University of Nottingham
UK | CHINA | MALAYSIA

Role profile

Job title	Research Fellow (Title will be 'Research Associate' where an appointment is made before PhD is completed)	Job family and level	Research & Teaching Level 4 (Appointment will be Level 4 Career training grade where an appointment is made before PhD has been completed)
School/ Department	Mathematical Sciences	Location	University Park Campus

Purpose of role

This postdoctoral research fellow position will have specific responsibility for developing research objectives and managing their own research whilst working with Prof. Gary Mirams on his Wellcome funded £2M Senior Research Fellowship "*Developing cardiac electrophysiology models for drug safety studies*".

	Main responsibilities (Primary accountabilities and responsibilities expected to fulfil the role)	**% time per year**
1	**Research** ▪ Develop research objectives and proposals for own and/or collaborative research area. ▪ Plan and conduct research using recognised approaches, methodologies and techniques within the research area. ▪ Collaborate with academic colleagues on areas of shared interest for example, collaborative or joint research projects. ▪ Plan and manage own research activity and resolve problems, if required, in meeting own/team research objectives and deadlines in collaboration with others.	60%
2	**Engagement, Communication and Dissemination** ▪ Analyse and illuminate data, interpret reports, evaluate and criticise texts and bring new insights to research area. ▪ Prepare papers for publication in leading journals and/or contribute to the dissemination at national/international conferences, workshops and meetings resulting in successful research outputs.	30%
3	**Project Administration** ▪ Co-ordinate the operational aspect of research networks, for example, arranging meetings and updating web sites etc. and contribute to collaborative decision making with colleagues in area of research. ▪ Utilise and contribute to organising research resources and workshops as appropriate.	10%

Background: Mathematical models of cardiac electrophysiology are beginning to be used for safety testing of new pharmaceutical compounds, to identify potential for increased pro-arrhythmic risk as a drug side effect [1]. There are substantial challenges in identifying the most appropriate models, parameterising them whilst considering uncertainty and variability, and designing experiments to do these tasks efficiently [2-5].

Aims: The grant will be developing and refining mathematical cardiac electrophysiology models for ion channels and cardiac cells for use in predicting pharmaceutical drug-induced changes to cardiac activity and subsequent risk in the clinic.

Team: You will be joining a team working on the project based in the School of Mathematical Sciences in Nottingham: the principal investigator Prof. Mirams; two senior postdoctoral research associates/fellows; two postdoctoral research associate/fellows; a dedicated research software engineer; and a number of PhD students based in Nottingham and in partnership with industry. We are a strongly collaborative team with shared open-source code development working jointly on a shared research programme – we work closely with other computational groups, experimental laboratories, industrial partners and international drug regulators. Post holders will undertake research visits to conduct their own experiments and collaborate with experimental electrophysiology groups: particularly in UMC Utrecht in the Netherlands; and the Victor Chang Cardiac Research Institute in Sydney, Australia. As a result of the unique collaborative opportunities described above, applicants should have a very strong interest in interdisciplinary and team-based research. You will be responsible for writing up your work for publication and can use your initiative and creativity to identify areas for research, work collaboratively in interdisciplinary teams, develop research methods, and extend your research portfolio.

Your particular focus (depending on the strengths and interests of the successful candidate) could include:

- Use of dynamic-clamp (real time simulation/experiment interaction) in model building.
- Cell-specific electrophysiology model construction.
- Working on methods for experimental design, to optimise parameter identifiability, but also to perform model selection and to minimise the effect of experimental artefacts.
- Building on the Cardiac Electrophysiology Web Lab (https://scrambler.cs.ox.ac.uk/) to record and reproduce the process of fitting a model to data and testing it.

We are looking for expertise in **any one of**:

- Mathematical modelling involving numerical simulations, e.g. ODE, PDE or agent-based modelling, ideally for the dynamics of a biological system
- Statistics/data science – for instance, fitting mechanistic models to real experimental data and performing uncertainty quantification/inference in a frequentist or Bayesian framework.
- Experimental electrophysiology (e.g. manual patch clamp) – for instance, using voltage-clamp protocols to characterise an ion channel current. In this case you will have a desire to combine extended overseas visits to collaborators' labs to undertake your own experiments with learning to do your own experimental design and computational ion channel modelling here in Nottingham.

