Hi-Throughput Colorectal Crypt Monoclonality Simulation

Markus Gerstel – Systems Biology Doctoral Training Centre – University of Oxford – markus.gerstel@dtc.ox.ac.uk

Biological Background

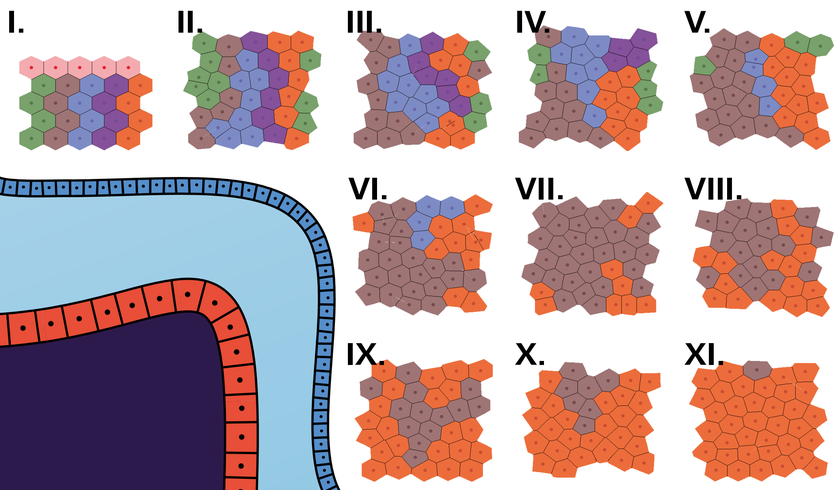
Colorectal crypts are recesses in the colon and rectum epithelium. Stem cells at the bottom of the crypt replicate and force other cells to migrate out of the crypt, specialising on their way. Cells detach from the epithelium at the tip between crypts.

The high cell replication rate at the bottom of crypts favours DNA mutation and can lead to uncontrolled cell proliferation, ultimately resulting in **colorectal cancer**.

The question to be answered by these simulations is how long it takes for one ancestorial cell to take over the crypt (**monoclonality**).

Monoclonality

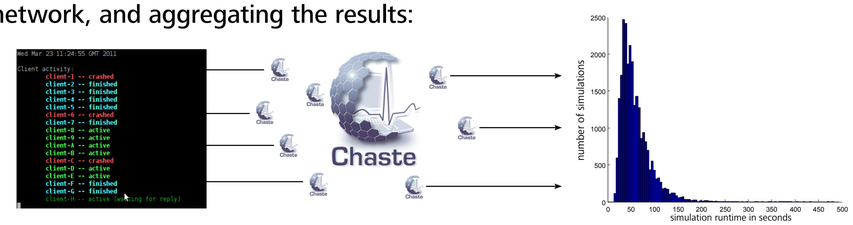
Shown below is a single simulation run of a 5x5 cylindrical crypt. Five ancestorial stem cells (**I.**) are competing against each other. The crypt will quickly become tri- (**VI.**) and biclonal (**VII.**) before finally reaching monoclonality:



Computational background

The simulation of cell replication and movement is based on **Chaste** (**C**ancer, **H**eart and **S**oft **T**issue **E**nvironment), a software package developed at the University of Oxford. Cells are represented by an interconnected damped spring mesh of their point centres. The cell shape is then defined by the voronoi tesselation.

To facilitate hi-throughput simulations Chaste was extended by a **parallel Chaste toolkit**, coordinating independent instances of Chaste over a local network, and aggregating the results:

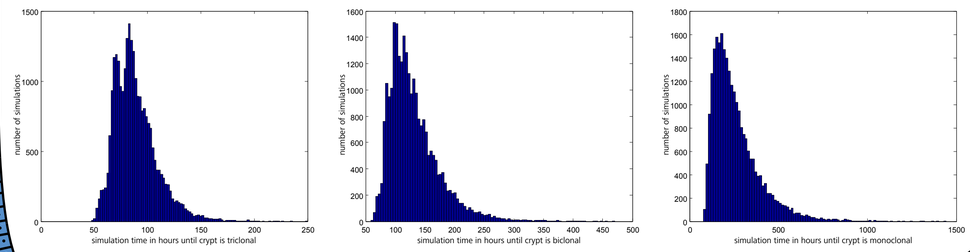


In these simulations the Parallel Chaste Toolkit controlled on average 27 instances of Chaste. The mean runtime of individual simulations was 59 seconds. Chaste is freely available from http://www.comlab.ox.ac.uk/chaste/

Results

Using **14 computers** and **27 parallel instances** of Chaste a total of **25.711 crypts** were simulated over a single night. A single processor would have needed **424 hours (~17.7 days)**. The results suggest that time-to-monoclonality follows a continuous distribution with a strong peak close to the minimum time:

	triclonality	biclonality	monoclonality
min	47.5 h	59.2 h	79.1 h
mean	88.6 h	131.2 h	260.9 h
max	250.0 h	470.7 h	1443.5 h



stem cells proliferate at the bottom of the crypt, get pushed out and differentiate on their way

EPSRC
Engineering and Physical Sciences Research Council

UNIVERSITY OF OXFORD

Systems Biology Doctoral Training Centre