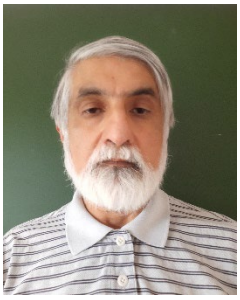
Modelling collective cell behaviour in development and disease

Philip K. Maini

Wolfson Centre for Mathematical Biology, Mathematical Institute, Oxford, UK

maini@maths.ox.ac.uk



Synopsis: Understanding collective movement is a major and important challenge. In the context of cell movement, we present two case studies: (i) cancer and (ii) neural crest (normal development). Using partial differential equation models, and hybrid cell-based models, we show how modelling can increase our understanding of collective cell invasion and migration.

Collective movement occurs throughout nature across a multitude of scales, from the long-distance movement of whales, to flocking starlings, to bacterial pattern formation. Understanding what are the hallmarks of collective movement is still an open question. With colleagues, I have been studying this problem in the context of cell movement and I will present some results from this work in the context of disease spread and normal development. Understanding how cancer cells invade tissue is an important part of preventing the disease spreading. Several models have been proposed for this. Recently, we proposed a partial differential equation model for this phenomenon in which cells co-operate. That is, instead of having a generalist population that can overcome obstacles and invade, we consider two specialist populations. In this context, we consider two barriers to invasion: normal cells and the extracellular matrix, and we consider two cancer cell types: one that produces lactic acid that can kill normal cells, and one that produces matrix-degrading enzymes. We analyse the travelling wave behaviour of this system via linear stability analysis and numerical simulation. We then analyse in more detail show a simplified sub-model, with degenerate cross-diffusion and a continuum of steady states, and find that it poses challenging problems for travelling wave analysis.

We then study normal development in the context of the cranial neural crest. These are cells that leave the neural tube and migrate to form part of the skull. Neural crest cells give rise to many parts of the body and nearly one-third of birth defects arise from abnormal behaviour of neural crest cells. Moreover, neural cells are the precursors of melanocytes, which can form melanoma, one of the most aggressive cancers. We use a hybrid cell-based model as an hypothesis testing and hypothesis generating tool and, in a long-standing collaboration with experimental colleagues, we have uncovered new biological insights concerning this process. Some of these results will be presented.