Relevant Publications

1. G. R. Mirams *et al.*, "Simulation of the effect of compounds on multiple ion channels provides improved early prediction of th.eir clinical torsadogenic risk," *Cardiovasc. Res.*, **91**(1):53–61, (2011).
2. Mirams, G.R., Pathmanathan, P., Gray, R.A., Challenor, P. & Clayton, R.H. Uncertainty and variability in computational and mathematical models of cardiac physiology. *J. Physiol.* **594,** (2016).
3. Beattie, K.A., Hill, A.P., Bardenet, R., Cui, Y., Vandenberg, J.I., Gavaghan, D.J., de Boer, T.P. & Mirams, G.R. Sinusoidal voltage protocols for rapid characterisation of ion channel kinetics. *J. Physiol.* **596,** 1813–1828 (2018).
4. CL Lei, M Clerx, D.J. Gavaghan, L. Polonchuk, GR Mirams, K Wang (2019). Rapid characterisation of hERG channel kinetics I: using an automated high-throughput system. Biophysical Journal **117**(12):2438-2454 (2019) doi:10.1016/j.bpj.2019.07.029.

5. CL Lei, M Clerx, DG Whittaker, DJ Gavaghan, TP de Boer, GR Mirams (2020) Accounting for variability in ion current recordings using a mathematical model of artefacts in voltage-clamp experiments. *Philosophical Transactions of the Royal Society A* **378**:20190348. doi:10.1098/rsta.2019.0348

Person specification

	Essential	**Desirable**
Skills	▪ Excellent oral and written communication skills, including the ability to convey complex information clearly and accurately. ▪ Ability to creatively apply relevant research approaches, models, techniques and methods. ▪ Ability to work both independently and collaboratively as part of a multidisciplinary and multicultural team.	

Knowledge and experience	▪ Expert knowledge of:
	  ▪ **EITHER** mechanistic biological modelling;
	  ▪ **OR** statistical inference for modelling;
	  ▪ **OR** experimental electrophysiology (e.g. patch clamp).
	▪ Proven ability to produce research of high quality in mathematical modelling **OR** statistical inference **OR** experimental electrophysiology; or closely related disciplines.
	▪ Very good programming skills, including use or development of scientific computing software (for example one/some of Matlab, R, Python, Stan, C++, etc.). Including experience writing code for
	  ▪ **EITHER** numerical solution of differential equations;
	  ▪ **OR** optimisation/inference.
	  ▪ **OR** post-processing experimental traces
		▪ Published papers in relevant academic journals.
		▪ Experience of developing new approaches, models, techniques, or methods in research area.
		▪ Experience of
		  ▪ **EITHER** developing electrophysiology models
		  ▪ **OR** model selection, experimental design, uncertainty quantification
		  ▪ **OR** experimental work on cardiac ion channels or cardiac cells

Qualifications, certification and training	• PhD (or close to completion) or equivalent in a relevant branch of mathematics, statistics, physics, control engineering, biosciences, or a closely related discipline,	

Athena SWAN Silver Award

The University strongly endorses Athena SWAN principles, with commitment from all levels of the organisation in furthering women's careers. It is our mission to ensure equal opportunity, best working practices and fair policies for all.

Expectations and behaviours

The University has developed a clear set of core expectations and behaviours that our people should be demonstrating in their work, and as ambassadors of the University's strategy, vision and values. The following are essential to the role:

Valuing people	Is always equitable and fair and works with integrity. Proactively looks for ways to develop the team and is comfortable providing clarity by explaining the rationale behind decisions.
Taking ownership	Is highly self-aware, looking for ways to improve, both taking on board and offering constructive feedback. Inspires others to take accountability for their own areas.
Forward thinking	Driven to question the status quo and explore new ideas, supporting the team to "lead the way" in terms of know-how and learning.
Professional pride	Sets the bar high with quality systems and control measures in place. Demands high standards of others identifying and addressing any gaps to enhance the overall performance.
Always inclusive	Ensures accessibility to the wider community, actively encouraging inclusion and seeking to involve others. Ensures others always consider the wider context when sharing information making full use of networks and connections.

Key relationships with others