Abstracts

Short courses

Jean-Frederic Gerbeau (INRIA & Ecole Polytechnique, Paris)
Fluid-structure interaction in the cardiovascular system. Forward and inverse problems

My lecture will be divided in 3 parts.

In Part 1, I will review various concepts useful to Fluid-Structure Interaction algorithms: energy conservation, added-mass effect, implicit and explicit coupling. I will explain state-of-the-art algorithms which can be more than 10 times faster than previous methods.

In Part 2, I will address Data Assimilation techniques for computational hemodynamics, including fluid-structure problems. I will discuss identifiability issues and I will show applications to the estimation of boundary conditions or arterial wall stiffness from clinical data.

Part 3 will be devoted to the numerical simulation of cardiac valves. I will present two approaches to simulate valves in 3D. In particular, I will present a recent algorithm to handle contact for immersed solids.

Hans G. Othmer (Minnesota)
From crawlers to swimmers – mathematical and computational problems in cell motility

Cell locomotion is essential for early development, angiogenesis, tissue regeneration, the immune response, and wound healing in multicellular organisms, and plays a very deleterious role in cancer metastasis in humans. Locomotion involves the detection and transduction of extracellular chemical and mechanical signals, integration of the signals into an intracellular signal, and the spatio-temporal control of the intracellular biochemical and mechanical responses that lead to force generation, morphological changes and directed movement. In these lectures we will discuss some of the mathematical and computational challenges that the integration of these processes poses and describe recent progress on some component processes. A basic background in ordinary and partial differential equations is assumed.

Lectures by senior participants

Helen Byrne (Oxford)
PDE models of angiogenesis

Angiogenesis is the process by which new blood vessels form from pre-existing vessels in response to externally supplied growth factors. It is tightly regulated during wound healing and placental development and aberrant during macular degeneration. It heralds a tumours transition from a relatively harmless, localised mass to one that grows rapidly, spreads to other parts of the body and is potentially life threatening. Angiogenesis is typically initiated by cells which, when deprived of vital nutrients, release chemicals that diffuse through the surrounding tissue matrix. These angiogenic factors elicit multiple responses when they bind to receptors on endothelial cells that line nearby blood vessels. For example, small capillary tips emerge from the existing vessels and migrate, via chemotaxis, towards the source of the angiogenic factors. At the same time, endothelial cells in the developing capillary sprouts proliferate, causing the sprouts to elongate. When two tips collide (or when a tip comes into contact with a vessel), they fuse or anastamose, forming a hollowed tube through which blood may flow, increasing the supply rate of vital nutrients to the tissue. A large number of mathematical and computational models have been proposed to describe angiogenesis. These models range from deterministic, continuum models that focus on macroscopic variables such as capillary tip and vessel densities, to cell-based models which distinguish between individual capillary tips and account for the detailed morphology of the emerging vascular network.

In this talk, I will show how existing (and new) PDE models of angiogenesis can be derived by coarse-graining discrete, cell-based models. Of particular interest will be investigating how volume exclusion effects at the cell-scale influence the system dynamics at the macroscale.

Mark Chaplain (St Andrews)
Mathematical modelling of gene regulatory networks

Gene regulatory networks (GRNs) play an important role in maintaining cellular function by correctly timing key processes such as cell division and apoptosis. GRNs are known to contain similar structural components, which describe how genes and proteins within a network interact – typically by feedback. In many GRNs, proteins bind to gene-sites in the nucleus thereby altering the transcription rate. If the binding reduces the transcription rate there is a negative feedback leading to oscillatory behaviour in mRNA and protein levels, both spatially (e.g. by observing fluorescently labelled molecules in single cells) and temporally (e.g. by observing protein/mRNA levels over time). Mathematical modelling of GRNs has focussed on such oscillatory behaviour. In this talk we will present various spatial models of GRNs (e.g. the Hes1 system, p53-Mdm2, NFkB) and then extend the approach to examine spatio-temporal models of synthetic GRNs e.g. n-gene repressilator and activator-repressor systems.

Peter Stewart (Glasgow)
The fluid mechanics of the optic nerve

The optic nerve is formed by a dense collection of nerve fibres which connect the photoreceptors in the retina to the thalamus in the brain. This nerve is surrounded by a sheath, which contains a thin layer of cerebrospinal fluid at the intracranial pressure. The central retinal artery and vein, which supply the retinal circulation, pass through the centre of the optic nerve as they enter the eye, but about half way back from the globe they deviate and pass through the nerve sheath into the surrounding fatty tissue. Hence, these blood vessels form an interesting point of coupling between the eye and the brain. In this talk I will show how modelling of the flow of CSF along the nerve sheath and the flow of blood in the central retinal artery and vein can be used to quantify the condition of the brain, suggesting a non-invasive method for estimating the intracranial pressure and providing a methodology for quantifying traumatic brain injuries. In particular, I will demonstrate how a large increase in CSF pressure is transmitted into the retinal artery and vein, leading to a spreading shock wave through the retinal circulation and the possible rupture of retinal blood vessels (ie retinal haemorrhages).

