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What is Genetics?

Genetics is the most fundamental of the biological sciences – it underpins all of biology and all biomedical research. It is the core discipline for understanding that grandest of phenomena – evolution and, as the famous evolutionist Dobzhansky once said, 'Nothing in biology makes sense except in the context of evolution'

Sydney Brenner, who was awarded a Nobel prize in 2002 for his work on *C.elegans*, predicted 'Genetics will disappear as a separate science because, in the 21st century, everything in biology will become gene-based, and every biologist will become a geneticist' [*Trends in Genetics* 9:104, 1993].

Modern genetics encompasses an enormous diversity of topics. These can be divided into two broad categories: function, how the genetic blueprint operates during the lifetime of an organism; and evolution, how the genetic systems we see today have come about.

Function can be studied at many levels. At the level of the genome, we are interested in how DNA is copied, transcribed and repaired, how genes work and how chromosomes are organised. During development, we would like to know how groups of genes work together to orchestrate cell division and differentiation. The end-product is an adult organism whose behaviour, physiology, morphology and ecology are determined by a complex interaction between the environment and the genes it carries. Disentangling the effects of genes and environment is a further area of interest.

All organisms are the product of **evolution**. To understand the overall biology of an organism we must appreciate both the evolutionary steps that shaped it and the forces that are acting to change or maintain it now.

Sydney Brenner's prediction has proved to be largely correct, with genetics one of the most important disciplines in both the basic and biomedical sciences today. Several other Part II courses cover some aspects of genetics, but we offer a broad grounding in the subject, which will equip you for a wide range of careers, both in and outside science.

'Genetics is the most exciting subject to study. It was so 40 years ago when I started, and it is even more so now, a time when the complete genomic sequences of organisms for bacteria to humans are being made available'

Professor Michael Ashburner FRS

The Genetics Department and the Part II Class



As a Department, Genetics is small, friendly and has a much less formal atmosphere than many larger Departments. Final year students become integrated into the life and work of the Department and interact daily with the academic staff. Our Part II class has averaged about 30 students for the past few years - small enough for the entire class to know each other and the staff and large enough to make an impact on the Department. The familiar atmosphere of the Department gives students easy access to staff and arranging supervisions, or more informal meetings, is straightforward.

A large ground floor seminar room is set aside for the use of the Part II course, and our first floor library is shared among all members of the Department - although the majority of users at any one time are usually Part II students. The library has a wide range of books and journals, and computer links to the necessary e-resources. These facilities allow students to ensconce themselves in the Department during the day. The departmental tea room is shared by all members of the department including, of course, Part II students, and this encourages a sense of belonging and familiarity.

The Department houses a wide spectrum of interests, with a common theme being the application of genetic tools to the understanding of biological problems. Areas of research include cell and chromosome biology, epigenetic inheritance, mammalian developmental biology, insect and worm development and neurobiology, plant development, microbial genetics, infectious disease dynamics, functional genomics and systems biology, and various aspects of evolution and population genetics. The breadth of interests of the Department means that it is possible to obtain tips and contacts in a wide range of research areas, which could help with your career planning. For more details, please see 'Research in the Department of Genetics' on page 19, or: http://www.gen.cam.ac.uk/research-groups

Genetics Part II logo designed by Luke Cahill (Part II 2011/12)





Staff Christmas gathering; Outreach Team at the University Science Fair; Genetics' Summer BBQ.





Genetics Bake Off competition with staff and student winners; Outdoors Christmas event with Pizza Mondo 2021; Online Christmas Event 2020.









Course Aims and Objectives

The Genetics Part II course aims to provide both a **broad overview** of the subject, and to give you an opportunity to study some selected areas **in depth**.

During the year, we aim to give you:

- A thorough grounding in the theoretical and practical foundations of basic genetics.
- An appreciation of the breadth of genetics; how genetics is applied in other disciplines.
- Detailed knowledge of selected areas.
- The chance to discuss and think about moral and ethical questions arising out of the applications of genetics to modern life, e.g. genetic counselling and CRISPR/Cas.
- Experience of research through a term-long project working within a research group.
- The ability to muster information about a topic, to critically assess it, and to communicate this information effectively in speech and writing.

What does the course entail?

The course is organised into **4 modules**, each being made up of ~24 lectures, accompanied by seminars or discussion sessions. These modules aim to cover the range of genetics from cellular to organism level and will show how the latest developments (in areas such as genome sequencing, functional and computational biology, and stem cells and organoid technology) are being applied to the problems of how genes in different species are organised, expressed and interact, to give the final phenotype.

There is no option system; instead, you are encouraged to attend all the lectures to ensure that you acquire the necessary breadth of background in the subject. Lectures generally take place at 9 am and 11 am, Monday to Friday, with 'extras' usually in the afternoons.

Teaching in the Department takes a variety of forms. Apart from lectures, we provide interactive

seminars, examples and data handling classes, and journal clubs. We offer supervisions with teaching staff around the time of their lectures. You will also be assigned an Adviser within the Department, with whom you meet regularly, to support your progress during the year.

In the Michaelmas term, you are offered sessions to help you make the transition to Part II, for example: sessions on essay writing, study skills, basic statistics and introductions to the online resources available via the UL and to bioinformatics [see page 12 – Extras]

You have an opportunity to show your individual worth through your research project, and the project oral presentation [see page 14]. You are also encouraged to submit regular essays or specimen answers throughout the year, on which you receive feedback. This practice is vital preparation for the exams.

Teaching in the Department takes a variety of forms

NST Part II and Part II BBS

You can take Genetics as a single subject in Part II of the Natural Sciences Tripos. This route will automatically involve a research project. Alternatively, you can take Genetics as your major subject in Part II Biological and Biomedical Sciences, or you can take a single Genetics module as a Part II BBS minor subject:

Single subject Genetics in Part II NST (NST2GN)

You will do **all four modules** plus the module-linked problem solving and journal criticism sessions, and the SAG discussions. You will also undertake a **research project and linked literature review.**

Four paper subject in Part II BBS (414)

You **will take the four Genetics modules** (including module-linked journal and problem sessions), together with another one paper (your minor subject) and complete a **dissertation**. You can select your minor subject from the list of permissible options available. Students choosing the BBS route will have Genetics as their 'home' department and have access to exactly the same facilities as single subject NST students.

