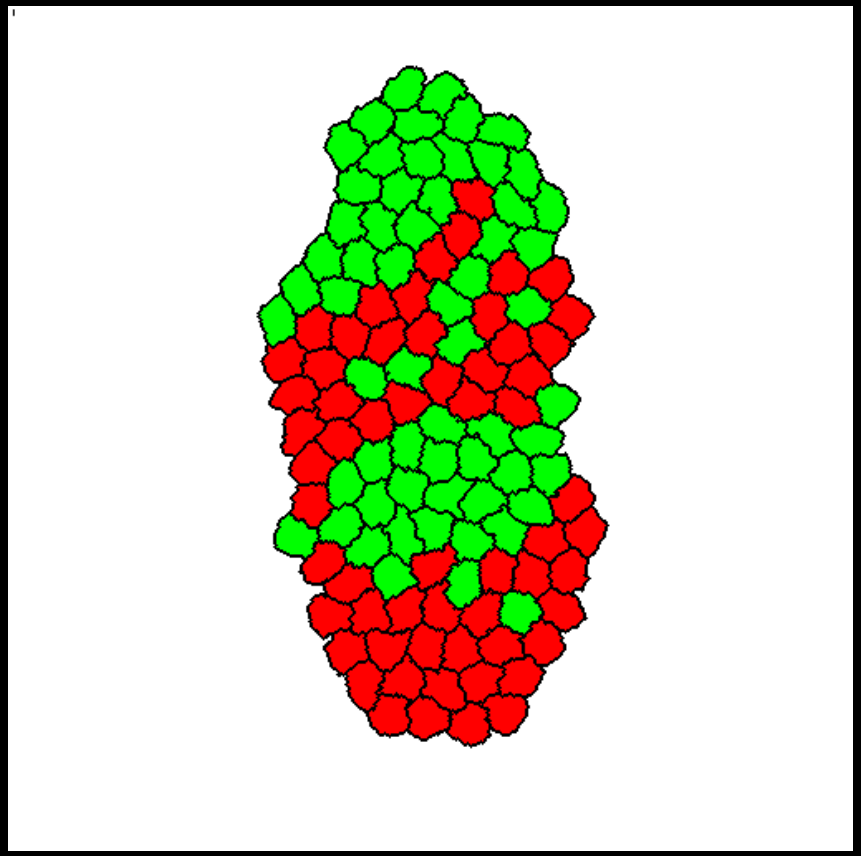
Modeling development with Cellular Potts Model

