Multiscale multicellular simulations using Cell Based Chaste

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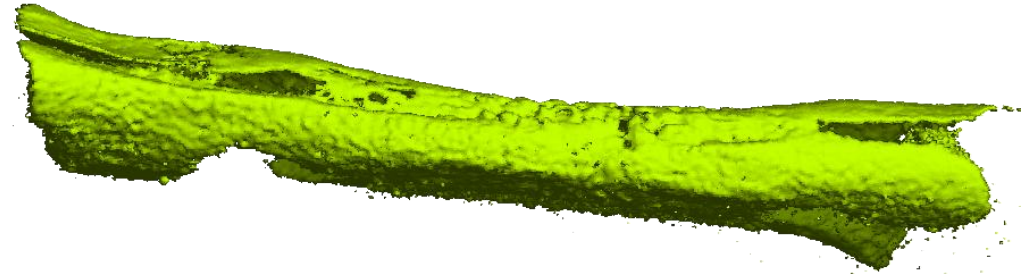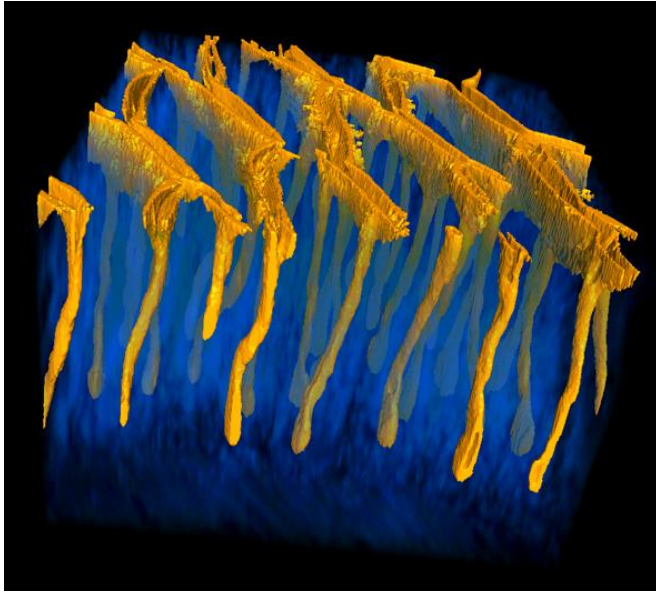
15th August 2012

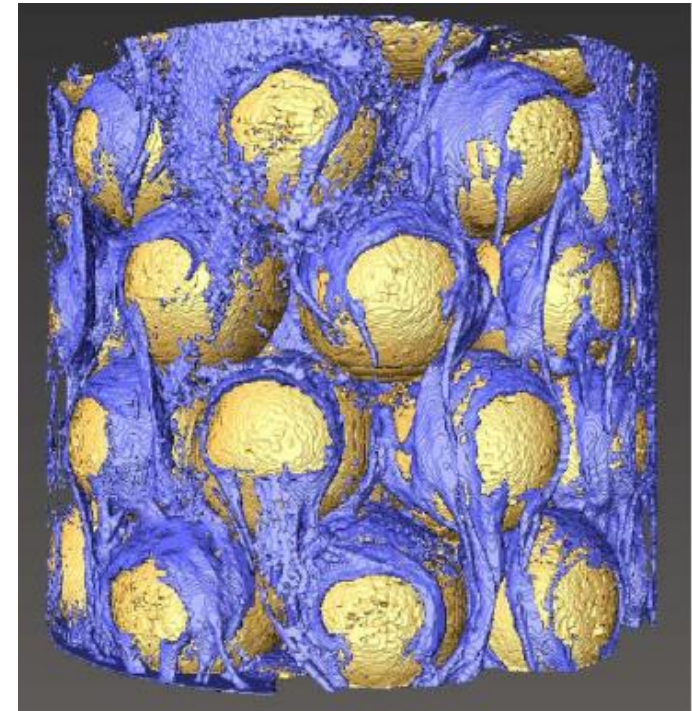http://www.cs.ox.ac.uk/people/james.osborne/

Motivation and framework

Modelling/ simulation interests

- Tissues and collections of cells:
  - How cells move, divide and die
  - Interact with each other and the environment
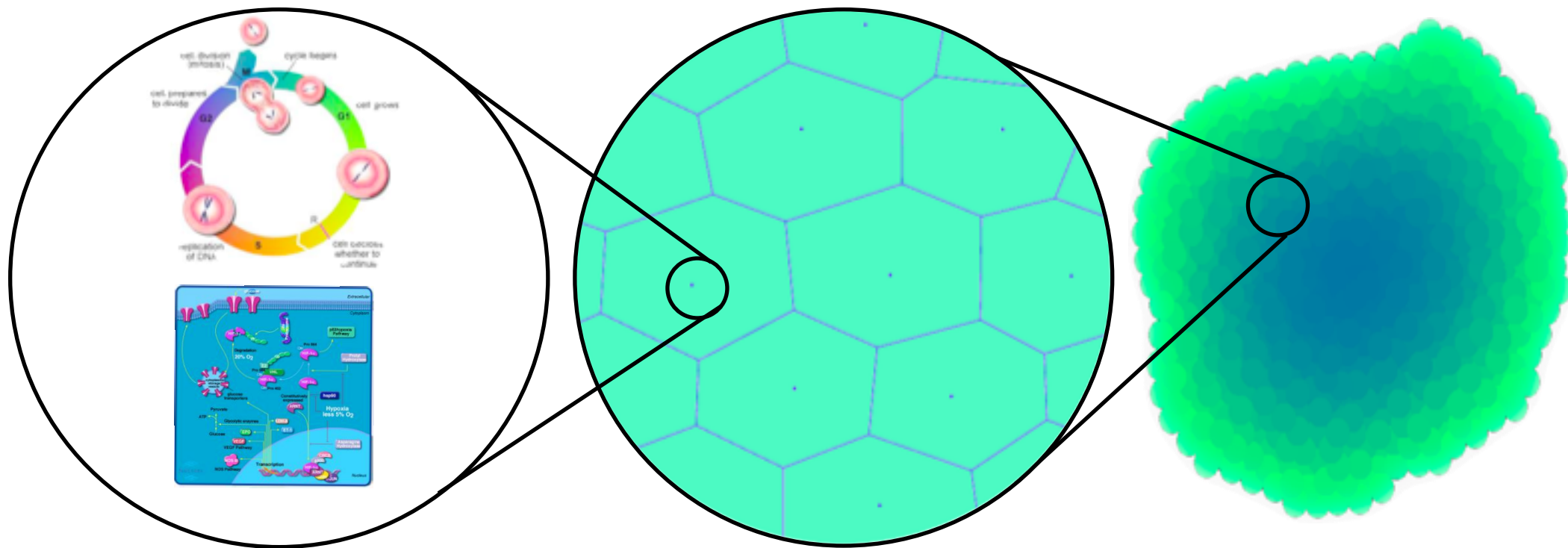 - How cellular level properties influence tissue level behaviour