Student talks

Gissell Estrada Rodriguez (Edinburgh)
Fractional Patlak-Keller-Segel equations for chemotactic superdiffusion

The long range movement of certain organisms in the presence of a chemoattractant can be governed by long distance runs, according to an approximate Levy distribution. This talk clarifies the form of biologically relevant model equations: Patlak-Keller-Segel-like equations involving nonlocal, fractional Laplacians from a microscopic model for cell movement. Starting from a power-law distribution of run times, we derive a kinetic equation in which the collision term takes into account the long range behaviour of the individuals. A fractional chemotactic equation is obtained in a biologically relevant regime. Apart from chemotaxis, this work has implications for biological diffusion in numerous processes.

Arnina Goodlad (Dundee)
Collective behaviour in schooling fish: the impact of behavioural rules and noise on overall group dynamics

Moving as a part of a collective group is a phenomenon required by many different species to carry out typical biological processes such as reproduction, migration and foraging. In this paper we present a simple model describing the collective motion of marine animals whereby individuals update their position and velocity through three key behavioural rules: repulsion, orientation and attraction. To investigate the impact that varying the strength of each of these rules has on the group, we introduce weighted terms to each of the rules in the equation. We use numerical simulations to identify different group formations with clear phase transitions, and the strengths of each of the behavioural rules required for the different formations observed. We then consider the disruption caused when noise is introduced to the system, and how this subsequently leads to changes in the group behaviour.

Aleksandra Plochoka (Edinburgh)
Robustness of the cytoskeleton

You and I are but a collection of trillions of cells. Why are we not falling apart? Consider this question on an inter-cellular level: to hold the cells together, the stickiness protein (E-cadherin) has to be delivered to the cell boundaries, where it is biologically relevant. This delivery is done along a network of highways (the microtubule cytoskeleton) via stochastically moving molecular motors. The cytoskeleton network self-organises to adjust to the functions of the cell and its developmental stage. Recently it was discovered that in epithelial cells cytoskeleton self-organisation is governed primarily by cell geometry [1]. In this talk, I will present our recent work. Using a probabilistic toy model and stochastic simulations, we show that cytoskeleton self-organisation is independent of most of the biological parameters. This means that the following result is robust: it is the cell geometry that determines our tissue properties.

[1] Gomez, Chumakova, Bulgakova, Brown, Nature communications 7 (2016): 13172.

Florian Sonner (Erlangen)

Averaging of periodically forced PDE-ODE fast-slow systems for simplified plaque model

Atherosclerosis is a widespread disease of arteries, where cholesterol accumulates in the artery walls, resulting in the growth of plaque through a chain of biochemical processes. Recently a model for the growth phase of plaque has been proposed by Yang et al. [YJNRR15]. This model contains fluid-structure interaction between the blood flow and the artery wall together with biochemical reactions which result in plaque growth. Apart from the inherent difficulties of fluid-structure interaction, this model exhibits multiple timescales: The blood flow driven by the heart beat, biochemical reactions inside the artery wall and finally the growth of the plaque itself, the latter taking place over the span of months or years. These phenomena make a direct numerical simulation of the model prohibitively expensive and call for temporal multiscale strategies [YRJNR17], [FRW16]. As a first step toward the analysis of multiscale algorithms for this problem, we investigate a fast-slow system consisting of a fast parabolic equation with periodic forcing, coupled through the differential operator to a slow ordinary differential equation, taking the role of the slow growth process. We prove that the slow component converges toward the solution of an averaging-type limit equation under the assumption of Lipschitz continuity of the involved objects [Son18]. The rate of convergence is of first order in a small parameter characterizing the timescale separation. All results are stated and proved in a framework where the fast component is described by an evolution process. Finally, we present some numerical results confirming the findings, outline the numerical challenges associated with solving the limit equation and discuss how our findings may carry over to the plaque problem.

References:

[FRW16] S. Frei, T. Richter, and T. Wick. Long-term simulation of large deformation, mechanochemical fluid-structure interactions in ALE and fully Eulerian coordinates. Journal of Computational Physics, 321:874–891, 2016.

[Son18] F. Sonner. Averaging of periodically forced pde-ode fast-slow systems. 2018. In preparation.

[YJNRR15] Y. Yang, W. Jäger, M. Neuss-Radu, and T. Richter. Mathematical modeling and simulation of the evolution of plaques in blood vessels. Journal of Mathematical Biology, 72(4):973–996, 2015.

[YRJNR17] Y. Yang, T. Richter, W. Jäger, and M. Neuss-Radu. An ALE approach to mechanochemical processes in fluid-structure interactions. International Journal for Numerical Methods in Fluids, 84(4):199–220, 2017.