One Genetics module taken as a Part II BBS Minor subject

Two of our modules are offered as Minor subjects to Part II BBS students who are not taking Major subject Genetics: **M3 Human Genetics, Genomics & Systems Biology** (120) and **M4 Evolutionary Genetics & Adaptation** (121). In addition to the lectures, you will be expected to attend relevant journal and problem solving sessions for that module.

The Department also offers a stand-alone module in **Bioinformatics** (128) that is available as a minor subject to BBS students. More information about the Bioinformatics minor subject can be found here: <u>https://bioinfotraining.bio.cam.ac.uk/undergraduate</u>

BBS information can be found at : <u>http://www.biology.cam.ac.uk/undergrads/nst/bbs</u>

There is also a separate brochure for Part II BBS as a whole, from the Faculty of Biology.

MVST - Are you a Medic or a Vet?

In most years 20-50% of the class has comprised Medical and Veterinary students, so if you are concerned about your relative lack of subject background, there will be others in a similar situation. Access to appropriate Moodle Part I course sites is provided, and background reading suggestions are provided, prior to the course, to help you catch up.

See page 27 - 'Preparation and previous courses of study'.

Genetics in IA and IB

Lecturers from the Department of Genetics contribute to a variety of IA and IB courses, so you will probably have already encountered many of us at some stage in your degree course.

For example, in the following NST courses:

Biology of Cells (IA)

Lectures from: Dr David Summers (Hunting the Gene; LT), Prof Steve Russell (The Genetic Revolution; LT) and Dr Marisa Segal (Cell Proliferation; LT).

Lent Term Practicals on fungal, bacterial and *Drosophila* genetics (delivered by Dr Marco Geymonat).

Evolution & Behaviour (IA)

Lectures & practical from: Dr John Welch (Evolutionary Genetics & Adaptive Evolution in Populations; MT)

Mathematical Biology (IA)

Lectures from: Dr Aylwyn Scally (Linear algebra; MT).

Cell & Developmental Biology (IB)

Lectures from: Dr Charlotte Houldcroft (Prokaryotic strategies; MT), Prof Cahir O'Kane (Genome function & evolution; MT, plus Cell and organelle regulation; LT), Dr Marisa Segal (The eukaryotic cytoskeleton and mitotic cell division; LT), Dr Ben Steventon (Xenopus & Zebrafish development; ET) and Dr Naomi Moris (Mammalian development; ET).

Practicals on mobile elements in *Drosophila* and fluorescence microscopy from Prof Cahir O'Kane (MT) and on the cytoskeleton from Dr Marisa Segal (LT).

Evolution and Animal Diversity (IB)

Lectures from: Dr John Welch & Dr Aleksei Belyi (Genes, genomes and infectious disease; LT).

Mathematical & Computational Biology (IB)

Lectures & practicals from : Prof Henrik Salje (Introduction, MT and Dynamic models, LT); Prof Richard Durbin (Bioinformatics, MT and Bayesian methods, LT); Dr Alexia Cardona (Python, MT); Dr Aylwyn Scally (Linear Algebra, LT).

Or in the following MVST courses:

Molecules in Medical Science (MIMS) (IA)

Lectures from: Dr Christine Farr (Genetics in human and animal medicine; LT, ET)

Human Reproduction (IB)

Lectures from: Dr Felipe Karam Teixeira (Human genetics and whole genome association studies; LT)

The Part II Modules

Michaelmas Term

- Module 1: Genomes, Chromosomes and the Cell Cycle
- Module 2: Early Development & Patterning: Genetic and Cellular Mechanisms

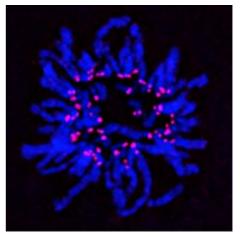
Lent Term

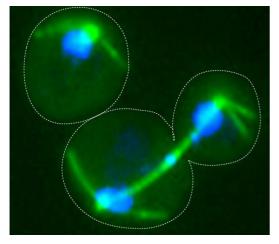
- Module 3: Human Genetics, Genomics & Systems Biology
- Module 4: Evolutionary Genetics & Adaptation

MODULE 1 – Genomes, Chromosomes and the Cell Cycle

This module will first explore how eukaryotic genomes are organised. We will examine histone modifications, nucleosome structure and organisation of the chromatin fibre. Topics discussed will include the novel paradigm of compartmentalisation via liquid-liquid phase separation, which allows intranuclear organisation in the absence of a membrane.

We will then compare eukaryotic chromosomes in interphase and during M phase, consider mechanisms for compaction in mitosis and examine two key functional elements: the centromere and telomere.





We will explore the control mechanisms that promote correct cell cycle progression and the accurate segregation of genes and chromosomes into daughter cells at cell division, centred on key cell cycle protein kinases, phosphatases and checkpoints. Then we will examine how DNA viruses exploit eukaryotic chromosomes and circumvent the cell cycle.

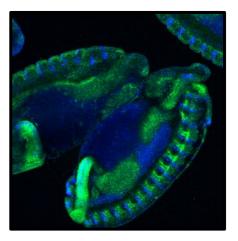
Finally, we will consider prokaryotes and the importance of their mobile genetic elements in spreading antibiotic resistance in bacteria.

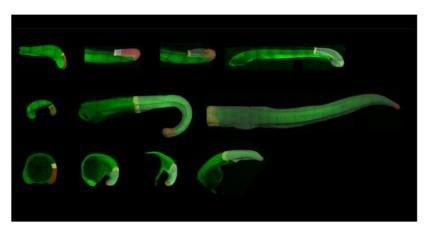
Taught by: Rosana Collepardo, Christine Farr, Marco Geymonat, Charlotte Houldcroft & Ash Zarkan

MODULE 2 - Early Development & Patterning: Genetic and Cellular Mechanisms

This module will cover how the early embryo develops from a fertilised egg to form the body plan. It will focus on our understanding of how gene regulatory and signalling interactions drive cell fate decision-making within cells, and combine this with our understanding of how dynamic cell behaviours drive the shaping of tissues through morphogenesis.

You will therefore learn about the key principles of embryonic development, taking examples from a range of early developmental events, such as cell fate determination, germline development, gastrulation, segmentation, and somitogenesis, in both invertebrate and vertebrate systems.





During the course of the module you will be introduced to a range of modern techniques applicable to the study of development including molecular, genetic and imaging technologies.

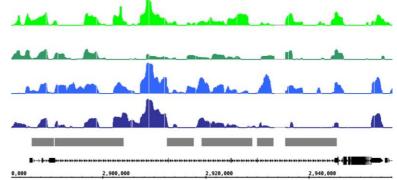
The module will compare mechanisms across a broad range of experimental organisms and processes, in order to highlight the essential principles of developmental biology.