Multiscale cell centric framework

"Fundamental unit of biology would seem to be the cell"

Multiple possible models at each scale

Modelling populations of cells

Cell-level models
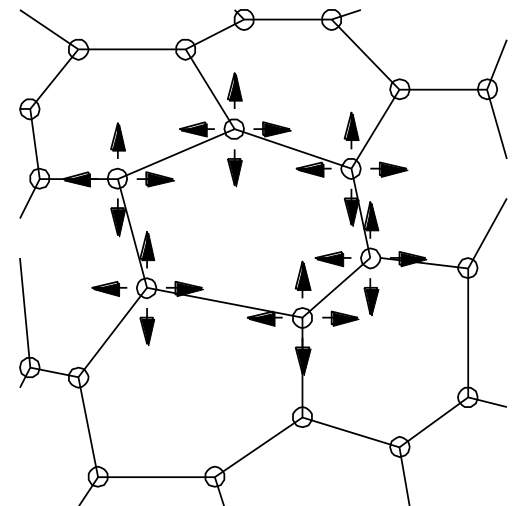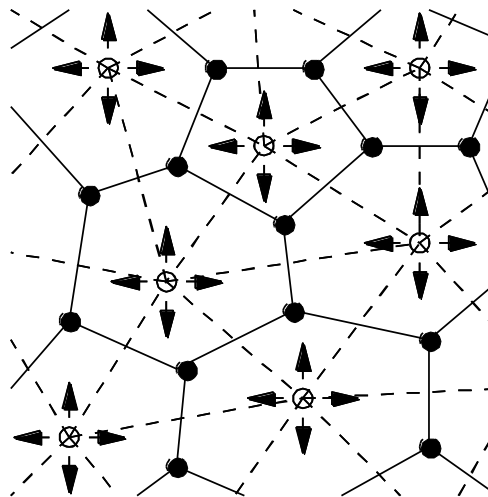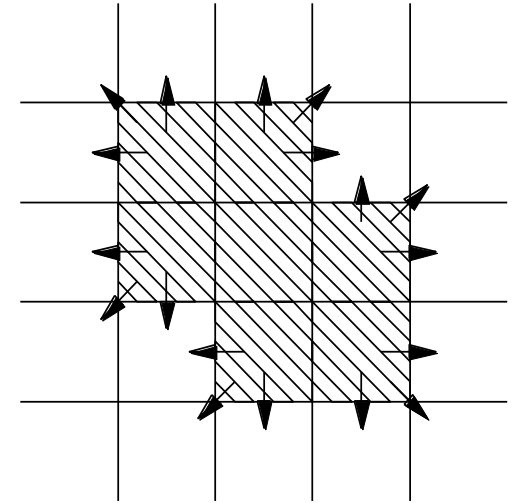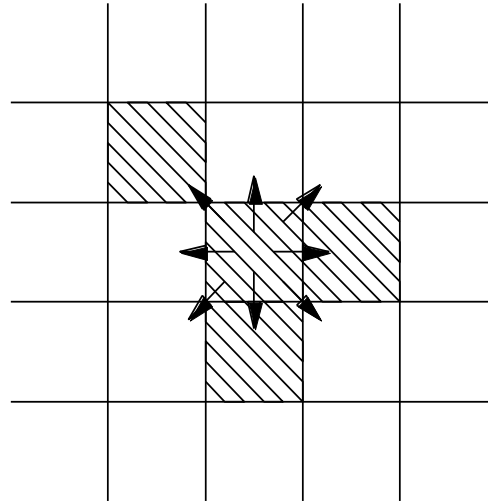
- Here we explicitly consider individual cells

- Track cell movement, size, shape

- Influences from 'above' and 'below'

- Cellular automata, cellular potts, cell-centre based models, vertex models
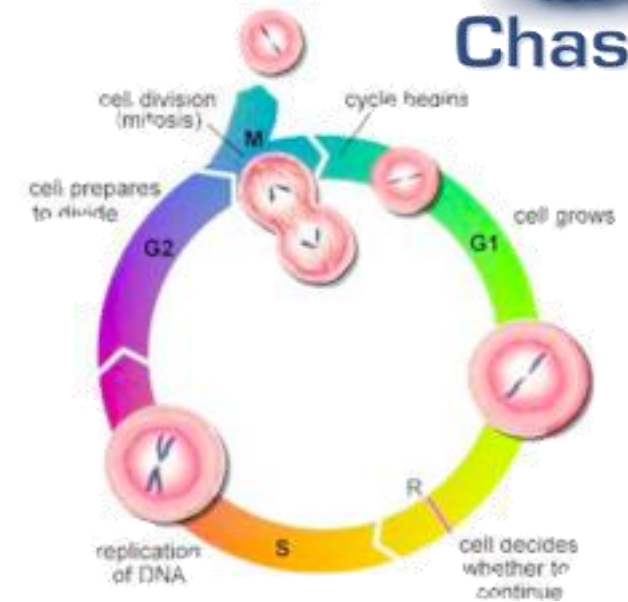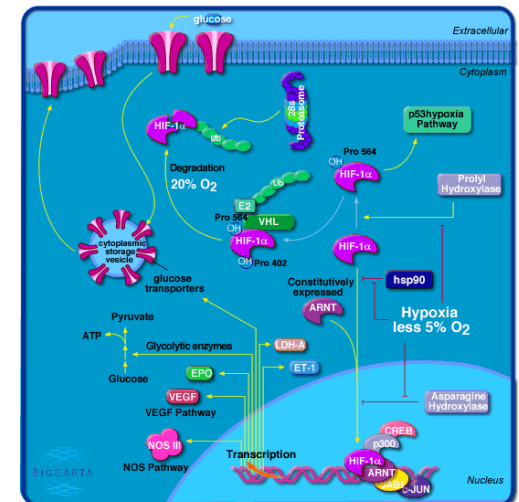
Modelling sub-cellular processes

