

THE UNIVERSITY OF MANCHESTER

PARTICULARS OF APPOINTMENT

FACULTY OF BIOLOGY, MEDICINE & HEALTH

SCHOOL OF HEALTH SCIENCES

DIVISION OF INFORMATICS, IMAGING & DATA SCIENCE

POSTDOCTORATE RESEARCH ASSOCIATE IN COMPUTATIONAL SYSTEMS BIOLOGY

VACANCY REF: BMH-023687

Salary:	Grade 6 £36,024-£44,263 per annum, depending on relevant experience
Hours:	1 FTE, 35 hours per week, full time
Duration:	Fixed Term starting as soon as possible until 31 October 2026
Location:	Manchester Oxford Road

Enquiries about the vacancy, shortlisting and interviews:

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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 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

The integrated structure of our faculty enables a truly translational approach to biology, medicine and health - from pure discovery science through to clinical application and patient care. It also encourages collaborative working, enabling staff to deliver innovative, world-leading research that has a very real and positive impact on people's lives, as well as high-quality education and training to over 11,000 undergraduate and postgraduate students.

Our Strategic Partnerships

The faculty has established 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 <https://mft.nhs.uk/withington/research/manchester-academic-health-science-centre-mahsc/> - 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.

We also play a leading role in <https://healthinnovationmanchester.com/>, 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 also has research and funding links to a number of commercial organisations including Unilever, AstraZeneca, GlaxoSmithKline and Boots, who 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 <https://www.staffnet.manchester.ac.uk/people-and-od/benefit/> 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 <http://www.manchester.ac.uk/connect/jobs/equality-diversity/awards/> 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, <http://www.manchester.ac.uk/study/experience/student-life/city/>, we welcome applicants of all nationalities. To help international job applicants plan for life in the UK, we have put together some useful <http://www.staffnet.manchester.ac.uk/employment/joining-the-university/international-staff/> travel to the UK, accommodation and a number of other practical considerations.

Background:

The post is associated with a Wellcome Trust Discovery Award “Defining the spatiotemporal gene expression dynamics controlling embryonic patterning” led by Hilary Ashe and Magnus Rattray. The project is an ambitious multi-disciplinary collaboration that will combine cutting-edge cell biology, mathematical modelling and machine learning to gain fundamental insights into gene expression and embryonic development. You will be part of a team of four post-doctoral researchers (two computational and two experimental) working on the project, along with associated PhD students and lab technicians.

The ability of cells to generate complex gene expression patterns is fundamental to multicellular life. While quantitative and live imaging has transformed our understanding of transcription, recent technological advances made by ourselves and others place us on the cusp of a similar revolution in decoding mRNA stability and translation regulation. Therefore, our overarching aim is to determine how gene expression dynamics are regulated and integrated in space and time to direct embryonic cell fate decisions. We will leverage the unique advantages of the *Drosophila* embryo to tackle this problem. Firstly, we will combine quantitative single molecule imaging, spatial transcriptomics and spatiotemporal modelling to uncover transcription, mRNA stability and translation regulation at single cell resolution in the embryo. Secondly, we will dissect the mechanisms underpinning these gene expression dynamics. Thirdly, we will perturb these control mechanisms in the embryo to determine the effect on cell fate decisions. Finally, we plan to build a ‘digital twin’ model of the *Drosophila* embryo, incorporating the gene regulatory networks and their dynamics, which we will use to derive and test predictions about how embryonic patterning tolerates gene expression perturbations. Together, our data and models will reveal how the integration of spatiotemporal gene expression dynamics underpins robust embryonic patterning. For related recent work see References [1-4].

References:

- [1] Forbes Beadle, L., Love, J. C., Shapovalova, Y., Artemev, A., Rattray, M., & Ashe, H. L. (2023). Combined modelling of mRNA decay dynamics and single-molecule imaging in the *Drosophila* embryo uncovers a role for P-bodies in 5' to 3' degradation. *PLoS Biology*, 21(1), e3001956.
- [2] BinTayyash, N., Georgaka, S., John, S. T., Ahmed, S., Boukouvalas, A., Hensman, J., & Rattray, M. (2021). Non-parametric modelling of temporal and spatial counts data from RNA-seq experiments. *Bioinformatics*, 37(21), 3788-3795.
- [3] Bowles, J. R., Hoppe, C., Ashe, H. L., & Rattray, M. (2022). Scalable inference of transcriptional kinetic parameters from MS2 time series data. *Bioinformatics*, 38(4), 1030-1036.
- [4] Hoppe, C., Bowles, J. R., Minchington, T. G., Sutcliffe, C., Upadhyai, P., Rattray, M., & Ashe, H. L. (2020). Modulation of the promoter activation rate dictates the transcriptional response to graded BMP signaling levels in the *drosophila* embryo. *Developmental cell*, 54(6), 727-741.