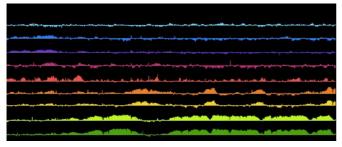
This is an inter-departmental module, with teaching shared by Genetics, PDN & Zoology. Contributors from Genetics: Julie Ahringer, Daniel St Johnston, Ben Steventon, Felipe Karam Teixeira]

MODULE 3 - Human Genetics, Genomics & Systems Biology

Human genetics, the genetic basis of human disease and the role of genomics in tackling it are the focus of this module. Humans are a problem for the geneticist because, for all sorts of good reasons, we don't do experiments on ourselves. Human genetics has always needed to exploit technology to obtain answers to the problems it poses. The sequencing technologies that underpin our ability to analyse genomes will be examined, followed by the organisation of the human genome, the role of repetitive DNA, and of epigenetics (including genomic imprinting).

We will explore how we assemble genome sequence and measure sequence variation and introduce rare disease genetics. We will then move onto genetic approaches aimed at characterising common diseases, including genome-wide association studies (GWAS).





We will introduce the genomics approaches that underpin functional analysis of genomes, including technologies for measuring gene expression, analysing transcription factor activity and chromatin states, and introduce modern proteomics.

Finally, the module will review the application of gene therapy approaches to deal with human disease.

Taught by: Gos Micklem, Richard Durbin, Michael Imbeault, Carol Edwards, Felix Day, Steve Russell, Paul Flicek and Christine Farr.

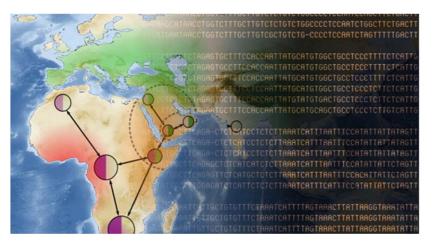
[This module is also available as a BBS Minor subject]

MODULE 4 - Evolutionary Genetics & Adaptation

Modern evolutionary theory has its roots in the union of Mendelian genetics with Darwin's theory of evolution, two of the great unifying themes of biology. This course will consider the process of evolution from a genetic perspective, exploring the central topics of natural selection, adaptation and genetic drift, and combining a variety of empirical and theoretical approaches. Alongside this, the course will explore how genomes themselves are shaped by selection, drift and their evolutionary history.



The first half of the module will explore the genetic basis of adaptation. Do we expect evolutionary change to involve few or many genes, and how might we go about identifying the genes underlying a particular trait? What kinds of genes control evolutionary changes in morphological traits? We look at the genes underlying convergent evolution as a way of understanding the predictability of evolutionary change. Genomic data contain a wealth of



information about the history of populations and natural selection, and population genetics provides a framework to reconstruct these processes.

The final lectures in this section will show how mathematical models of population genetics can be used to describe and reconstruct the action of natural selection, genetic drift and mutation.

The second half of the module will look at the evolution of genomes and conflict within genomes. We will begin by considering one of the conundrums of evolutionary biology—why most species reproduce sexually—from a theoretical and empirical perspective. Sexual reproduction leads to conflicts between genes within the genomes, and we will explore its consequences for genome evolution. We will then examine the evolution of key features of genomes—sex chromosomes, introns, repetitive DNA and gene expression. Finally, we will consider the evolution of quantitative traits that are controlled by many genes, and what constrains the evolution of these traits.

This is an inter-departmental module, with teaching shared by Genetics & Zoology. Contributors: Frank Jiggins, Aylwyn Scally, John Welch, Chris Jiggins, Bill Amos, Nick Mundy, Emelia Santos, Lucy Weinert, Richard Durbin, Edwige Moyroud. This Module is also available as a BBS Minor subject.

'Extras'

Social Aspects of Genetics (SAGs)

A series of interactive discussions, with invited speakers from the Sanger Institute, Addenbrooke's, and elsewhere. Topics include medical ethics (e.g. issues surrounding gene therapy, genome sequencing and over-the-counter DNA testing kits), bioethics (e.g. genome editing technologies, such as CRISPR), biofuels, antibiotic resistance, plant GMOs, scientific publishing & "open research", and genetics & race.



Michaelmas Term Information Sessions

Sessions will cover study skills (including essay writing workshops and information on plagiarism and how to avoid it). Introductions to bioinformatics and to statistics will be run, along with briefings on coursework preparation and the end-of-year examinations. In addition, there will be sessions outlining the PhD application process, and on careers in genetics.

Journal Sessions

Sessions are held for each Module, in which students learn to read, understand and criticise papers from the primary scientific literature.

Problem-solving/Data-handling sessions

In these sessions, students work in groups solving genetics problems or interpreting experimental data. This forms vital practice for the exams, and indeed for any future career in a lab.

Computational Practical sessions

In recognition of the need for more training in programming and bioinformatics, Module 3 will include an introduction to some of the computational approaches covered in the lectures.

Meetings with your Adviser

During the Michaelmas term you are encouraged to arrange weekly meetings with your assigned Adviser, who will answer any queries you have about the course and its organisation and will help sort out any problems that arise during the year.

Seminars

The Department runs two main seminar series, which Part IIs are encouraged to attend. One series is given by external speakers; and in the other series current Postgraduate students give a brief lunchtime presentation on their research.

Supervisions

Supervisions on the lecture material are provided by the lecturers themselves. Each lecturer will provide a list of times when they are available to give supervisions, together with possible essay

titles and topics for discussion. We encourage you to submit essays to lecturers, who will provide you with feedback.

Revision Seminars

There is no formal teaching in the Easter Term, but revision seminars are organised for each Module, to allow you to ask questions about the aspects you don't feel you have understood, and to help with your preparation for the exams.

The Part II Examination

The examination for Genetics Part II (NST2GN) consists of five written papers, and a research project. There is also a brief oral examination, although this does not make a numerical contribution to the final mark.

Each module in the course will be examined by a separate 3 hr written paper in the final examination, so you can expect questions on Module 1 to be in Paper 1 and so on. Each paper will include both essay-based questions and questions designed to assess the skills acquired in the data handling/ problem-solving components of the course and the journal sessions.

There is one additional paper, the Integrated Paper. This is a 2 hr paper and will contain a mix of broad-based questions designed to test your ability to integrate knowledge from across the course, as a whole.