- Simple agent based models
- Cell cycle
- Other metabolic pathways
  - Reaction networks
  - Typically a system of non-linear ODEs
- Coupled to extracellular concentrations
- Influence cell division, cell size/shape, cell-stromal and cell-cell adhesion, cell fate

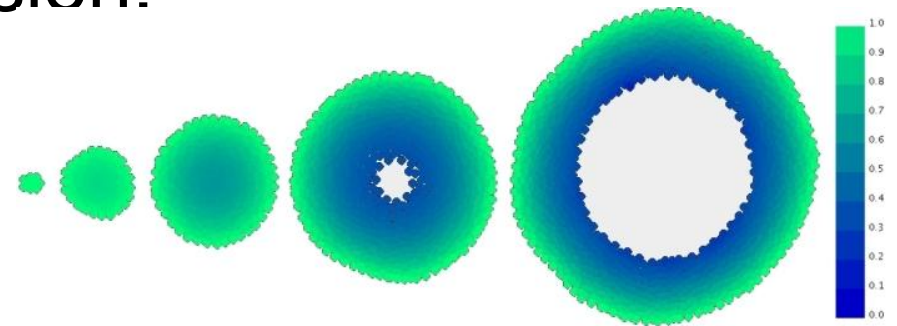http://teachline.ls.huji.ac.il

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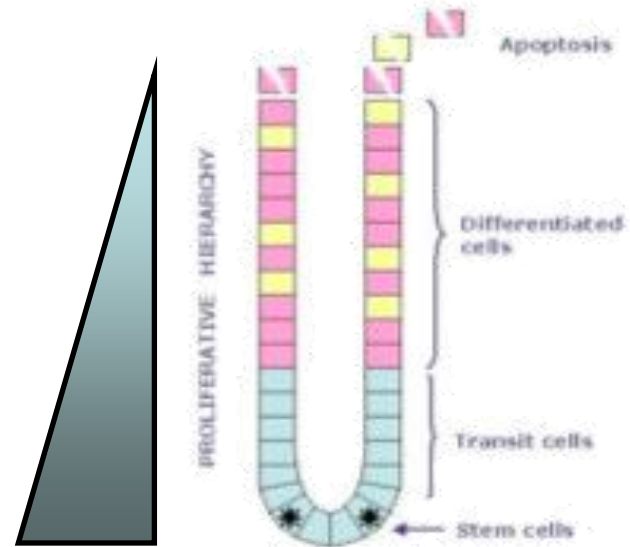
Modelling tissue-level processes

- Geometrical constraints
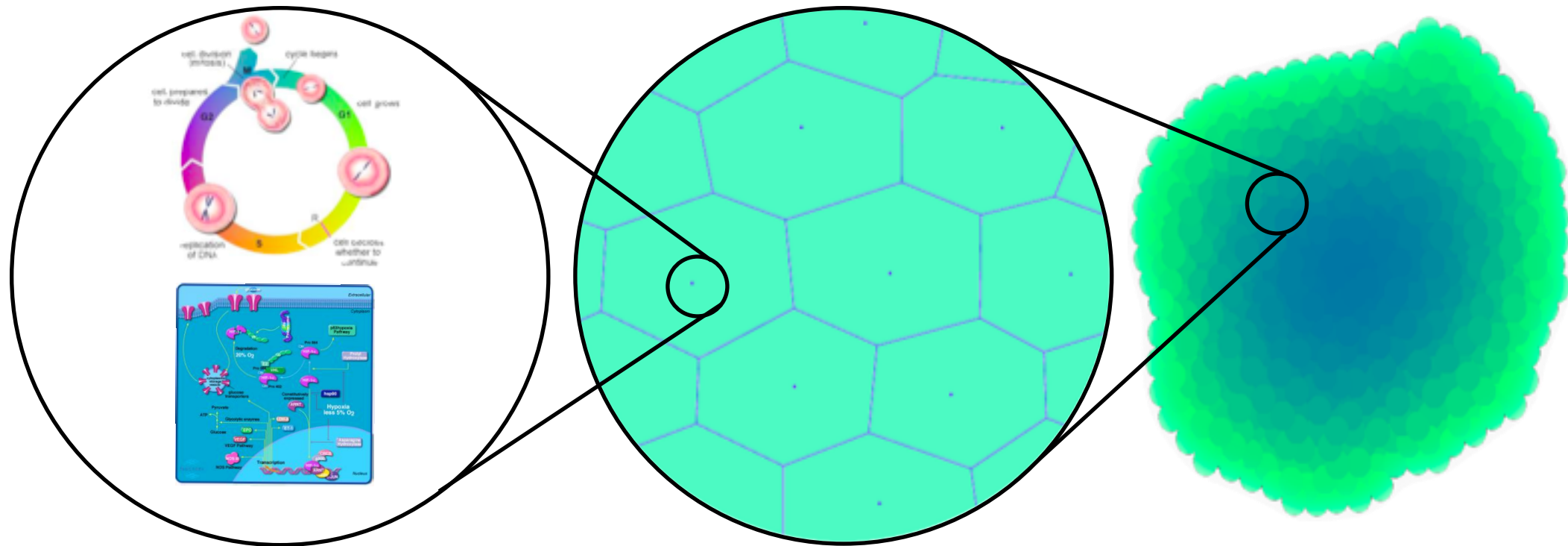- Imposed gradients
- Vascular networks
- Juxtacrine signalling
- Field equations:
  - nutrient or inhibitor diffusion.
  - cells as sinks/sources,
  - on a growing domain
- Fluid flow
  - Mechanotransduction

Putting it all together

Multiple possible models at each scale.
Also need to specify interactions between scales.

