Available PhD Project:

Supervisors: Dr Olivier Restif, Dr Lucy Weinert

https://www.research.vet.cam.ac.uk/research-staff-directory/principal-investigators/disease-dynamics/Olivier-Restif
https://www.research.vet.cam.ac.uk/research-staff-directory/principal-investigators/disease-dynamics/lucy-weinert

Project Title: Modelling the evolution of bacterial pathogens in the real world

Background:
The apparently limitless ability of pathogens to defeat control measures through evolution poses growing threats to human and animal health as well as food security. In particular, antimicrobial resistance (AMR) in bacteria is often perceived as an unavoidable outcome that can only be slowed down by careful use of available antibiotics and development of new ones. However, these strategies remain highly empirical and based on rudimentary assumptions about the evolutionary processes involved. Indeed, most of our knowledge and theoretical modelling of AMR evolution stems from in vitro experiments where bacteria are grown in rich medium and exposed to fixed concentrations of drugs. Very different conditions in living hosts or in the environment can lead to different growth dynamics of bacterial populations, creating variable selective pressures in the presence of antibiotics. For example, Streptococcus pyogenes readily evolves resistance in vitro, yet clinical isolates have remained susceptible to penicillin for over 60 years.

At the genetic level, evolution of AMR can involve de novo mutations as well as transfer of genes on mobile elements, which occur on different time scale with contrasting selective pressures. With rapid progress in sequencing, we now have access to large datasets that bear witness to the recent evolutionary history of bacterial pathogens in relation to disease outbreaks or antibiotic use. The Department of Veterinary Medicine is a leader in farm animal disease epidemiology, mathematical modelling of infectious diseases, and bacterial genomics, hence providing the perfect environment for a targeted PhD studentship in line with the BBSRC priorities.

Aims.
The student will develop mechanistic models for the evolution of AMR in bacterial pathogens. The models will be validated using genome sequence and epidemiological data from several bacterial species, including Streptococcus suis, Salmonella enterica and Escherichia coli, obtained from both the wild, and from experimental evolution studies. The project will contribute to answering fundamental questions about the evolution of adaptations in host-pathogen systems, and also has a clear applied component, relevant to food production.

Objectives.
(i) To develop a new dynamical framework for the circulation of bacterial species and mobile AMR genes, in the absence of disease and treatment.
(ii) To estimate key parameters in real systems, by fitting models to genomic data from asymptomatic carriage.
(iii) To model selection pressures created by interspecific competition and antibiotic treatment, within and between hosts, using data from clinical cases and experimental infections (collected as part of an MRC grant).
(iv) To simulate alternative drug regimens and treatment strategies that may reduce or counter selection for AMR.

Learning opportunities.
By bringing together mathematical modelling, bioinformatics and epidemiological data, this project will fill a gap in the field of bacterial evolutionary epidemiology, which is lagging years behind research on viral pathogens. With joint expertise from Restif and Weinert (Vet Medicine) and Welch (Genetics), the student will learn a variety of programming, statistical and genomic skills at the cutting edge of science. The student will benefit from interactions with other modelling experts within the Disease Dynamics Unit, as well as microbiologists, veterinarians and geneticists.

BBSRC DTP: As a Targeted BBSRC DTP student the successful candidate will complete DTP training courses and will undertake two rotation projects in their first year (one in their PhD laboratory and a second in a lab of their/their Supervisor’s choosing. On successful completion of these, they proceed to
their PhD project. Students must also complete a three-month internship (PIPS), usually before the last six months of the Programme. The full programme must be completed within 48 months.

**Funding:**
UK and EEA students who meet the UK residency requirements ([see here](#)) will be eligible for a full 4 year BBSRC studentship. This will cover a stipend at the standard Research Council rate (£14,553 per annum for 2017/18), research costs and tuition fees at the UK/EU rate, to start 1st October 2018.

**How to apply:**

- **Preliminary Stage:** Please send your CV, transcripts and a cover letter to Fiona Roby (email: fr288@cam.ac.uk) by 9th February 2018. The cover letter should outline your research interests and experience and explain why you think you would be a good fit for this project. Please also include contact details for two referees who may be contacted in the event you are shortlisted. Shortlisted candidates will be invited to interview in February 2018 (date to be confirmed).

- **Secondary Stage** (only if successful at interview stage): Following interviews the successful candidate will then need to submit a full official application to the University of Cambridge via the Applicant Portal - note there is a £50 fee for this application. A full offer will only be made once all conditions required by the University have been met.

**Deadline to apply:** 9th February 2018