Renske Vroomans



Master's and PhD in Utrecht

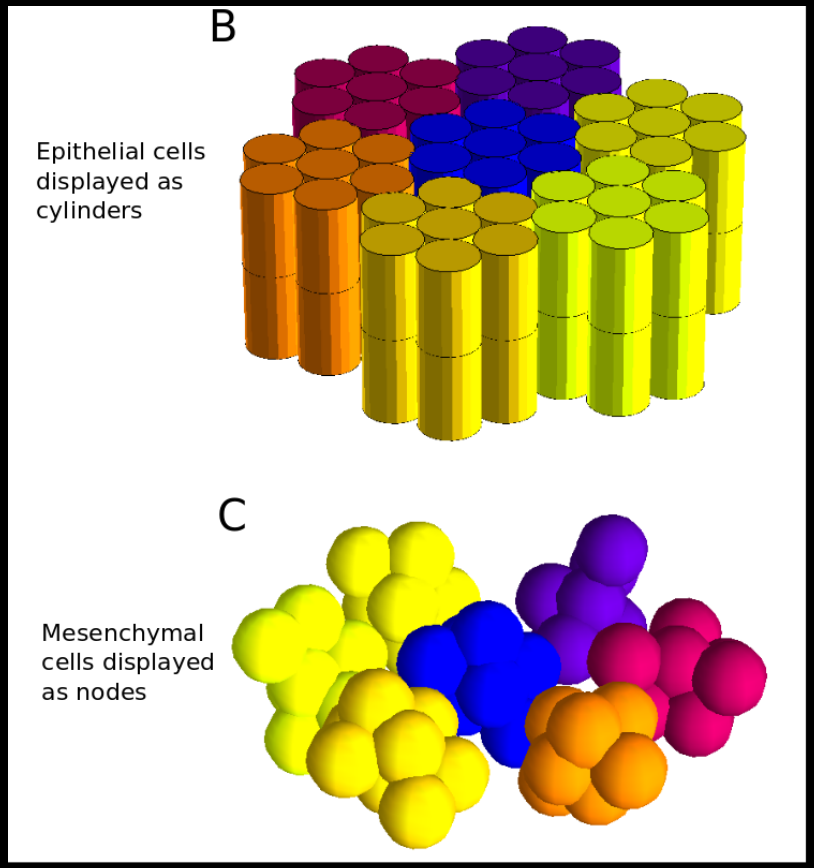
T cell migration

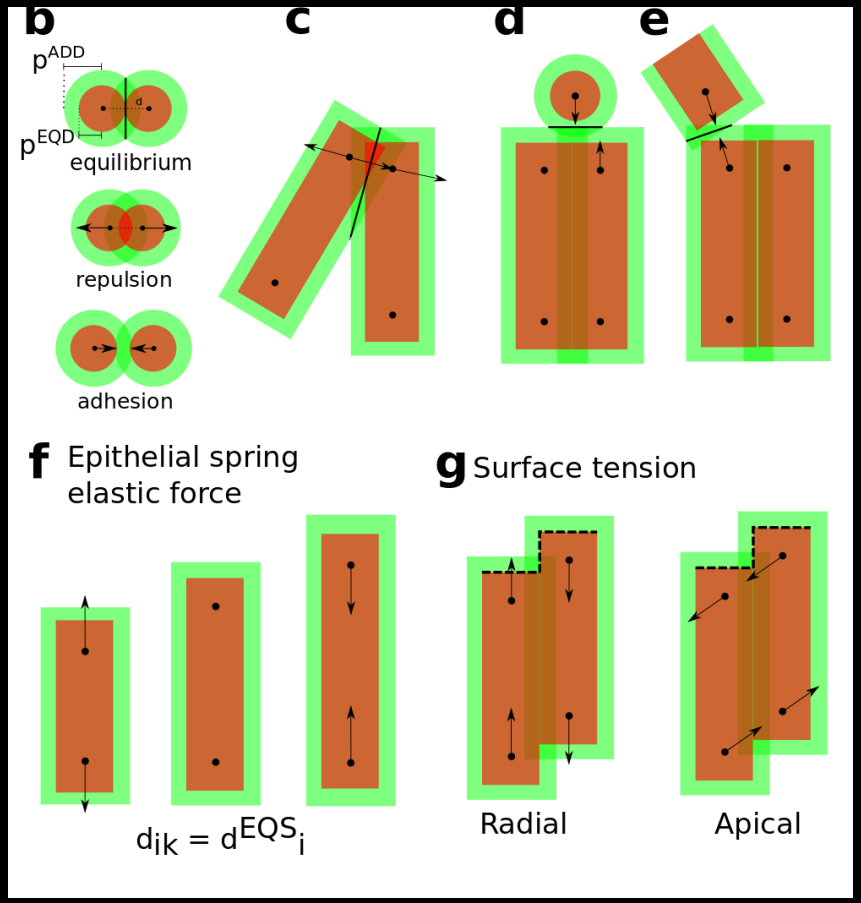
Plant hormones in fruit development

Evo-devo of animal segmentation

Tcell receptor sequences in database

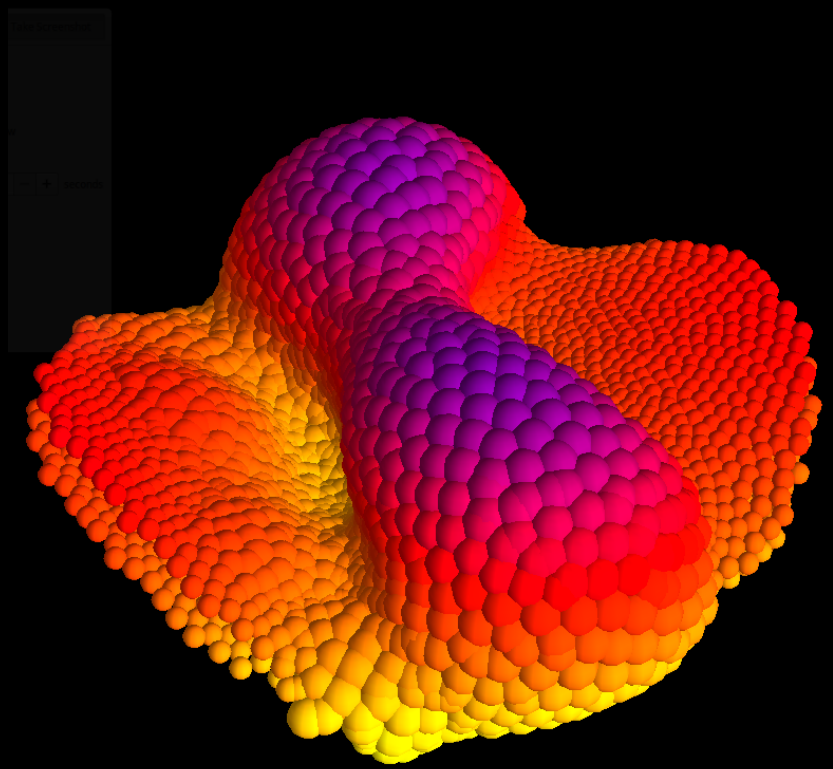
Currently: EmbryoMaker





Marin-Riera *et al.*, 2015

Epithelial morphologies



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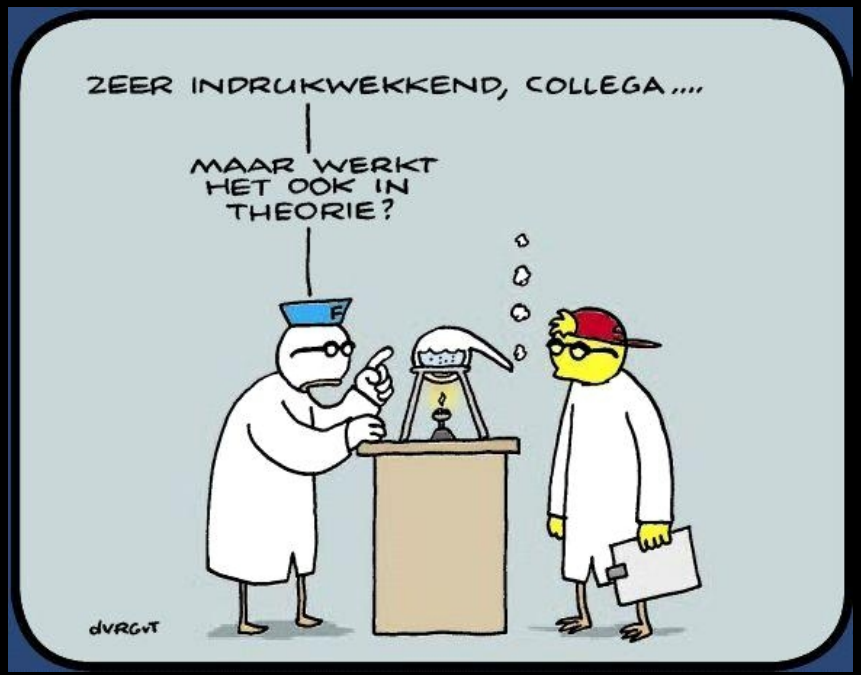
Why do we make models

- to inform the next experiment
- to test difficult hypotheses
- to identify gaps in our knowledge
