

Simulations of epithelial cell monolayer

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Modelling approaches for biological and physiological systems span the range from detailed models of subcellular molecular processes, to biomechanical models at the tissue level. The focus of this summer research project was development of cell-based simulations of 2D sheets of epithelia using a multiscale approach that bridges across spatial and temporal scales within a single, generic modelling framework.

CHASTE (Cancer, Heart and Soft Tissue Environment) is a multi-scale modelling framework, developed at University of Oxford, that comprises of three interlinked modules: a model of sub-cellular behaviour (for example, progress through the cell cycle, or programmed cell death); a model of the movement and mechanical interaction between cells; and a model of the transport of key nutrients, signalling molecules or waste products at the tissue level. The CHASTE software and related libraries (for numerical computation, visualization of simulation results, etc.) were installed and configured on a department server. Simulations are written using a test-driven development paradigm and are designed to run in parallel.

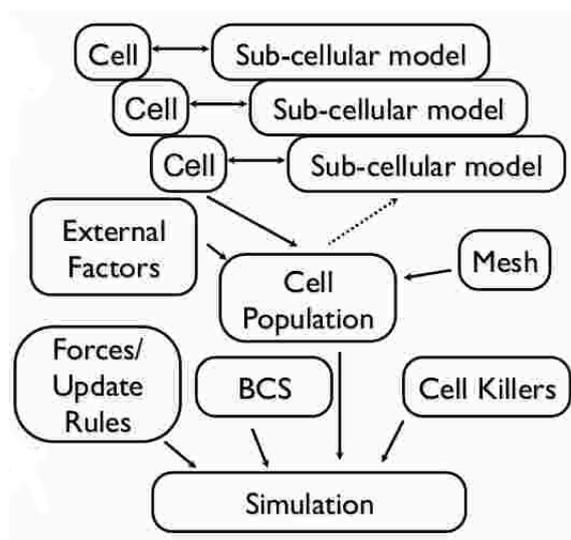


Figure 1

Structure of a CHASTE simulation: Cells are defined by their sub-cellular model and arranged in a mesh. The cell population is subject to external factors (e.g. chemicals, nutrients, forces). Users can define boundary conditions, cell killers, and other simulation parameters (e.g. time step, duration, cell volume tracking, etc.) to keep the population in check.

Cell-based models are broadly categorized as on-lattice or off-lattice models based on how the individual cells are represented geometrically and how the physical and chemical interactions between cells are treated. Cellular Automata and Cellular Potts are on-lattice models that represent cells as collection of one or more lattice sites that undergo growth through stochastic relabeling rules. Node-based models where cells are represented as overlapping spheres and vertex dynamics model in which cells are described by polygons are examples of off-lattice models that offer greater flexibility in defining cell-cell interactions. Vertex dynamics model is particularly appealing for modelling epithelia as the relatively regular shape of cells (with near planar interfaces between neighboring cells) is well represented.

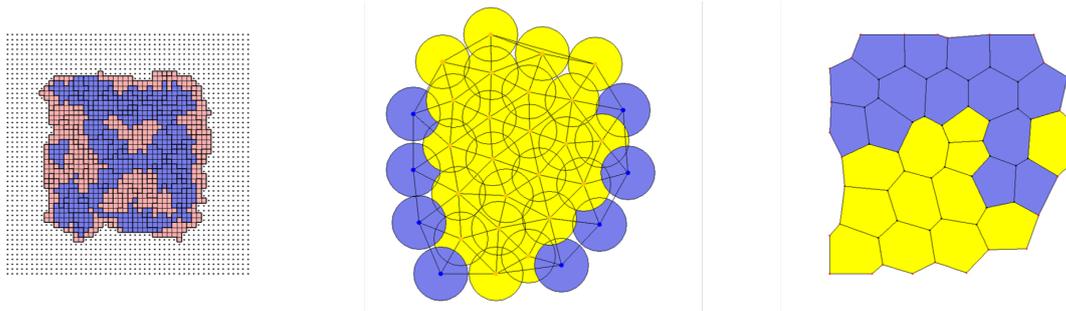


Figure 2

Left to right: CHASTE simulation consisting of two cell types (yellow and blue) using cellular potts, node-based and vertex dynamics models.

Biological processes are inherently multiscale. Therefore, simulations developed using CHASTE that incorporate features from multiple scales are useful for understanding complex biological processes like tumour growth and embryonic development. Cells interact with each other and the environment to influence tissue development. During this summer, we developed simulations of tissue growth, cell sorting, cell migration, contact inhibition and stem cell proliferation using the models described above. Inspection of similar simulations using different models allows us to find relative strengths and weaknesses of each model. The results obtained thus also inform our choice of model for subsequent simulations and lead to development of better models.

REFERENCES

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