Cell Based Chaste: running multicellular simulations

What is Chaste?

- Library of numerical code, for solving problems in computational biology
- Started in 2005
- 2 main components: Cardiac and Cell Based

"Cancer Heart and Soft Tissue Environment"|

- Aim: to produce a robust, easily extensible, reliable, re-usable and well documented code base
  - XP - Test driven development
  - Tested continuously/nightly/weekly
  - Over 250,000 lines of source code and over 200,000 lines of tests (C++)
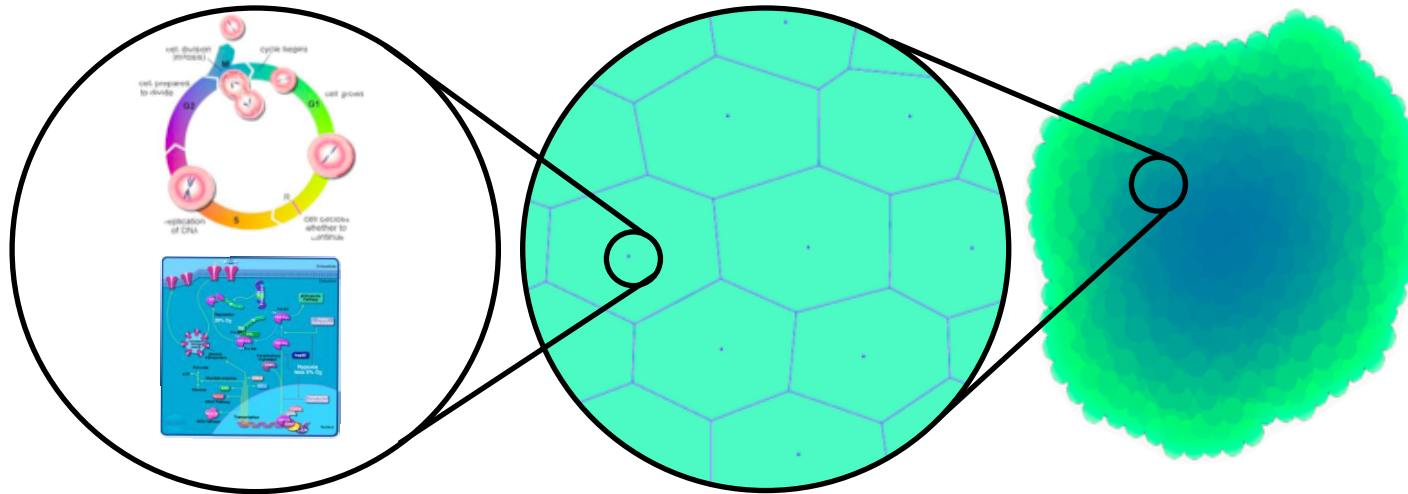 - Open source - BSD Licence http://www.cs.ox.ac.uk/chaste/

Cell-base functionality

Sub-cellular level:
- rule based;
- stochastic;
- ODE based cell cycles models/ other networks

Cell level:
- cell centre;
  - OS,
  - voronoi
- vertex based;
- cellular Potts;
- cellular automata

Tissue level:
- external factors;
- juxtacrine signalling;
- PDEs: reaction diffusion, etc, on growing domain

Setting up a simulation

Going from Biological Model to simulation

- Type of cell level model
  - interaction forces/rules
  - boundary forces/rules
- Sub cellular model
  - proliferation,
  - growth, death .etc.
- Diffusible species
  - how these interact with cells
  - How they diffuse
  - boundary conditions
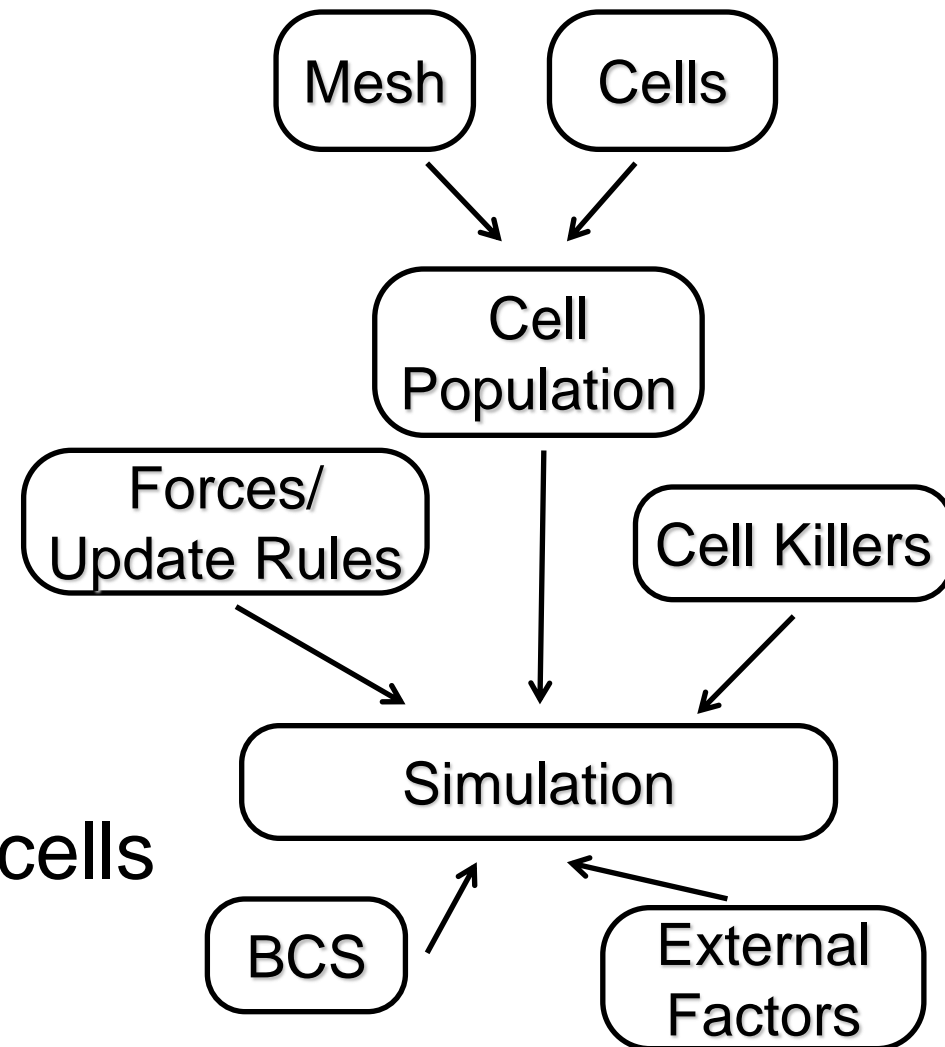
Example Simulations

