University of Nottingham
UK | CHINA | MALAYSIA

Role profile

Job title	Senior Research Fellow in Cardiac Electrophysiology Modelling (Fixed-term)	Job family and level	Research and Teaching Level 5
School/ Department	School of Mathematical Sciences	Location	University Park Campus

Purpose of role

This senior postdoctoral role will have specific responsibility for research, for developing research objectives and proposals with Prof. Gary Mirams and Prof. Simon Preston on a project entitled "*A continually-learning framework for uncertainty quantification and translation of preclinical studies to human cardiovascular safety*".

Background: Dedicated in-vivo cardiovascular safety studies in dogs or non-human primates are routinely performed when progressing pharmaceutical drug candidates toward first-in-human trials; but the UK government has a target of reducing these studies by at least 50% by 2030. Before these studies, both computational mechanistic and statistical regression models are used to predict increased cardiovascular risk [1-3]. But critically, the pharmaceutical industry currently lacks a rigorous, quantitative framework to determine when animal studies are genuinely adding predictive value for human clinical risk, beyond what is known from earlier in-vitro and in-silico data.

Aims: you will plan and conduct work using appropriate approaches or methodologies and techniques to develop and use computational models of dog electrophysiology to predict dog cardiovascular safety study outcomes. The predictive value of the models will be assessed as part of a framework to score each preclinical cardiovascular safety assay in a drug development cascade. By propagating uncertainty through both mechanistic and statistical regression computational models[1], a framework will generate probabilistic forecasts [4,5] of downstream study outcomes and ultimately human clinical pro-arrhythmic risk. When an in-vivo study ceases to provide information that materially updates the human risk prediction (in-vivo results are no longer 'surprising' given existing in-vitro and in-silico evidence) the framework will provide a principled, quantitative basis for skipping studies for particular compounds, or retiring those studies completely.

Team: You will be joining a team working on this project based in the School of Mathematical Sciences in Nottingham: the investigators Prof. Mirams and Prof. Preston and a statistical postdoctoral research associate/fellow. We are a strongly collaborative team developing shared open-source codes – we work closely with other computational groups, experimental laboratories, industrial partners (AstraZeneca and GSK as part of this project) and international drug regulators.

[1] A second postdoctoral research associate/fellow position is funded by this project, and they will specialise in the statistical modelling and decision theoretic aspects of the project.

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.

Relevant Publications

[1] GR Mirams, Y Cui, A Sher, M Fink, J Cooper, BM Heath, NC McMahon, DJ Gavaghan, D Noble (2011) **Simulation of multiple ion channel block provides improved early prediction of compounds' clinical torsadogenic risk**. *Cardiovascular Research*, 91(1):53-61. doi:10.1093/cvr/CVR044.

[2] KA Beattie, C Luscombe, G Williams, J Munoz-Muriedas, DJ Gavaghan, Y Cui, GR Mirams (2013) **Evaluation of an In Silico Cardiac Safety Assay: Using Ion Channel Screening Data to Predict QT Interval Changes in the Rabbit Ventricular Wedge**. *Journal of Pharmacological and Toxicological Methods*, 68(1):88-96. doi:10.1016/j.vascn.2013.04.004.

[3] GR Mirams, MR Davies, SJ Brough, MH Bridgland-Taylor, Y Cui, DJ Gavaghan, N Abi-Gerges (2014) **Prediction of Thorough QT study results using action potential simulations based on ion channel screens**. *Journal of Pharmacological and Toxicological Methods*, 70(3):246-254. doi:10.1016/j.vascn.2014.07.002.

[4] RC Elkins, MR Davies, SJ Brough, DJ Gavaghan, Y Cui, N Abi-Gerges, GR Mirams (2013) **Variability in high-throughput ion-channel screening data and consequences for cardiac safety assessment**. *Journal of Pharmacological and Toxicological Methods*, 68(1):112-122. doi:10.1016/j.vascn.2013.04.007.

[5] S Boulet, U Moreno, R Michelet, LBS Aulin, C Kloft, E Comets, S Zohar (2024). **Bayesian framework for multi-source data integration-Application to human extrapolation from preclinical studies**. *Statistical Methods in Medical Research* 33(4): 574-588. doi:10.1177/09622802241231493.

	Main responsibilities (Primary accountabilities and responsibilities expected to fulfil the role)	**% time per year**
1	**Research** ▪ Undertake original research of international excellence in a branch of cardiac electrophysiology modelling. ▪ Acquire, analyse, interpret and evaluate research findings using approaches, techniques, models and methods selected or developed for the purpose. ▪ Deliver research as part of a collaborative team and contribute to the achievement of specific research objectives. ▪ Seek and secure research funding.	35%

2	**Engagement, Communication and Dissemination** ▪ Assist in the co-ordination of the research and related administrative tasks, including liaising with external project collaborators in academia and industry. ▪ Publish results of research in internationally leading peer-reviewed journals. ▪ Establish your reputation nationally, by writing up research work for publication and contributing to the dissemination of findings at national/international conferences. ▪ Build relationships and collaborate actively with internal and external contacts, nationally and internationally, to complete research projects to advance the discipline and increase knowledge exchange	35%
3	**Administration** ▪ Provide support, guidance and supervision to other staff within the research team, where appropriate in own area of expertise. ▪ Supervise undergraduate and/or postgraduate students projects and placements, as appropriate. ▪ Participate in co-supervision of projects at the Masters and PhD level.	20%
4	**Any other duties appropriate to the grade and role of the post holder**	10%

Person specification

	Essential	Desirable
Skills	▪ Ability to devise, advise on and manage a research programme. ▪ Excellent communication and organisational skills, including the ability to communicate with clarity on complex information. ▪ Ability to work independently and as part of a multidisciplinary and multicultural team.	

Knowledge and experience	▪ Consistent track-record in developing, performing and publishing peer-reviewed research of international quality in cardiac electrophysiology modelling.
	▪ Excellent programming skills, including use or development of scientific computing software (for example one/some of Python, C++, etc.). Including experience writing code for
	  ▪ numerical solution of differential equations; and
	  ▪ optimization/inference
		▪ Background knowledge in uncertainty quantification
		▪ Experience of working in interdisciplinary teams.
		▪ Experience obtaining competitive external research funding
		▪ Experience of supervision of junior colleagues.

Qualifications, certification and training (relevant to role)	▪ PhD or equivalent in a relevant branch of mathematics, physics, bioengineering or a closely related discipline.	

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