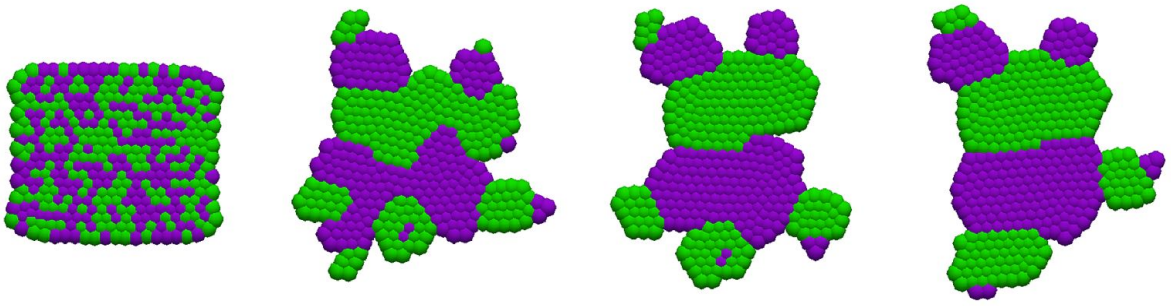
An overlapping spheres model of cell–cell interactions

Embryonic epithelia, the sheets of tissue that line structures and cavities in the embryo, achieve complex shape changes including bending and folding through the coordinated action and rearrangement of individual cells. Recent technical advances in molecular and live-imaging studies of epithelial dynamics provide an excellent opportunity to better understand how cell-level processes facilitate these large-scale tissue rearrangements. In combination with experimental approaches, computational modelling allows us to challenge and refine our current understanding of biological processes and to explore experimentally intractable questions. To this end a variety of 'cell-based modelling' approaches have been developed to describe how processes at the cell scale determine tissue-level behaviour.

In one such approach, the 'overlapping spheres' model, each cell is represented by a point in space with one or more parameters defining the radius (or principal axes) of an ellipsoid centred at that point [2]. Many mechanical descriptions of cell–cell contact have been used, from a simple linear potential to the more complex Hertz and Johnson–Kendall–Roberts (JKR) models. On top of mechanical interactions, biological processes such as cell growth, division and death are often modelled.

A prototypical in silico experiment that can be performed using an overlapping spheres model is that of cell sorting by differential adhesion [1]. In this experiment, two cell types in a random initial configuration can sort into homogeneous regions as a result of different mechanical interactions between different cell types.



Cell sorting due to differential adhesion. Image from Osborne et al [1].

Project

The paper by Pathmanathan et al [2] gives all the information necessary to implement a simple overlapping spheres model from scratch, and the paper by Osborne et al [1] gives details of how to perform a cell sorting experiment using such a model.

The candidate will:

- code up a simple overlapping spheres model in MATLAB with linear interactions and a forward-Euler time stepping scheme
- recapitulate the cell sorting experiment, exploring in some detail how the model parameters influence the rate of cell sorting over time

Many extensions of this project are possible, depending on the interests of the candidate, for example:

- exploring the limitations of the forward-Euler time stepping scheme and implementing more sophisticated numerical schemes
- implementing more sophisticated mechanical interactions between cells, such as Hertz or JKR
- adding biological processes such as cell growth, division and death, using them to perform other in silico experiments
- exploring the functional form of the noise added to cells during cell sorting, improving the formulation to allow length-scale correlation
- implement more sophisticated methods for determining whether two points in space are close together: for instance, use of k-d trees or spatial partitioning algorithms

Prerequisites

Knowledge of MATLAB or other programming experience will be helpful, but this can be gained during Michaelmas Term. All mathematical knowledge can be obtained from the relevant papers and individual study.

References

[1] Osborne J M, Fletcher A G, Pitt-Francis J M, Maini P K, & Gavaghan D J. **Comparing individual-based approaches to modelling the self-organization of multicellular tissues.** *PLOS Comput. Biol.*, 13(2):e1005387, 2017.

[2] Pathmanathan P, Cooper J, Fletcher A, Mirams G, Murray P, Osborne J, Pitt-Francis J, Walter A, & Chapman S J. **A computational study of discrete mechanical tissue models.** *Phys. Biol.*, 6(3):036001, 2009.