If you are taking **NST Part II Genetics**, the current weightings of each part of the examination are:

Papers 1- 4 (16% each)	64%
Integrated Paper	10%
Research Project (a literature review, research project & report) See the following pages for information about the project	26%

If you are taking Genetics as **BBS Part II major subject** the current weightings of each part of the examination are:

Genetics Papers 1-4	64%
Minor Subject	16%
Dissertation See page 17 for information about the dissertation	20%

The Research Project

In the Lent Term each Part II Genetics student carries out an individual research project. This forms an important part of the course and allows you to engage in your own research work within an established group in the Department. It gives you an opportunity to work alongside graduate students and post-doctoral scientists who are carrying out upto-date work in the field, and to become familiar with the atmosphere of an experimental laboratory.

Each student selects a project from a list of options suggested by members of staff. Projects are chosen during October/ November, which gives plenty of time to plan them before the beginning of Lent Term.

From mid-November and over the Christmas vacation you will be asked to write a review of the scientific literature in your chosen field.

Then your actual research will start at the beginning of the Lent term. Your findings are written up and the report handed in at the beginning of the Easter vacation.

As well as providing an exciting opportunity for you to demonstrate initiative and ability, the project gives you some idea of what research is really like.

Project Presentations

All students give a short oral presentation on their research project to the rest of the class, and a few of the lecturers. A chance to try to lecture better than the lecturers!

As well as providing an exciting opportunity for you to demonstrate initiative and ability, the project gives you some idea of what research is really like.



In the time available, exciting results can emerge: some projects have evolved into PhDs for the student concerned, and others have contributed to published scientific papers.

For example,

Eve Ainscough [Part II 2018/19] contributed to:

Elmer JL, Hay AD, Kessler NJ, Bertozzi TM, **Ainscough EAC** & Ferguson-Smith AC : Genomic properties of variably methylated retrotransposons in mouse. **Mob DNA** (2021) 12(1): 6 doi: 10.1186/s13100-021-00235-1

Raag Agrawal [Part II 2018/19] contributed to :

... **Agrawal R**, Prabakaran, S. : Big data in digital healthcare: lessons learnt and recommendations for general practice. **Heredity** (2020) 124(4) 525-534 doi: 10.1038/s41437-020-0303-2

... Mi Kieu Trinh [Part II 2018/19] contributed to :

Trinh MK, Wayland MT, Prabakaran S. : Behavioural analysis of single-celled aneural ciliate, *Stentor roeseli*, using machine learning approaches. **The Royal Society Interface** (2019) 16(161): 20190410. doi: 10.1098/rsif.2019.0410.

... Alistair Dunham [Part II 2015/16] contributed to :

Nene NR, **Dunham A**, Illingworth CJR : Inferring fitness effects from time-resolved sequence data with a delay-deterministic model. **Genetics** (2018) 209(1) 255-264.doi: 10.1534/genetics.118.300790.

... Tim Freeman [Part II 2014/5] contributed to :

Shaw C , Lonchamp J, Downing T, Imamura H, **Freeman T M**, Cotton J A, Sanders M, Blackburn G, Dujardin J C, Rijal S, Khanal B, Illingworth C J, Coombs G H, Carter K C. : In vitro selection of miltefosine resistance in promastigotes of Leishmania donovani from Nepal: Genomic and metabolomic characterization. **Molecular Microbiology** (2016) 99(6) 1134-48. doi: 10.1111/mmi.13291

... Jessica Patel [Part II 2010/11; Part III 2011/12] contributed to :

Corrigan AM¹, Shrestha RL, Zulkipli I, Hiroi N, Liu Y, Tamura N, Yang B, **Patel J**, Funahashi A, Donald A, Draviam VM. : Automated tracking of mitotic spindle pole positions shows that LGN is required for spindle rotation but not orientation maintenance. **Cell Cycle** (2013) 12: 2643-2655

... Matthew Thomas [Part II 2009/10] contributed to :

Yalcin B, Zhao L, Stofanko M, O'Sullican N, Kang ZH, Roost A, **Thomas MR**, Zaessinger S, Blard O, Patto AL, Sohail A, Baena V, Terakai M & O'Kane CJ : Modeling of axonal endoplasmic reticulum network by spastic paraplegia proteins. **eLife** (2017) 6:e23882 doi <u>10.7554/eLife.23882</u>

Examples of projects offered:

- Deterministic and stochastic models for inferring fitness effects in viral populations
- Bioinformatic identification and characterisation of KRAB-ZPPs transcripts and their isoforms in purified *ex vivo* mammalian cells
- Dissecting the C-terminal region of human Topoisomerase IIa
- Determining the function of long non-coding NAs using Cas9/CRISPR genome editing
- Heat responsive transposon and its possible role in acclimation to heat stress
- Genomics of Drosophila Sox100B transcription factor
- Visualising single neurons that monitor activity in mushroom bosies (memory centre) of larval Drosophila a Brainbow approach
- The role of Par-1 in polarising the cortex
- Genome reduction and pathogenicity in bacteria
- Polarising the epithelial microtubule cytoskeleton
- Manipulating mother-daughter controls for asymmetric expression and age-sensitive protein mobility
- Comparing recombination maps in Pan genome sequence data
- Characterisation of cellular immune response in resistant and susceptible Drosophila lines to the parasitoid wasp Leptopilina boulardi
- Using micro-injection to down-regulate genes involving retro-element suppression in maize endosperm
- Viewing the axonal ER network in live Drosophila that are mutant for hereditary spastic paraplegia genes
- Optogenetic activation of modulatory neurons to test behavioural odour discrimination in Drosophila larvae
- Analysis of cell behaviour and gene expression during mouse ES cell differentiation
- Characterisation of Tem1 phosphorylation in the control of mitotic exit network and the spindle orientation checkpoint in yeast
- Investigating the molecular mechanism behind gene repression via a Retinoblastoma-like protein in *C. elegans*
- Identification of mammalian metastable epialleles
- Exploring the expression pattern and alternative splicing of regulators of genomic imprinting
- Inferring gene flow between human populations
- Understanding the number of SARS-COV-2 circulating strains within communities
- Studying the expression of the master differentiation factor of germline stem cells at the single molecule level
- Exploring the role of gene duplications in cold adaptation and diversification of Antarctic Notothenioid fish genomes.