Tracking cell lineages

Cell sorting
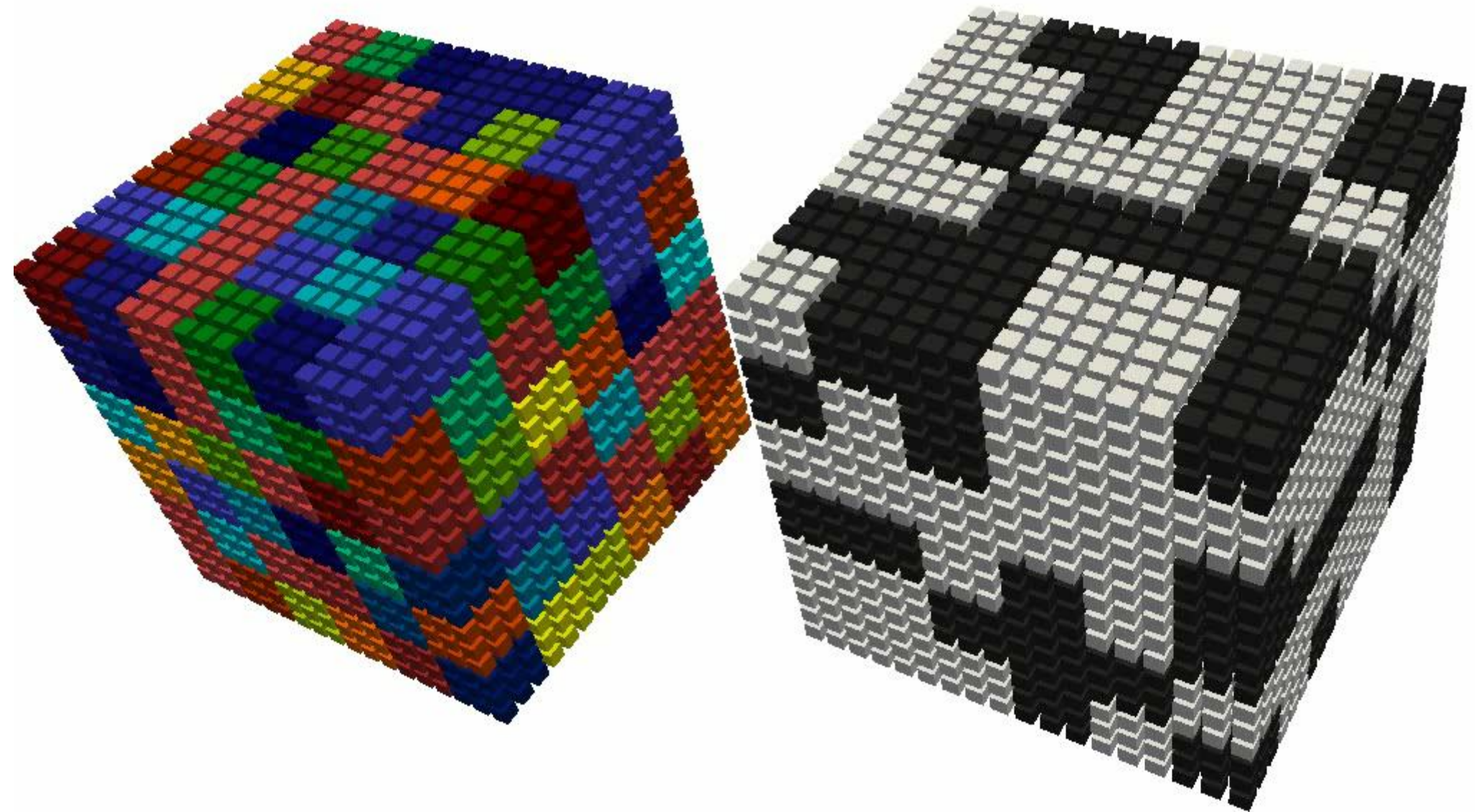
Other examples
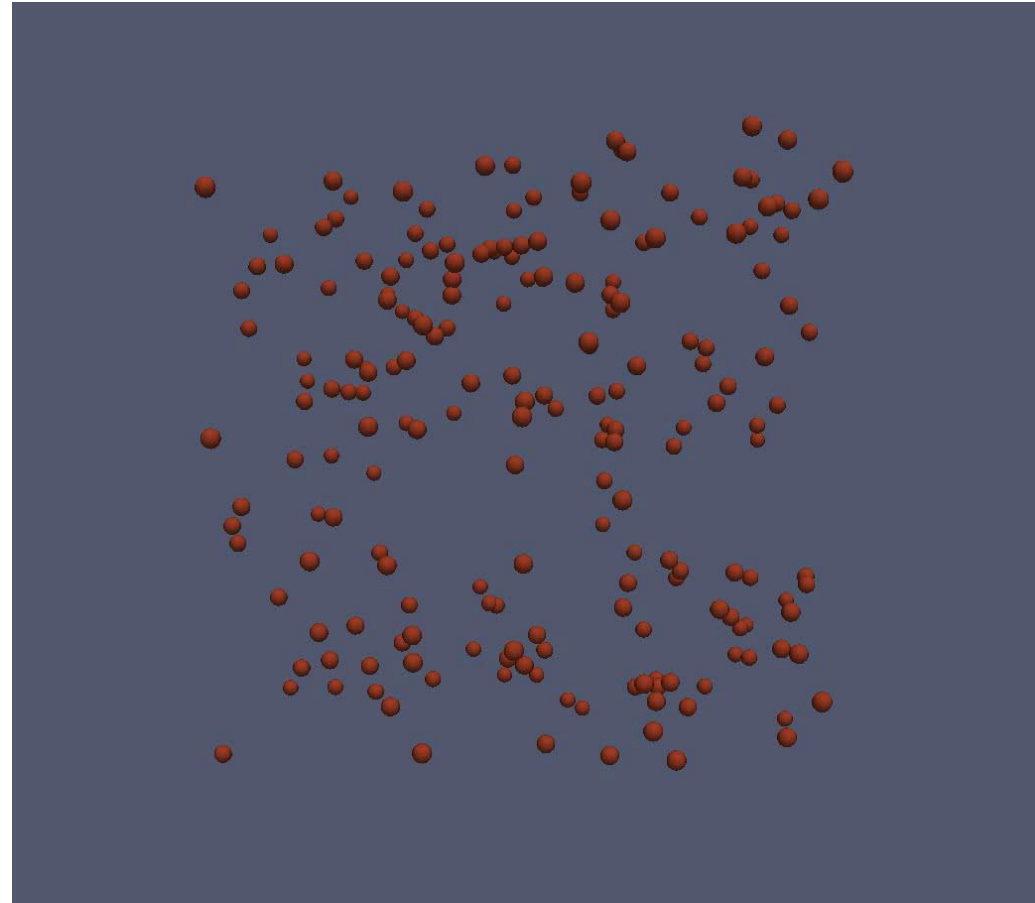