Project Details	
Project Code	MRCPHS24Ca Kaouri
Title	Calcium signalling in In-Vitro Fertilization: developing a non-invasive diagnostic tool using mathematical modelling and data analysis
Research Theme	Population Health Sciences
Summary	In-Vitro Fertilization is the primary treatment of infertility, with ~2.5 million cycles performed annually. Success rates are, however, declining partly due to waiting 5 days to select the best embryo to transfer to the woman. A rapid (day 1) indicator of embryo viability, based on experimental data, will be developed through mathematical modelling of the calcium signalling in fertilising eggs and their movements, and shared with IVF clinicians.
Description	IVF is the primary treatment of infertility with ~2.5 million treatments and ~500,000 births annually. The success rate has been ~25% for many decades but it has been decreasing while the IVF industry is projected to grow to 37.7 billion (USD) by 2027 with an ~10% annual growth rate. Success rates have been declining mainly because of culturing embryos for 5-6 days in order to select the 'best' single embryo for transfer to the patient. This is not ideal because in vitro conditions never full mimic in vivo conditions. Moreover, the embryos take more of the clinic's resources and the process is more psychologically taxing for the patient. The project will pave the way for providing the IVF clinics with a novel diagnostic tool: a rapid (day 1) quantitative indicator of embryo viability. This novel methodology is based on monitoring calcium (Ca2+) signalling in fertilising eggs and the associated egg movements and flows. The methodology was pioneered through a collaboration between the Swann lab (Cardiff Biosciences) and labs in Oxford and Cambridge in 2011 but has not progressed, partly due to the lack of accurate, sophisticated mathematical modelling. A patent based on the latter experiments (granted to Cambridge Enterprise Ltd) has been recently allowed to lapse because of lack of quantitative progress. This timely PhD project will close the translation and innovation gap through advanced mathematical modelling, simulation and data analysis.This ground-breaking diagnostic technology will be eventually deployed to IVF clinics, pushing the frontier in IVF. Ca2+ waves and oscillations are integral in fertilization. There is an optimal Ca2+ pattern associated with successful IVF but monitoring Ca2+ damages the egg. It has, however, been recently observed that Ca2+ waves cause subtle movements (spasms) and flows in eggs; these could be detected non-invasively, through low-cost imaging, such as Particle Image Velocimetry. To advance this technology, the coupling between Ca2+ waves and egg cytoplasmic movements must be elucidated through modelling and more experiments. It is also unclear how to optimize the signal to noise for tracking egg movements as these vary over time and from one egg to another. This is an ambitious project at the forefront of smart, data-driven healthcare technologies and lies at the Mathematical Sciences/ Life Sciences interface. The student will develop advanced modelling, coding and data analysis skills while benefiting from the collaboration with the Swann lab which is at the forefront of the IVF field (Swann is Co-Supervisor 3). The student will observe experiments on fertilising eggs and drive data extraction. The model predictions will inform testable

	experimental questions, shedding light on factors underlying IVF success. The student will employ sophisticated statistical methods to parametrise, validate and test the models.The student will, thus, communicate across Biology, Medicine and Mathematics, generating predictions that can be used in further experiments. At least three high-impact papers will be generated from the thesis and the student will present in at least two international conferences. At the end of the project the student will be ideally positioned to pursue an exciting career in academia or in industry. The student will join the vibrant community of Mathematical and Computational Biology and Medicine across the three participating GW4 universities. The supervisory team has an excellent publication record, regularly presents at international conferences and communicates their results to the public. Infertility challenges all developed countries and investments have been made by the EU in multidisciplinary consortia such as the European IVF-monitoring Consortium and the European Society of Human Reproduction and Embryology. Thus, the work will have world-wide impact on a large community of scientists and patients in the UK and abroad.
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