The BBS Dissertation

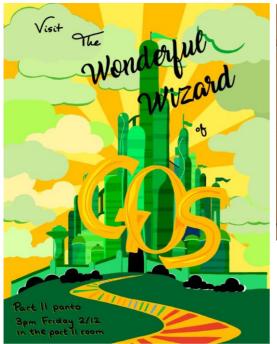
BBS students will have the chance to select a dissertation topic from a list circulated early in the Michaelmas term. All BBS students will have the chance to give a short oral presentation on their dissertation research to the rest of the Genetics class at the end of the Lent Term. Past topics have included:

- Can we assign a function to 80% of the DNA in the human genome?
- The biology of CRISPR/CAS systems and their uses in eukaryotic genome engineering
- How can genomic data be used to understand cancer evolution and to assist with cancer therapy?
- How does a cell make a decision to divide or stop dividing?
- How have bdelloid rotifers avoided sex for so long?
- Discuss the concepts presented in C H Waddington's 1942 paper in *Nature* 'Canalisation of development and the inheritance of acquired characteristics'
- Transgenerational epigenetic inheritance in mammals fact or fiction?
- Many human cancers are aneuploid. Yet aneuploidy has detrimental effects on human development and has been shown to reduce cellular fitness : Consider this conundrum
- Why do endosymbiotic bacteria have small genomes?
- Cell and gene therapy the future of human monogenic disorders
- Have regulatory changes been more important for the evolution and divergence of species than changes in protein coding sequence?
- Discuss recent developments in the mechanistic understanding of cell size control
- Transposable elements and their impact on human health new opportunities in the era of large scale human genome sequencing
- Can the bacterial endosymbiont Wolbachia eliminate vector-borne disease?
- Safeguarding genome integrity: DNA damage and repair in heterochromatic domains of eukaryotic genomes
- Molecular mechanisms underlying mitochondrial dynamics
- Genetic Mechanisms of pattern formation on the surface of plants and animals
- What can single cell 'omics approaches really tell us about biology?
- Understanding the ability for chikungunya virus to persist endemically in populations
- How important was the impact of archaic admixture on the human genome?
- How are important are mutations of large effect for adaptation by natural selection?
- What has experimental evolution taught us about how new species arise?

Social Aspects of Life in the Department

Research in Genetics Day

This one-day review of research in the Genetics Department takes place at the end of the Michaelmas Term. This informal meeting is an excellent way to appreciate who does what within the Department. Part II students are encouraged to attend.





The Christmas Party and Student Panto At the end of the Michaelmas Term, the Part IIs dazzle the department, traditionally with a Panto. This could be your chance to not only demonstrate your thespian skills, but also to exact revenge on the academic staff

who have tortured you in lectures! This Department can, shall we say, boast several members of staff who can easily be represented as compelling pantomime characters – and they love it! (Poster from the 22/23 Part II Class Panto; Photo from 21/22 class decorating the Christmas Tree, also holding their Panto Poster)

Happy Hour

Once a month, departmental Lab Groups take turns to host invite our popular Happy Hours. All from the department are invited for drinks and snacks.

The Summer Garden Party

After the exam results are announced we hold a Summer Garden Party; a chance to relax and celebrate with the rest of the Department once the year's hard work is over with food and drinks.

(Photo from 2020/21 class enjoying pizza and prosecco at the Summer Garden Party to celebrate the end of their exams)



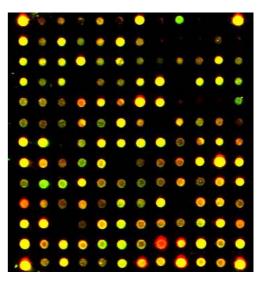
Research in the Department of Genetics

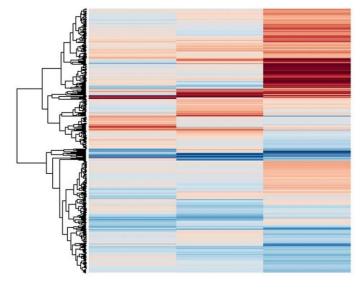
The range of research subjects in the Genetics Department is very broad, but it can be roughly divided into the 'themes' below. Of course, many Groups fit more than one 'theme'. This breadth benefits students in several ways. First, it means that the Department is well balanced between whole-organism and molecular approaches. Second, for those wishing to go on to research, there will almost certainly be someone with useful contacts, to help you get into almost any branch of genetic research. Each research group has its own web page, with more details about their work, accessed from: http://www.gen.cam.ac.uk/research-groups.

*An * indicates a Group which is based outside the main Department building. Most are sited just across Tennis Court Road*

Functional Genomics and Systems Biology

Professor Steve Russell. F is for Fruit Fly and Steve is a big fan. His is one of several groups using *Drosophila* as a model in research. Steve's group is studying the function of the Sox family of transcriptional regulators during embryonic development with a particular focus on the role the proteins play in the formation of the CNS. Along with classical genetics and developmental biology, they are utilising modern functional genomics and proteomics approaches. Recently they have been using clever genetic and biochemical approaches to better understand effective insecticide design.

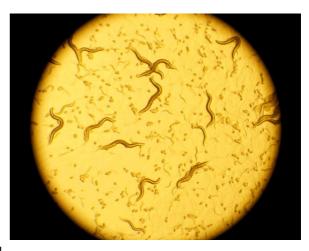


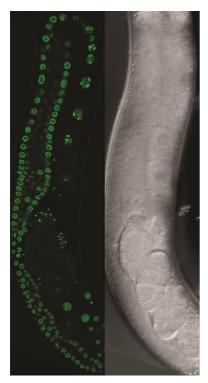


Professor Gos Micklem. Gos works in the field of integrative genomics – applying high throughput experimental methods and using bioinformatics to solve real world problems. Some work focuses on developing new tools and providing community resources (such as their data warehouse system InterMine). His research ranges across a number of fields and includes *de novo* genome sequencing and annotation to obtain insights into gene function and evolution, genomic studies of parasite action, cancer biology, and synthetic biology.

Developmental Biology

Professor Julie Ahringer FRS, FMedSci *. Julie is interested in how chromatin regulation plays a central role in transcriptional control and genome organisation, because dysregulation is implicated in human disease. Her group uses the power of functional genetics and genomics in the nematode *C. elegans* to address fundamental questions by analysing epigenetic state and function in wild-type and mutant animals and tissues. *C. elegans* is an excellent system for studies of chromatin function due to its small well-annotated genome, powerful RNAi technology, and rich resource of chromatin mutants. Another reason that Julie and her colleagues study *C. elegans* is because it's beautiful!

