Project Details	
Project Code	MRC23IIAREx Richards
Title	Modelling human embryo development: a combined mathematics and lab approach
Research Theme	Infection, Immunity, Antimicrobial Resistance and Repair
Summary	During this PhD, you will use mathematics, computer programming and lab-based experiments to investigate how the human embryo develops, focusing on the very first few days after fertilisation when the embryo grows from a single egg to several hundred cells. The findings will have important implications for improving IVF treatment. Unlike most PhDs, this is an excellent opportunity to be trained in both the experimental and mathematical aspects of modern research.
Description	Background: Understanding the earliest stages of human embryo formation is not only of fundamental interest, but also has great significance for health and wellbeing since most embryos fail to develop beyond implantation. It is inherently challenging to study in vivo development of the human embryo, and there are ethical and logistical constraints to in vitro research. However, we recently created the first realistic model of the human blastocyst, called the blastoid. This system can provide high-quality data at a level that has simply not been possible before and which can be used to inform and validate mathematical modelling. Importance: This topic is of substantial importance to improve the success rates of IVF. Better ways of scoring blastocyst quality in IVF clinics could dramatically improve fertility, issues that have devastating health, psychological and economic impact, and which will only become more acute as women increasingly delay having children until their 30s. Key research question: What are the fundamental rules underlying human embryo development and how can these improve scoring of IVF embryos? The approach: This PhD will leverage the opportunity presented by our blastoid model. It will employ a truly multi-disciplinary approach to study the fundamental mechanisms that underlie early embryo development. The student will undertake a cross-disciplinary PhD, including designing mathematical models, performing image analysis, conducting time-lapse imaging experiments, and working with our IVF collaborator. This approach will allow the student to learn a highly-desirable combination of quantitative and experimental skills, leading to excellent future career prospects. Project plan and objectives: This cross-disciplinary studentship will be based within the Living Systems Institute at the University of Exeter. The student will also spend time at the University of Bristol. The student will join the new Quantitative Health Network to obtain a broad understanding of the role of mathematical modelling throughout human health. The project itself will include: Objective 1. Mathematical simulation of blastocyst formation. Building on our proof-of-principle model (https://tinyurl.com/2p8rxuh5), a Cellular Potts model will be developed to simulate cell shape, motion and lineage specification. This will involve a combination of MATLAB and C++. Objective 2. Time-lapse microscopy of developing blastoids. In the lab, the student will culture and capture time-lapse images of blastoid development. Our knock-in fluorescent protein reporters for each lineage will allow individual cell types and shapes to be identified. Objective 3. Image analysis. Based on our

	existing code, the student will design image analysis software that automatically extracts and tracks cell shape and position in the developing blastoid. This information will be used to inform and validate the mathematical model. Objective 4: IVF scoring. Using our collaboration with the Aria Fertility IVF clinic, improved ways of automatically scoring human embryos will be investigated. This will involve visiting the clinic and using images of human embryos to fit the model parameters. We have designed the project so the student will have significant scope to take ownership. This particularly applies to Objective 1 (where there are several possible modelling approaches) and Objective 3 (with several image analysis options). However, objectives 2 and 4 can also be tailored as required. Importantly, the proportion of time spent on each objective can be adjusted and so the student will be able to balance the project as best suits their needs. Outreach: Public involvement will also play an important part of this studentship. The student will work with Rachel Etherington (the TREE Communities Engagement Manager) to interact with individuals with fertility issues. This will help shape the project direction and disseminate results to a lay audience.
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