Project Title: Using fast and efficient computer simulations for understanding the mechanobiology of sperm motion in the design of artificial reproduction technologies

Project Number: IMURA0393

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Research Academy Themes:
Highlight which of the Academy’s Theme(s) this project will address?
(Feel free to nominate more than one. For more information, see www.iitbmonash.org)
1. Advanced computational engineering, simulation and manufacture
2. Infrastructure Engineering
3. Clean Energy
4. Water
5. Nanotechnology
6. Biotechnology and Stem Cell Research

The research problem
One of the criticisms of current techniques of artificial reproduction is that they may be selecting the wrong sperm to fertilize eggs and make babies. In the real biological environment, sperm cells have to swim through an obstacle course in which only 1 in about 300 million sperm can eventually fertilize an egg. In contrast, modern artificial techniques may be unintentionally selecting poor quality sperm, with potentially disastrous consequences for offspring. One alternative is to design microfluidic devices that can replicate the complex environment of the reproductive tract. But in order to do this, we need to understand how sperm cells swim up the reproductive tract.

Project aims
A collaborative project between engineering and medical researchers at Monash University is currently under way. This project will contribute by building a computational model of a swimming sperm cell. Sperm use whip-like propellers called flagella, and a technique called Smoothed Dissipative Particle Dynamics
(SDPD) will be used to discretize equations describing the hydrodynamics of motion of the viscous fluid environment. The motion of flagella is generated by intracellular protein motors, which are in turn regulated by the complex biochemical circuitry within the sperm cell. To fully understand sperm behaviour it is necessary to integrate current understanding of biochemical signalling and regulatory networks with the hydrodynamical description of flagellar propulsion. The advantage of using particle-based approaches such as SDPD is that they can be set up for parallel computation using powerful algorithms in existing molecular-dynamics packages that can run efficiently on GPU architectures.

There are two principal aims in this project:
1. to develop SDPD simulations of a sperm cell swimming using flagellar propulsion in a viscoelastic fluid medium;
2. to predict the dependence of flagellar stroke patterns, swimming speed and trajectories on viscoelastic characteristics of the fluid and driving forces exerted by internal flagellar motors.

Expected outcomes

This is a challenging project in the emerging and highly interdisciplinary field of computational bioengineering, and is aimed at advancing fundamental understanding as well as developing new computational techniques. This is an ideal stepping-stone to either an academic or industrial career in advanced fluid computation. The project will provide you in-depth training in cutting-edge simulation techniques, particularly in micro/nano fluidics and bioengineering. The interdisciplinary nature of the project will give you a broad exposure to a number of areas, since you will be communicating with experimental biologists and fluid mechanicians, as well as experts in numerical methods, high-performance computation, high-end graphics and data visualization. We expect high-quality publications in top high-impact interdisciplinary journals.

The project requires a strong background in mathematics, computation and programming. The work will involve numerical analysis, discretization of partial differential equations, linear and nonlinear stability analysis, probability and statistics, etc. The project also involves understanding the physics of mechanical behaviour and flow properties of complex materials such as polymer solutions. Prospective applicants should note that THIS IS NOT AN EXPERIMENTAL PROJECT and there is no scope for microbiological, biochemical, bioinformatics experiments.

The virtual sperm cell developed in this study will provide germ cell biologists a predictive tool to test theories and perform what-if analyses. Predictions of the effect of fluid medium viscoelasticity on sperm swimming will lead to improvements in current approaches to male fertility characterization and artificial reproduction. For instance, the health of sperm is currently judged by preparing samples in simple aqueous buffers and observing swimming motion under the microscope. In real life, however, these cells are designed to operate in a highly viscoelastic environment. Understanding the effect of the physical properties of the external medium on sperm swimming can help design experimental protocols that better reproduce the actual environment in the reproductive tract.

How will the project address the Goals of the above Themes?

The models and simulations developed in this study address Goal 1. The subject of these simulations are sperm cells and the submicron scale fluid flow that governs their motion – this addresses Goals 5 and 6.

Capabilities and Degrees Required

- Undergraduate degree in chemical/mechanical engineering or physics/mathematics
- Strong undergraduate performance in mathematics, computation, fluid mechanics/transport phenomena/ reaction engineering