Summary Project Proposal

Supervisor(s):

Dr Eamonn A Gaffney, Centre for Mathematical Biology, Oxford (gaffney@maths.ox.ac.uk)

Title of Project: **The Dynamics of The Eukaryotic Axoneme**

Description of project: The eukaryotic axoneme is a ubiquitous organelle found within cilia and flagella, which are filamentous cell appendages whose beating drives fluids in numerous physiologically important settings, including sperm swimming and egg transport in reproduction, mucociliary clearance within the lung, circulation within the cerebrospinal fluid system, symmetry breaking in early developmental biology and the virulence of numerous medically important pathogenic parasites. Dynein molecular motors contract within the axoneme, exerting internal forces and moments; mechanically, these are balanced by a combination of viscous drag from the medium surrounding the cell and a passive elastic restoring response of the cilium or flagellum. The resulting dynamics gives rise to a propagating waveform which drives the surrounding fluid, and for free cells, results in swimming.

Nonetheless, the details of the collective behavior of the dyneins are poorly understood, suffering from numerous competing hypotheses. However consider the combination of cell videomicroscopy and mechanics. From movies of a swimming cell for example, one can determine viscous drags and moments on the flagellum using fluid dynamical theory. Similarly, passive restoring forces and moments can be extracted using the mechanics of filaments (see figure). A force and moment balance subsequently reveals the collective mechanical behaviour of the dyneins, allowing the objective testing of the numerous competing hypotheses for the regulation of dynein forces within flagellated cells using data acquired from a wider group of flagellum dynamicists.

These are examples of numerous possible projects considering various aspects of eukaryotic flagellar dynamics, which can be pursued in close collaboration with biological experts, for instance within The Centre for Human Reproductive Science, University of Birmingham or The Faculty of Fisheries and Protection of Waters, U. South Bohemia, Czech Republic or The Dunn School of Pathology in Oxford, according the cell type under study.

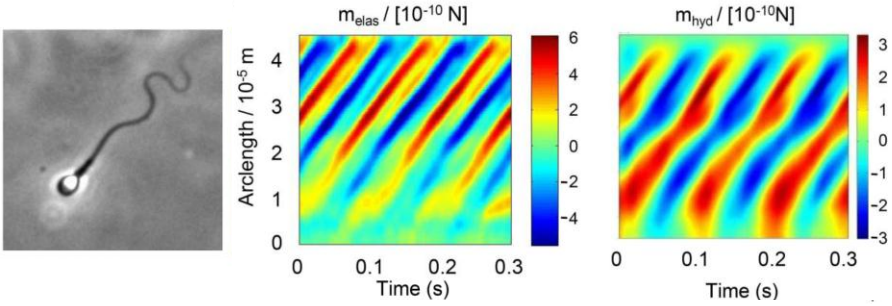

Figure: *Left.* A frame from the video-microscopy of a human sperm. Using the captured video of this sperm, the *centre* panel gives the bending moment density as the cell swims due to elastic restoring forces on flagellum; this bending moment is as a function of time (horizontal axis) and arclength along the sperm from the sperm head (vertical axis). The *right* panel inherits these axes and illustrates the bending moments due to viscous drag. The bending moments due to dynein contraction can readily be determined from these using moment balance.

Reasonable expected outcome of a summer project: One example for a summer project would be improving data extraction algorithms, a second example would be a summer project using of fluid and filament mechanics to extract dynein behaviour from current videomicroscopy archives.

Background The student should have an undergraduate knowledge of viscous fluid dynamics and at least a rudimentary knowledge of MATLAB.

Background reference:

EA Gaffney, et al, Mammalian Sperm Motility: Observation and Theory. Ann. Rev. Fluid Mech. 43:501-28, 2011