12 newly sequenced *Drosophila* genomes.

Evolution of the innate immunity gene regulatory network in *Drosophila* - Andrew Clark - March 2nd (A Friday!!)

When insects are challenged with a bacterial pathogen, there is rapid induction of a few hundred genes, culminating in production of potent antimicrobial peptides. Comparison of the genes in this network across 12 *Drosophila* species, affords the opportunity to test a set of hypotheses regarding the evolution of this gene regulatory network. Infections of multiple species and microarray analysis of the dynamics of transcript abundance reveals intriguing departures from immune pathways in *Drosophila melanogaster*.

Embryology of *Drosophila* - Alfonso Martinez - March 6th

I shall be discussing issues of noise regulation in gene regulatory networks during cell fate decisions. The premise of the exercise will be that studies in bacteria and yeast have shown that transcriptional noise is a pervasive occurrence and that when one extrapolates these findings to developmental gene regulatory networks, it looks as if it is a miracle that things work. Of course there are no miracles, just regulation. The lecture will explore these issues. There is a review I wrote which will be the basis of the lecture. Martinez Arias AM, Hayward P. “Filtering transcriptional noise during development: concepts and mechanisms” Nat Rev Genet. 2006 Jan;7(1):34-44.