

THE UNIVERSITY OF MANCHESTER

PARTICULARS OF APPOINTMENT

FACULTY OF BIOLOGY, MEDICINE & HEALTH

SCHOOL OF BIOLOGICAL SCIENCES

DIVISION OF EVOLUTION & GENOMIC SCIENCES

RESEARCH ASSOCIATE (EXPERIMENTAL EVOLUTION)

VACANCY REF: BM&H-13188

Salary:	Grade 6 £32,236 to £35,211 per annum (according to relevant experience)
Hours:	Full Time
Duration:	ASAP for 2 Years
Location:	Oxford Road, Manchester

Enquiries about the vacancy, shortlisting and interviews:

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Faculty of Biology, Medicine and Health

Introduction to the University of Manchester and the Faculty of Biology, Medicine and Health

The University of Manchester is the largest single-site university in the UK with around 38,000 students and more than 11,000 staff. We aim to become one of the top 25 research universities in the world by 2020 and are committed to delivering an outstanding teaching and learning experience; contributing to the social and economic success of local, national and international communities; producing the highest calibre graduates; and developing our staff to be amongst the very best of their peers.

To achieve our ambitious goals we aim to attract and retain the very best people to work across a range of academic disciplines and support functions.

The Faculty of Biology, Medicine and Health (FBMH)

The Faculty of Biology, Medicine and Health was created on 1 August 2016 when the Faculty of Life Sciences and the Faculty of Medical and Human Sciences will be brought together in a new, integrated structure to deliver a truly translational approach to the life sciences, ensuring smooth research pathways - from pure discovery science through to clinical application and patient care.



With a total annual income of over £300 million, and over 3,000 members of staff, the new Faculty is comparable in size to a medium-sized UK university. Thirty undergraduate and 90 postgraduate programmes offer our 11,000 students opportunities to develop the skills and knowledge they need for a successful career.

The Faculty's matrix structure facilitates interdisciplinary working and enables us to learn from each other and share best practice; and our eight, strategic Research Domains help to articulate our research strengths, drive large-scale, collaborative research activities and strengthen relationships with our research and healthcare partners.

The integration of discovery biology, clinical application and patient care within a single Faculty, particularly in a region with notable health inequality, provides us with a real opportunity to have a very significant and positive impact on people's lives.

Our strategic partnerships

The new Faculty inherited a number of key strategic partnerships that underpin its ambitions to develop ground-breaking research.

Working alongside six local NHS Trusts, the Faculty is a key member of the <u>Manchester</u> <u>Academic Health Science Centre (MAHSC)</u> - a federation of equal partners that unites leading healthcare providers with world-class academics and researchers. It aims to be a global centre for the delivery of applied health research and education and provide leadership for our local and regional health systems.

The Faculty also play a leading role in <u>Health Innovation Manchester (HInM)</u>, which was launched in September 2015, as part of the UK Government's decision to devolve health and social care responsibilities to Greater Manchester. HInM offers a unique opportunity to bring together health and social care, academic and life science related business resources across the region to deliver an innovative health ecosystem that can help accelerate innovation into our local health and social care systems, enhance our global scientific standing and act as a magnet for inward investment.

Key partnerships in the charitable sector include Cancer Research UK; Diabetes UK; and the Wellcome Trust; and the Faculty will also have research and funding links to a number of commercial organisations including Unilever, AstraZeneca, GlaxoSmithKline and Boots, who will help us to bring new drugs and products to the market.

Working for the University of Manchester

The University of Manchester strives to make our community a welcoming, caring and enthusiastic one, fuelling ambition with opportunities and support to help us all achieve our personal and professional goals.

Our diverse job opportunities include an attractive <u>benefits package</u> with family-friendly policies that provide for flexible working. We care deeply about career and personal development, offering a structured induction programme for new staff, an annual performance and development review, staff training for all career stages and mentoring opportunities to support your career development.

We have a genuine commitment to <u>equality of opportunity</u> for our staff and students, and are proud to employ a workforce that reflects the diverse community we serve.



As a global institution, situated at the heart of a lively, <u>culturally diverse city</u>, we welcome applicants of all nationalities. To help international job applicants plan for life in the UK, we have put together some useful <u>information on passports and visas</u>, travel to the UK, accommodation and a number of other practical considerations.

Project Title: Tackling antimicrobial resistance by understanding evolutionary landscapes

Project Description

The increasing prevalence of anti-microbial resistance (AMR) is one of the key health challenges of the 21st century. An important but neglected part of this problem is the interaction between the microbes and the aspects of their environment aside from antibiotics. Understanding of these interactions in relation to AMR offers the possibility of developing novel approaches that have the potential to produce not only better or more 'evolution-proof' antibiotics but also allow us to harness evolutionary processes themselves to allow antibiotic sensitive microbes to outcompete resistant ones. However, the evolutionary and environmental interactions and trade-offs are not well understood.