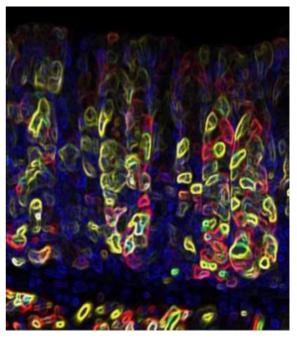




Professor Daniel St Johnston FRS, FMedSci *. Daniel makes fruitfly larvae with no heads or no abdomens, or in some cases, two heads or two abdomens. He studies the mechanisms involved in localisation in the egg of maternal determinants such as bicoid RNA, which control embryonic pattern formation. He uses *Drosophila* as a model system to investigate intracellular transport and the origin of anterior-posterior polarity. Daniel himself has a normal complement of body parts.

Dr Ben Steventon. Ben's research interest is in comparative developmental dynamics. He wants to know how, during embryo development, multiple tissues take shape in a highly coordinated manner to build the final body plan. Ben likes to use a musical analogy "Think of an orchestra without a conductor. Do players listen out for each other to keep in tempo? How does one section of the orchestra communicate with another?" His group is studying this using several model systems, but their favourite is the Zebrafish because, as everyone knows, Zebrafish Rock!

Dr Felipe Karam Teixeira. Felipe's interest is the development of the germline, the 'immortal' cell lineage that provides the continuity of life. In particular, he is interested in the genetic and molecular mechanisms controlling germline stem cell behaviour and protecting totipotency, using the *Drosophila* ovary as a model system. Half of his group work on gene expression regulation during stem cell self-renewal and differentiation, while half work on mobile elements and genome stability. Felipe himself is functionally and structurally very stable.



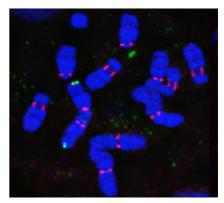
Dr Edwige Moyroud *. Edwige's group investigates the mechanisms of pattern formation on the petals of flowering plants and is known as "Team Hibiscus" because of their fascination with this plant and its beautiful bullseye pigmentation patterns. These patterns play crucial roles in both pollinator attraction and in pollen protection against UV damage. They also represent striking examples of evolutionary diversification by natural selection. Her group combines a range of genetics and developmental biology approaches with novel imaging, modelling and phylogenomic tools.

Dr Erik Clark. Eric is fascinated by developmental patterning systems and their evolution. Most of his research is on various aspects of anteroposterior patterning in the *Drosophila* blastoderm, but is he is also interested in arthropod evo-devo and vertebrate somitogenesis.

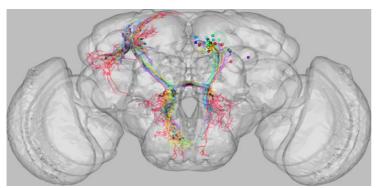
Chromosomes and Cell Biology

Dr Christine Farr. Christine's research focuses on centromeres and telomeres. Her lab has created vertebrate cell lines mutated for various chromosomally-associated proteins, as well as a series of human mini-chromosomes. These reagents are being used to study chromosome behaviour in mitosis.

Professor Rosana Collepardo. Rosana's research focuses on understanding DNA packaging inside cells using approaches that bridge genetics, theoretical chemistry and physics. She develops and applies multi-scale computational models to investigate the structure of the genome at the nanoscale level. Their recent work



has shown that nucleosomes are diverse and plastic and chromatin is liquid-like!



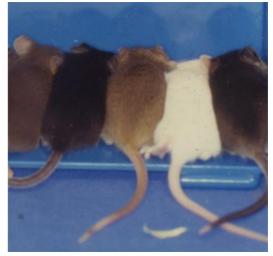
Dr Liria Masuda-Nakagawa. Liria is interested in brains and is using *Drosophila* to investigate the circuitry of odour discrimination and olfactory memory formation.

Professor Cahir O'Kane. Cahir studies how neurons work and how they go wrong during neurodegeneration in

Drosophila. Of particular interest are the processes that organise and traffic membranes, both pre-and post-synaptically. At this level, flies are about as smart as we are.

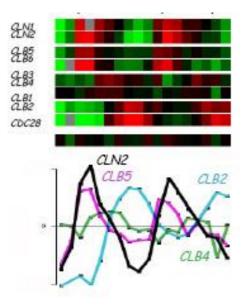
Epigenetic Inheritance

Professor Anne Ferguson-Smith FRS, FMedSci. Using mouse genetic models, the Ferguson-Smith lab studies the genetic and epigenetic control of developmental processes including stem cells, and the epigenetic control of genome function. The research combines both experimental and bioinformatics approaches to understand the link between genome and epigenome and the impact that this has on normal and abnormal development and physiology in tissues and in the whole organism.



Dr Michael Imbeault. Michael is interested in the impact of transposable elements on mammalian genomes. Using a mix of bioinformatic and molecular biology approaches his group is delving into how TEs, and DNA binding proteins that interact with them, contribute to disease risk factors and other complex traits.

Microbial Genetics



Dr Marisa Segal. Marisa's group uses the yeast *S. cerevisiae* to explore the mechanisms coupling mitotic spindle orientation with cell polarity, processes critical for the fidelity of chromosomal segregation and cell division. The principles emerging from these studies can be extended to learn how spindle orientation is controlled throughout metazoan development to generate cell diversity.

Dr Marco Geymonat. Marco is also a big fan of the yeast *S.cerevisiae* and is using genetics, biochemistry and microscopy to study cell polarity, spindle orientation and cell cycle progression.

Dr Ash Zarkan. Ash is seeking to understand the mechanisms of biofilm and persister formation in E. coli. The goal is to develop new therapies to inhibit E. coli biofilms and persisters, thereby reduce pathogenicity, improve antibiotic effectiveness and reduce recurrency in UTIs.

Dr John Archer *. A key challenge in understanding the genetic content and species composition of microbial habitats is the difficulty of culturing diverse fastidious microorganisms in pure



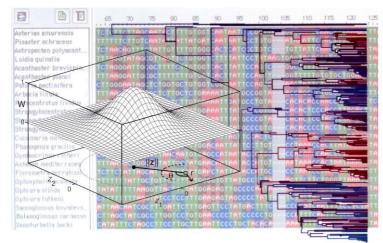
culture in the laboratory. John is applying metagenomics to capture the microbial population DNA sequence content of given environments. Such approaches have applications in environmental, biotechnological and medical sciences.