Overall Purpose of the Job:

The post-holder will be responsible for developing and refining systems biology models of *drosophila* embryogenesis. This will include developing both stochastic models of high-resolution live cell imaging from individual genes (e.g. modelling transcription and translation processes) and spatio-temporal modelling of gene regulatory networks involving hundreds of genes. The project

will require the integration of in-house and public datasets along with incorporating/adapting published gene regulatory network models for early embryogenesis. As well as developing models from the data, you will be required to carefully consider appropriate pre-processing, normalisation and signal processing, as these steps can be of critical importance for developing models from imaging and omics datasets. You will work with the rest of the team to improve and refine models through data-driven inference approaches. Models developed will be used to gain mechanistic insights and design/interpret perturbation experiments (e.g. using optogenetics), and data from these experiments will then feed back into improved models.

Key Responsibilities, Accountabilities or Duties:

The post-holder will,

- Apply and develop computational systems biology approaches for modelling biological time course datasets (e.g. from live cell imaging experiments).
- Collate existing regulatory network models and improve/refine models based in project data (e.g. spatial transcriptomics) and public data sources (e.g. published single nucleus RNA-Seq and ATAC-Seq datasets, ChIP-Seq data, genomic sequence analysis results etc).
- Work closely with experimental partners to better understand the domain, help address scientific hypotheses and support the project objectives
- Publish well-documented open source code implementing algorithms for general use
- Contribute to scientific publications using the above methods, e.g. describing methodology, providing high-quality images and statistical summaries
- Lead scientific publications describing novel methodological contributions for publication in high quality computational biology journals/conferences
- Present work at leading international conferences as talks, posters and demos
- Prepare well and contribute actively to regular project meetings
- Support research group and project-related activities as required, e.g. helping to organise visits and seminars from external researchers

PERSON SPECIFICATION

Essential Knowledge, Skills and Experience:

- Undergraduate or Masters degree (or equivalent) with a significant mathematical or computational element, e.g. in Mathematics, Computer Science, Engineering, Systems Biology, Physics or Statistics
- PhD (or equivalent) with a significant computational and/or statistical element
- Experience of computational systems biology
- Experience of scientific programming
- Good scientific publication record given career stage
- Self-motivated, hard-working and able to work in a team
- Good organisational and communication skills
- Fluent in written and spoken English

Desirable Knowledge, Skills and Experience:

- Good knowledge and understanding of Bayesian statistical principles
- Experience of omics and/or imaging data analysis
- Experience of modelling gene regulation (either stochastic single cell dynamics or gene regulatory networks)
- Experience of machine learning
- Experience of writing code in python
- Experience of using a High Performance Computing (HPC) environment (e.g. Ethernet Clusters, GPUs etc.)
- Experience of software development using version control (e.g. GitHub or similar)

Division of Informatics, Imaging and Data Sciences

Our Division uses big data to evaluate statistical links across all biological and medical fields.

The areas we focus on include looking at new medical imaging methods for understanding disease and informing care, discovering which groups of people are most likely to be at risk of disease within a given population group and developing informatics interventions in health care.

Our research

Informatics

Informatics research in the Division has an international reputation for research with a broad portfolio encompassing precision medicine, epidemiology, citizen driven health, public health, clinical trials and learning health systems.

Our staff come from disciplines such as clinical medicine, epidemiology, computer science, software engineering, statistics and mathematics, with a truly multi-disciplinary approach to research.

We collaborate closely with the NHS and with academic centres and industry, both nationally and internationally. Our [Christabel Pankhurst Institute](#) is a leading centre for health technology research and innovation and we have more than 350 academics from across the University involved in our multidisciplinary Digital Health and Care network which is part of the University's broad [Digital Futures](#) initiative.

Imaging

Our imaging research is working to develop, validate and apply novel imaging and image analysis methods. We develop imaging methods to solve a wide variety of problems, particularly in the biomedical field. For instance, to better understand a variety of diseases, their management and treatment.

There is a broad scope of published imaging research and studies ongoing across the imaging facility sites in Manchester, including both preclinical and clinical studies in oncology, neurology,

psychiatric disorders, musculoskeletal disease, cardiovascular disease, respiratory conditions and other inflammatory disorders.

We aim to facilitate wider use of imaging in research, clinical practice and industrial applications. We have multiple collaborations with industrial partners and have spun out five companies.

Data sciences

Our data sciences group works on the interpretation of datasets by building predictive models of biological systems using computer algorithms.

We have developed methods to uncover the patterns underlying gene expression changes in time and to uncover the complex network of molecular interactions between DNA and proteins which regulate this process.

We are also interested in how biological systems change and adapt over much longer evolutionary timescales using phylogenetic models. Models encode our hypotheses about how biological systems work.