This project will ask a range of fundamental questions directly: 1. Does genomic background determine the genes involved in antibiotic and post-antibiotic adaptation? 2. Are the genes that evolve in the absence of antibiotics the same or different following more or less adaptation to antibiotics? 3. How do resistance and competitive fitness evolve in the absence of antibiotics: does the rate differ for strains longer to adapted to antibiotics? Critically, the answers will allow us to detect signatures of antibiotic adaptation in the genomes of bacteria found in a hospital setting as well as those used experimentally. This work will allow us to shape antibiotic prescription regimes (e.g. altering usage periods of particular antibiotics, tailoring treatments to specific infections) in novel, evidence-based ways, founded in a molecular, genomic and population understanding of AMR evolution.

Two posts are available on this project. This appointee to this post will use experimental characterisation of bacterial evolutionary landscapes, deep sequencing of bacterial populations and analysis of fitness effects of variants based on protein structure. A complementary post will use statistical inference and stochastic modelling to characterise microbial evolution in experimental and clinical settings in response to anti-microbial treatments.

Background Information:

This post will be in the School of Biological Sciences, Faculty of Biology, Medicine and Health. The School is ideally suited for both experimental and computational biology research, being home to one of the largest UK academic grouping of computational biologists and an active community evolutionary biologists as well as a large number (300+) other research group with diverse interests. Manchester will thus provide an outstanding environment for the proposed research with an active and highly collaborative research-training environment, and access to professionally managed high-performance computing clusters.

Other relevant genomic technologies such as deep sequencing and other high-throughput analysis methods will be provided by the Faculty's core facilities. Here too support includes optimal experimental design, sample preparation, analysis and subsequent data processing. In all cases the researchers on the project will receive relevant training in all techniques.

The research groups coming together around this project have unique expertise to take an experimental approach to the evolutionary grand challenge of AMR. Gifford, Knight and Lovell have collaborative research groups focused on evolutionary mechanisms. We ask questions



through a mixture of wet-lab experiment (primarily using microbial systems), and computerbased analysis, modelling and simulation. The resulting 'evolutionary systems biology' aims to deal clearly with the interactions of organisms and their environments in the context of evolution, with particular focus on antimicrobials and resistance to them. While this project embodies a new collaboration, it builds on existing collaborations, notably between Knight and Gifford (e.g. Krašovec, R. *et al.* (2017) Spontaneous Mutation Rate Is a Plastic Trait Associated with Population Density across Domains of Life. *PLoS Biol.*, 15, e2002731) and between Gifford and Tobias Galla, a physicist and stochastic modeler, also a co-investigator on this grant. Other coinvestigators are Tim Felton, a clinical microbiologist, Tjeerd van Staa, who works on AMR in clinical records and Thomas House, concerned with modelling population dynamics.

Overall Purpose of the Job:

1) To experimentally evolve laboratory and clinical strains of bacteria (*Escherichia coli*), quantifying fitness gains accessible to strains resistant to different antibiotics, associated with

different adaptive landscapes.

2) Sequence the genomes of experimentally evolved organisms to assess to determine whether the antibiotic resistance mutations correspond to single or multiple peaks.

3) Contribute to the development, with other members of the team, of evolutionary models to simulate evolution and spread of antibiotic resistance in realistic contexts

4) Contribute to the scientific direction of the project and to write up, in collaboration with others, results for publication in high impact journals.

Key Responsibilities, Accountabilities or Duties:

You will take responsibility for:

- Setting up experiments, analysing and interpreting resulting data, and communicating results via presentations and the writing of papers for publication in leading journals.
- Making significant input to the scientific direction of the project, and writing, as necessary, in a timely and efficient way.
- Communicating research plans and findings with project collaborators.

You will also be expected to:

- Actively read the scientific literature relating to (and around) the project.
- Have frequent meetings with your supervisor and project partners to present work-in progress and discuss experiments.
- Be prepared to present work at national and international meetings.
- Produce high quality work for publication in peer-reviewed journals.
- Show willingness to contribute to the work of others in the lab by offering practical and intellectual help, including technical staff and post-graduate students.
- Take an active part in group meetings, and to make presentations at these when required.
- Assist in laboratory supervision of postgraduate and undergraduate students, if and when requested.
- Perform routine laboratory tasks and duties.
- Keep good general records and work with all levels of staff.



PERSON SPECIFICATION

Essential Knowledge, Skills and Experience:

- A PhD in evolutionary genetics or a related discipline
- Good laboratory skills
- Experience of, and enthusiasm for, laboratory-based evolutionary research.
- Experience in analysis and interpretation of experimental data, including statistical analyses of large and complex datasets
- Excellent computational and statistical skills, including proficiency in the use of programming languages such as R
- Experience using UNIX-like systems (e.g. Linux), including command-line
- Relevant publication record appropriate to stage of career including recent first authored research publications in internationally recognised peer-reviewed journals
- The ability to present information in an accurate and appropriate format, and to communicate effectively with a range of groups including both scientists and wider audiences
- Good written and spoken English
- Convey an appropriate rationale and interest in applying for this particular post
- Effective interpersonal skills and ability to work with colleagues at all levels

Desirable Knowledge, Skills, Experience and Qualifications:

- Expertise in experimental microbiology techniques
- Expertise in experimental evolution
- Experience of WGS analysis (e.g. using breseq or other pipelines)
- Experience of interacting with theoreticians and computer scientists
- Understanding of population genetic theory
- Understanding of microbial genetic model systems
- Understanding and experience of mechanisms of antibiotic resistance