Evolution and Population Genetics

Professor Frank Jiggins. Using insects as a model system, Frank's Lab is studying the evolution of hosts and parasites. A combination of population, quantitative and molecular genetics is being used to address the genes that cause variation in susceptibility to infection, the evolutionary processes that maintain this variation in populations and how coevolution with parasites has shaped the insect immune system.



Dr John Welch. John's research focuses on the processes that shape DNA sequence variation within and between populations. Ongoing research projects involve quantifying the contribution of natural selection to genomic change, inferring specific selection pressures that were faced by natural populations, and identifying the general conditions that promote or hinder an adaptive response.



Dr Aylwyn Scally. Aylwyn's research focuses on the evolution of populations and species, using computational analyses of large-scale genome sequence data. His particular interest is in human and primate evolution, but the methods and approaches involved in evolutionary genomics are applicable to organisms across the tree of life.

Professor Richard Durbin FRS. The focus of the Durbin group is sequence-based

analysis of genetic variation and genome evolution. Their computational research projects encompass a broad range of organisms, including ancient and modern human DNA samples, induced pluripotent stem cells and cichlid fishes. Richard can't get enough genome sequences so is leading the University's collaboration with the *Darwin Tree of Life* project, which is sequencing thousands of species from the British Isles.

Professor Henrik Salje. Henrik's research is on applied public health research, especially with regards to the spread of infectious pathogens. His work sits at the interface of mathematical modelling, genetics, population biology, big data, public health and field-based epidemiology. His group has recently published findings highlighting the age-specific mortality and immunity patterns of SARS-CoV-2.

Dr Charlotte Houldcroft. Charlotte is focussed on understanding how the genetic diversity of DNA viruses impacts human health and how ancient evolutionary processes have shaped the viral genomes circulating today. Charlotte's work on herpes virus genomes from ancient DNA samples suggest that the virus became widespread with Bronze age migrations into Europe and possibly with the emergence of kissing!

Beyond Part II

Part II Genetics offers a challenging, rewarding and socially enjoyable course, which combines whole organism biology and molecular studies effectively to provide a step towards a successful career.

Many in the Part II class will progress to PhD positions in Cambridge and elsewhere. This is normally the best option for an eventual career in either pure research (e.g. in a university or research institute), or industrial research (e.g. in a biotechnology or pharmaceutical company). There are prospects for research positions in both 'pure' areas such as cell biology, genome analysis, evolutionary and population biology, and more 'applied' areas such as agricultural and medical genetics, biotechnology, and genetic applications to environmental problems. Where funding is tight a background in genetics may give prospective candidates an edge. A PhD might for example lead on to a career in bench science, academic or industrial research, science administration and management, working in an advisory capacity, or publishing and disseminating scientific information.

Employment prospects are good for Cambridge graduates in general. Part II Genetics provides

Genetics is a

range of job

booming subject

that offers a wider

opportunities than

an excellent training also for those not wishing to continue in 'front-line' science. Many employers are realising that they require people with a good background knowledge of genetics and a broad scientific training, even for jobs that do not involve bench science. Therefore, there are Part II Geneticists doing well in traditional publishing, in the City, in the law, even accountancy!

Former Part II and PhD students from this department now hold significant scientific positions in the UK and world-wide:

many other areas of biology Oxford, Cambridge, the USA (Yale, California), and the Pacific rim (Singapore and Papua New They often work as research group leaders for companies such as Unilever, Guinea). AstraZeneca, Novartis and GlaxoSmithKline. Some have joined Cambridge area 'Start Ups'. Other science-related destinations have included publishing (e.g. Benjamin Lewin, who founded the important journal, 'Cell') and venture capital consultancy.

Part III Systems Biology

For those interested in the Part III Systems Biology course, Part II Genetics offers an ideal platform by providing a comprehensive grounding in the basic methods underpinning genomics as well as an introduction to modelling approaches from a developmental biology perspective. More information is available here:

https://www.gen.cam.ac.uk/postgraduate/genetics-partiii-mphil

Feedback from former Part II students

Kane Toh [who stayed on to do his PhD in the department]

The Part II Genetics course gave me a thorough and critical knowledge of genetics. This is excellent as students of genetics are particularly well-equipped to enter different sub-disciplines in biology, since all fields in biology must intersect with the fundamental study of genetics. In terms of its atmosphere, the Genetics Department is really welcoming towards its small cohort of Part II students, and our unique pantomime tradition brings the class and the research community together. With the thorough syllabus, excellent teaching and vibrant atmosphere, I am proud to have chosen genetics as my Part II subject!

Katherine White

The small class size means that everyone knows each other and there's a feeling of belonging to a department that you don't get in Part I. The course itself is broad enough that you'll find something that you really love and goes into enough depth so that it's interesting. If that isn't enough for you then there's the fact that tea breaks are scheduled into the timetable and the fun of putting on a pantomime for Christmas!

Sarah Jones

There is no denying that the Genetics course is extremely hectic, especially when you have to undertake a research project as well as keep up with all the lecture material, and it often feels as though there aren't enough hours in the day. However, due to the helpful atmosphere of the Department and the structure of the course, there is always enough support to help you through. Even if you do not want a career in science, the Genetics Department is a fantastic place to spend a year and will hopefully provide you with some great memories!

Joe Laycock

Imagine yourself surrounded by desert with neither water nor sustenance. Hungry and thirsty you espy an oasis surrounded by a banquet of magnificent proportion. A mirage? Why no, this is Part II Genetics. An overflowing cornucopia awaits, ready to cater for every taste with a bounteous panoply of succour. Classical versus modern, genomics, cell cycle, development, evolution, plants; even the most ravenous of desires will be sated. Extended essays, projects and bio-informatics provide appetising introductions to some of the delicacies of modern genetics. Rich, succulent, alluring; come, eat, for none shall go hungry.

How to Apply

All students are required to register their Departmental preferences on-line through CamSIS.

This booklet, together with our website <u>(https://www.gen.cam.ac.uk/undergraduate/genetics-for-pt1)</u> should provide the necessary background information about the Department of Genetics and our Part II course.

Students considering taking Part II Genetics are invited to come along to our **Part II Open Day** on **Thursday 16th March, 2.30 – 4 pm**, when there will be the opportunity to chat to teaching staff and Part II students about the course. You will find the Department of Genetics on the Downing site, near the Biffen Lecture Theatre.

