Modelling the mechanics of tissue morphogenesis

Alexander Fletcher and Michael Smutny

During embryonic development, mechanical forces are essential for cell rearrangements and tissue shape changes. Deciphering the nature of these forces and their interactions will help improve our understanding of embryogenesis, tissue regeneration and wound healing. **This project will use mathematical modelling to help understand how different mechanical forces interact in the development of the early central nervous system.**

A common approach to modelling the collective mechanical behaviour of developing tissues is to treat cells as individual objects. In vertex models [1], cells are considered as 2D polygons that represent cellular interfaces, with vertices forming where three or more polygons meet. The position of each vertex evolves according to a first-order differential equation that balances nonlinear forces on the vertex due to processes such as adhesion and friction. Rules for cell rearrangements, proliferation and death are represented via discontinuous jumps in the trajectory of the system defined by the vertex positions and cell adjacencies.

This project will develop a vertex model to gain a better understanding of cell and tissue dynamics in the early nervous system of the zebrafish embryo, an ideal organism to study experimentally due to ease of imaging and genetic perturbation. Specifically, the focus of the model will be to link local force generation to global cell and tissue deformations and movements in a tissue called the neural plate. We hypothesise that a combination of external forces such as friction from an underlying tissue called the mesendoderm [2] and convergence and extension [3] can drive cell and tissue rearrangements in the neural plate. However, experimental perturbations in the embryo are limited and quantitative physical model of tissues enable a description of how generation and balance of forces drive morphogenesis [4]. The aim of this project is to use the developed vertex model to better understand how mechanical constraints externally imposed on the neural plate tissue define cell/tissue shapes and movements.

This project would suit a student who is competent in programming and interested in the application of mathematics in biology. The student will start by reading relevant literature and understanding previous models. They will then adapt an existing vertex model to explicitly account for mechanical contributions from neighbouring tissues. If time permits, the student will extend this model to account for tissue curvature. This model could eventually be extended and refined during a PhD, based on further data generated by the Smutny lab, and used to model other tissues in the embryo such as collectively migrating cells that we are working on.

[1] Fletcher et al (2014). Vertex models of epithelial morphogenesis. Biophys J 106:2291-304.
[2] Montero & Heisenberg (2004). Gastrulation dynamics: cells move into focus. Trends Cell Biol 14:620-7.
[3] Smutny et al (2017). Friction forces position the neural anlage. Nat Cell Biol. 19:306-17.
[4] Alt et al (2017). Vertex models: from cell mechanics to tissue morphogenesis. Phil Trans R Soc B 372:20150520.