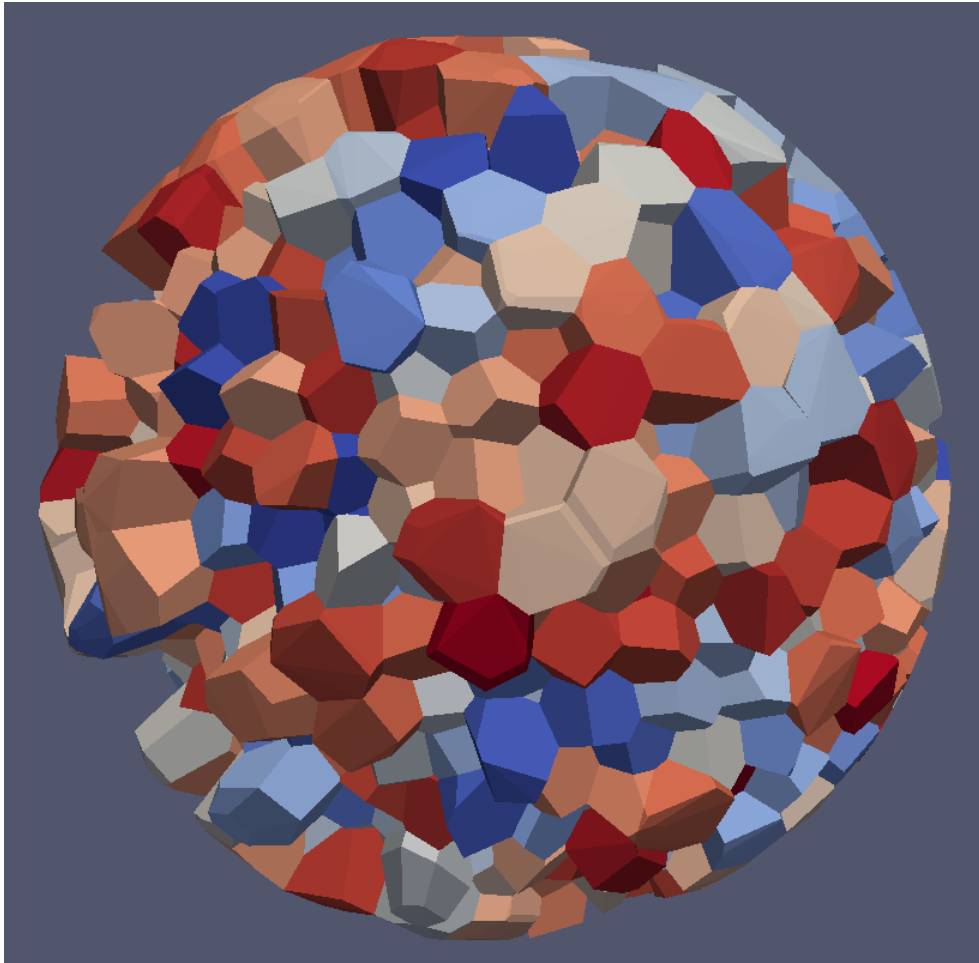
Simple model comparison
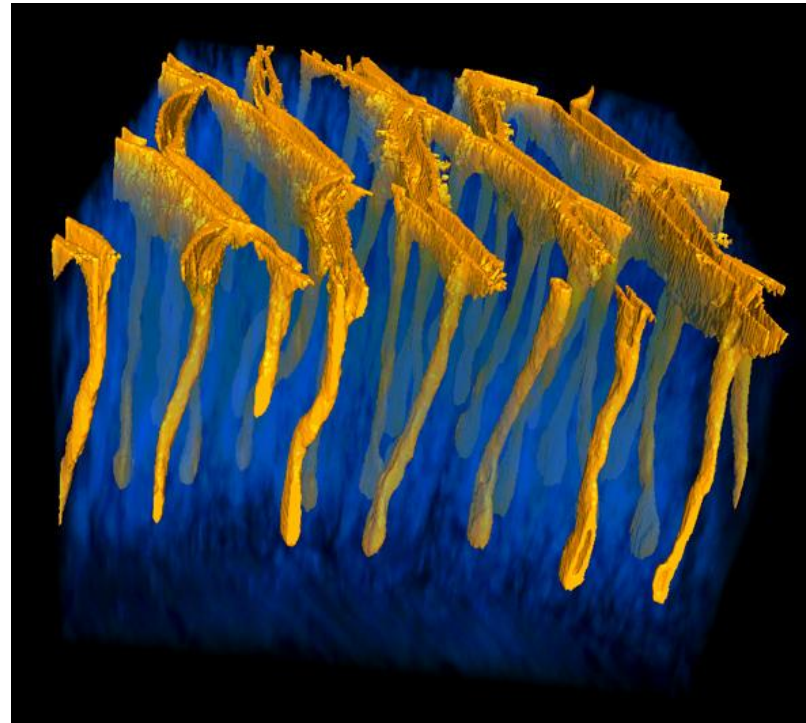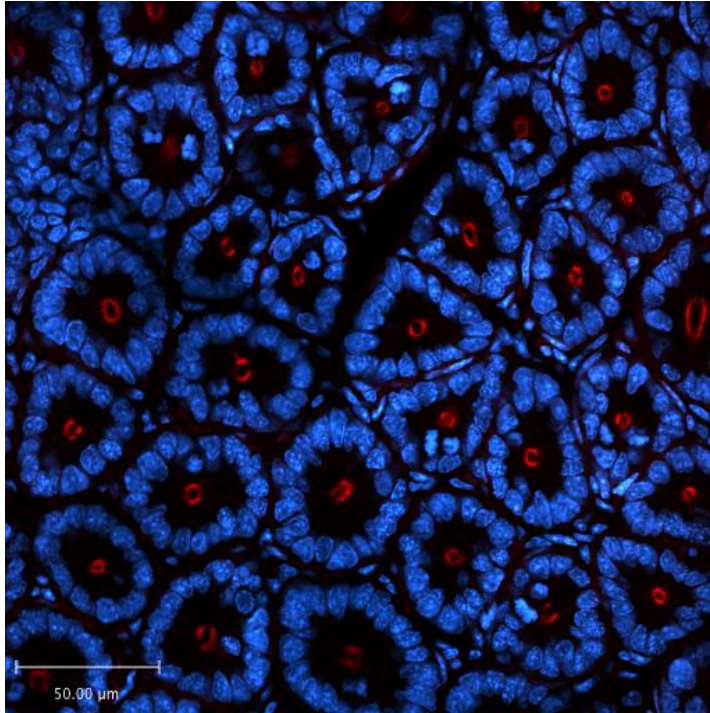
Colorectal crypt