Representatives of the Part II Genetics course will also be at the **Part II Subject Fair** on **Friday 17th March**, **12noon – 4pm**.



Information on the course is also available in the Genetics folder on the **NST Part II Subjects Fair Moodle site**.

Preparation and previous courses of study

There are no compulsory prior courses or prerequisites for admission to Part II Genetics; we are looking above all for students with a genuine interest in genetics, who will get the most out of our stimulating course.

Part II Genetics students from the Natural Science Tripos will typically have taken courses such as Part IA Biology of Cells, IA Evolution & Behaviour, IA Mathematical Biology, Part IB Cell & Developmental Biology (or IB Biochemistry & Molecular Biology), IB Evolution & Animal Diversity, and IB Mathematical & Computational Biology. However, these courses are *not* required. Medical and veterinary students may also elect to take this course before proceeding to their clinical studies, and often form a significant proportion of the class. Students with a background in the physical sciences or mathematics have also done well in Part II Genetics in the past, and we welcome applications from such students.

For all incoming Part IIs who have not taken IA Biology of Cells, IA E&B and/or IB CDB, access is granted, during the long vacation, to the previous year's version of the Moodle sites for these courses, so that they can consult lecture notes and other posted material. The Department can also suggest material for directed reading prior to the course.

Vacation Research

Hands-on experience is an invaluable bonus when it comes to getting a foot in the door in research. The way that undergraduates, wanting to carry out summer vacation research in the UK, are funded has undergone extensive change in the past couple of years. This has been to ensure that funding schemes meet the legal requirement that students receive the Real Living Wage. Information on possible sources of funding and on how to apply can be found on our website at: <u>http://www.gen.cam.ac.uk/undergraduate/vacation-research</u>

Interested students should approach Group Leaders directly to find out if they have research opportunities in their Labs. <u>See our listing of labs</u>. Obviously the earlier you apply, the better. Some closing dates for funding are as early as February.

The Stephen Johnson Research Bursary

The Department of Genetics offers a small number of undergraduate 10-week research bursaries, through the generosity of Stephen Johnson, a former Part II student. They are open to second year students, in either NST or MVST, who intend to read Part II Genetics as their final year option.

The research must be carried out under the supervision of a Principal Investigator who is a member of the Department of Genetics. A list of research groups and their fields of research can be found <u>here</u>. Students will receive stipends at the living wage level.

<u>Application forms can be found here (https://www.gen.cam.ac.uk/undergraduate/vacation-research)</u> and should be sent to the Secretary to the Head of Department at

hodsec@gen.cam.ac.uk along with a CV and a brief description of the proposed project, which must have been discussed with the head of the host laboratory.

The deadline for applications is Friday 05 May 2023, and successful applicants will be informed as soon as possible after this (no later than the end of May).

The Richard Wilson Research Bursary

The Department of Genetics is delighted to announce a Bursary to encourage research exchanges in genetics between The University of Cambridge and the University of Glasgow. Bursaries are funded by the generosity of the late Dr Richard Wilson, Glasgow Genetics Department, who spent 40 years conveying his enthusiasm for genetics and evolutionary biology to students and research colleagues alike.

The Richard Wilson Bursary supports funding of student exchanges between Glasgow and Cambridge and will facilitate undergraduate students at any stage from the University of Glasgow or Cambridge to study at the opposite University. Glasgow students coming to Cambridge for periods of 8-10 weeks will receive stipends at the living wage level. University of Cambridge students wishing to spend a summer in a lab at the University of Glasgow carrying out research in the general area of genetics should contact cq663@cam.ac.uk for further details.

Completed <u>applications</u> for all summer awards should be returned to the Secretary to the Head of Department at: <u>hodsec@gen.cam.ac.uk</u>

The deadline for applications is Friday 05 May 2023, and successful applicants will be informed as soon as possible (no later than the end of May).

General bursaries – open to all students

Genetics Society Summer Studentship Grants:

The Genetics Society has grants available to support students to gain experience in any area of genetics by doing a research project during the summer holiday prior to the final year of their degree. (Deadline 31 March 2023)

Experience Postgrad Life Sciences: Students will receive the Real Living Wage and will be accommodated at Corpus Christi. (Deadline 30 January 2023)

<u>Amgen</u>: Support for students participating in the Amgen Scholars Programme.

In addition, places where students have previously received studentships to come to the Department include:

BSDB (<u>http://bsdb.org/awards/gurdon-studentships-for-summer-vacation-work/</u>) BSCB (<u>https://bscb.org/competitions-awardsgrants/studentships/</u>) Balfour-Brown Fund (Cambridge Zoology, open to students who will take internships in other departments <u>https://www.zoo.cam.ac.uk/intranet/professional-services/introduction/trust-</u><u>funds/balfour-browne-fund</u>)

Colleges: Many colleges provide funds to help support students wishing to broaden their experience by conducting research over the summer period.

Collated information about undergrad funding can be found at: <u>https://www.biology.cam.ac.uk/undergrads/InfoCurrentStudent/undergrad-fund</u>

In this useful piece in <u>Varsity</u>, Bethan Clarke talks about the value of her experiences on an informal placement in the Steventon Lab during the summer between Part 1A and Part 1B.

Interested students should approach staff members directly to find out if they have vacation research opportunities, funding and space available <u>http://www.gen.cam.ac.uk/research-groups</u>

For further information on the Part II Genetics Course

- Come along and chat to us at the Part II Subjects Fair (Friday 17th March, noon-4pm) or at our Part II Open Day (Thursday 16th March, 2.30 – 4 pm).
- Visit our website : <u>https://www.gen.cam.ac.uk/undergraduate/genetics-for-pt1</u>
- Visit our folder on the <u>NST2 Subjects Fair Moodle site</u>
- Scan the QR code below
- For general information about the course e-mail: <u>undergrad.admin@gen.cam.ac.uk</u>
- To contact the course organisers: ptilorganisers@gen.cam.ac.uk



Several members of this Department teach IA and IB NST and MVST: Dr Christine Farr, Prof Cahir O'Kane, Dr Aylwyn Scally, Dr Marisa Segal, Dr Marco Geymonat, Dr John Welch, Prof Steve Russell, Dr Ben Steventon, Dr Felipe Karam Teixeira, Prof Henrik Salje, Prof Richard Durbin and Dr Alexia Cardona.

They can supply further information about the Department and the Part II course. All can be contacted by email at the generic address: first initial.surname@gen.cam.ac.uk (no spaces or apostrophes).