University of Nottingham
UK | CHINA | MALAYSIA

Role profile

Job title	Research Associate/Fellow in Statistical Modelling (Fixed term)	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	School of Mathematical Sciences	Location	University Park Campus

Purpose of role

This postdoctoral research associate position will have specific responsibility for developing research objectives and managing their own research whilst working with Prof. Gary Mirams and Prof. Simon Preston on an externally-funded 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 whether a drug candidate will cause increased cardiovascular risk [1-3]. But critically, the pharmaceutical industry currently lacks a rigorous, quantitative framework to determine when animal studies are genuinely adding new 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 a statistical decision-support tool that quantifies the information content, measurable 'value added', of each preclinical cardiovascular safety assay in a drug development cascade. By propagating uncertainty through both mechanistic[1] and statistical regression computational models, the 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 senior postdoctoral research associate/fellow with expertise in the mechanistic modelling needed in this project. 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

[1] No prior knowledge of the mechanistic models that are used is required for this role, a second research associate will be assisting with this aspect.

of this project) and international drug regulators. 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. ▪ 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. ▪ Identify opportunities and assist in writing bids for research grant applications.	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. ▪ Provide support, guidance and supervision to other staff, where appropriate in own area of expertise.	30 %
3	**Project Administration** ▪ Prepare proposals and applications to both external and/or internal bodies for funding, contractual or accreditation purposes. ▪ 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 facilities and workshops as appropriate.	10 %

Person specification

	Essential	Desirable
Skills	▪ Excellent oral and written communication skills, including the ability to communicate with clarity on complex information. ▪ Ability to creatively apply relevant research approaches, models, techniques and methods. ▪ Ability to fit statistical models to real-world data (optimisation or inference in a frequentist or Bayesian framework) using various approaches, and to interpret the results. ▪ Very good programming skills, including use or development of statistical inference software in a widely used programming language (for example R, Python, Stan, etc.) ▪ Ability to work independently and as part of a multidisciplinary and multicultural team	
Knowledge and experience	▪ Expert knowledge of statistical models and methods, especially in biological and medical settings, applied to real-world data. ▪ Proven ability to produce research of high quality in applied statistics, mathematical biology, or closely related discipline.	▪ Background knowledge of drug development (preclinical studies or clinical trials) ▪ Published papers in relevant academic journals.
Qualifications, certification and training	▪ PhD or equivalent, in a relevant branch of mathematics, statistics or a closely related discipline **OR** near to completion of a PhD.	

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