Paul Appleton, Dundee

- Crypts of Lieberkühn in the gut ~5 million in adults
- About 700 cells and renewal every 3-5 days
- 20-50 million cells per minute lost into gut, 10 per crypt
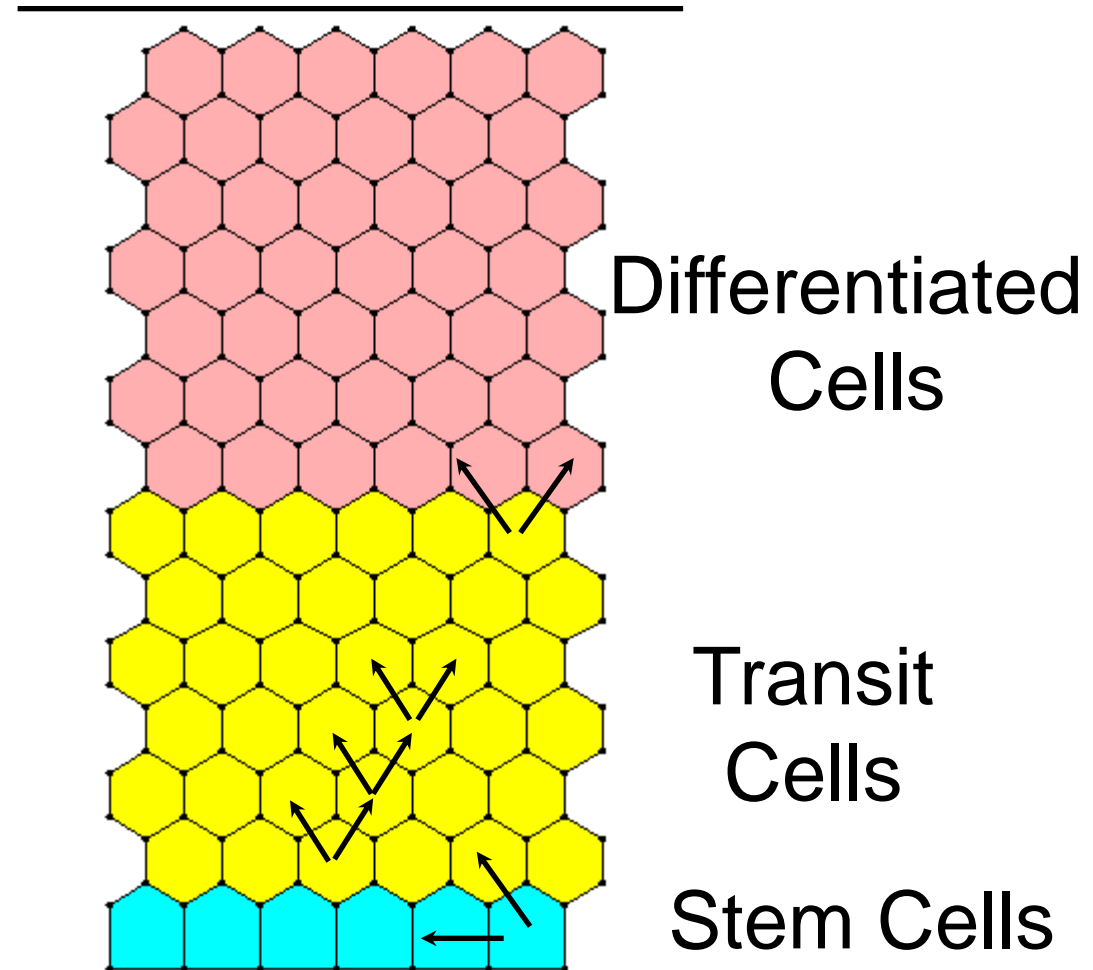- Mutations in crypt lead to onset of CRC

