Bridging from single to collective cell migration with non-local particle interactions models

Andreas Buttenschoen

Abstract

In both normal tissue and disease states, cells interact with one another, and other tissue components. These interactions are fundamental in determining tissue fates, and the outcomes of normal development, and cancer metastasis. I am interested in collective cell behaviours, which I view as swarms with a twist: (1) cells are not simply point-like particles but have spatial extent, (2) interactions between cells go beyond simple attraction-repulsion, and (3) cells "live" in a regime where friction dominates over inertia. Examples include: wound healing, embryogenesis, the immune response, and cancer metastasis. In this seminar, I will give an overview of my computational, modelling, and theoretical contributions to tissue modelling at the sub-cellular, cellular, and population level.

In the first part, I focus on the nonlocal "Armstrong adhesion model" (Armstrong et al. 2006) for adhering tissue (an example of an aggregation-diffusion equation). Since its introduction, this approach has proven popular in applications to embyonic development and cancer modeling. However many mathematical questions remain. Combining global bifurcation results pioneered by Rabinowitz, equivariant bifurcation theory, and the mathematical properties of the non-local term, we prove a global bifurcation result for the non-trivial solution branches of the scalar Armstrong adhesion model. I will demonstrate how we used the equation's symmetries to classify the solution branches by the nodal properties of the solution's derivative.

In the second part, I focus on agent-based modelling of cell migration. Small GTPases, such as Rac and Rho, are well known central regulators of cell morphology and motility, whose dynamics play a role in coordinating collective cell migration. Experiments have shown GTPase dynamics to be affected by both spatio-temporally heterogeneous chemical and mechanical cues. While progress on understanding GTPase dynamics in single cells has been made, a major remaining challenge is to understand the role of GTPase heterogeneity in collective cell migration. Motivated by recent one-dimensional experiments (e.g. micro-channels) we introduce a one-dimensional modelling framework allowing us to integrate cell bio-mechanics, changes in cell size, and detailed intra-cellular signalling circuits (reaction-diffusion equations). We use numerical simulations, and analysis tools, such as bifurcation analysis, to provide insights into the regulatory mechanisms coordinating collective cell migration.