Model comparison

Simplfied Crypt model
- Small periodic domain
- Solid base
- Simple stochastic generation based model for cell birth
- Cell sloughing
- Cell centre; vertex and cellular Potts model
- Parameterised by number leaving per hour

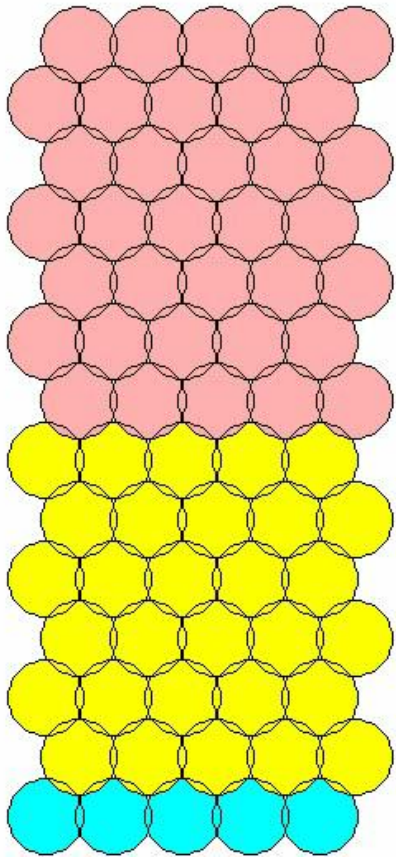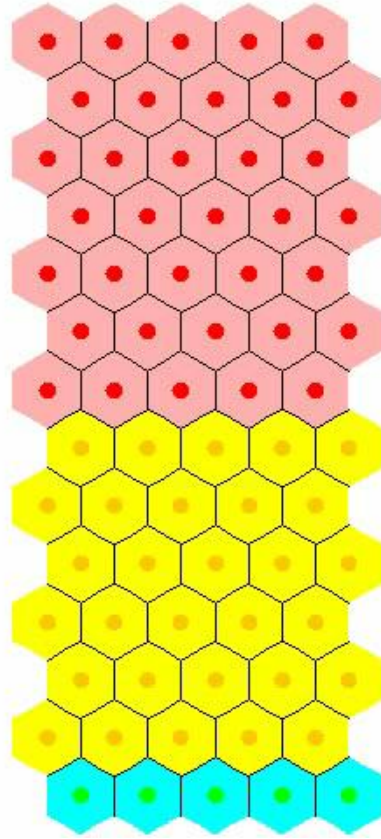Cells Sloughed

Differentiated Cells
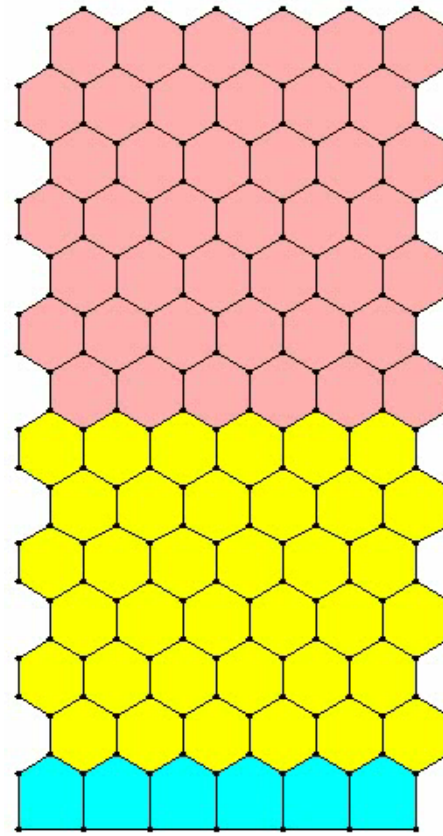
Transit Cells
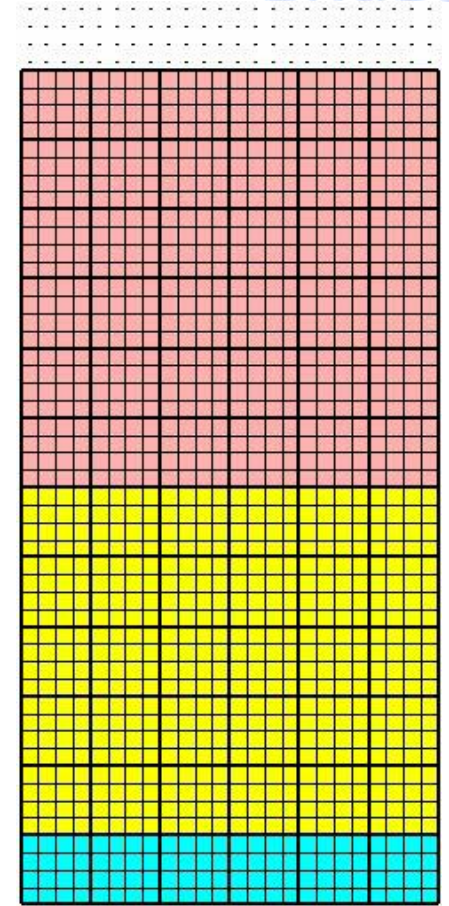
Stem Cells

Comparison of cell level models

OS based   Tessellation based   Vertex based   Cellular Potts

Compare: numbers of types of cells; distribution of cell types; time spent in crypt.

Where we're going

Specifying simulations:

- Ways to specify models at each scale effectively
- Specify connections between scales
- Equate parameters between modelling paradigms: force vs probability

Running simulations:

- Tools/ languages to build simulations from descriptions of system
- Protocol specification – Functional Curation: Jon Cooper
- Writing simulations - Matlab interface

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Chaste

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