- to understand mechanism and process
- to be surprised

lower-level properties <–> higher-level phenomena



What should a model of cells capture?

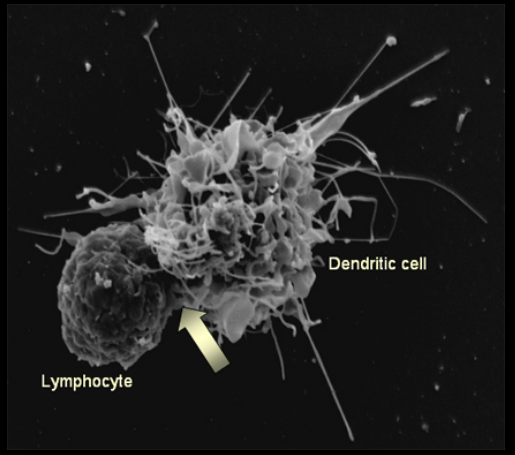
short answer: that depends on the question

CPM is suitable for mesoscale cell modeling:
between cells as points and cells as complex machines

What should a mesoscale model of cells capture?

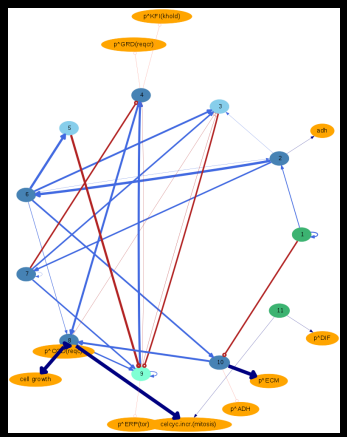
Cells have a size and shape
Cells can be more or less stiff
They experience 'spontaneous' membrane fluctuations
They can be more or less motile

Cells can interact and adhere

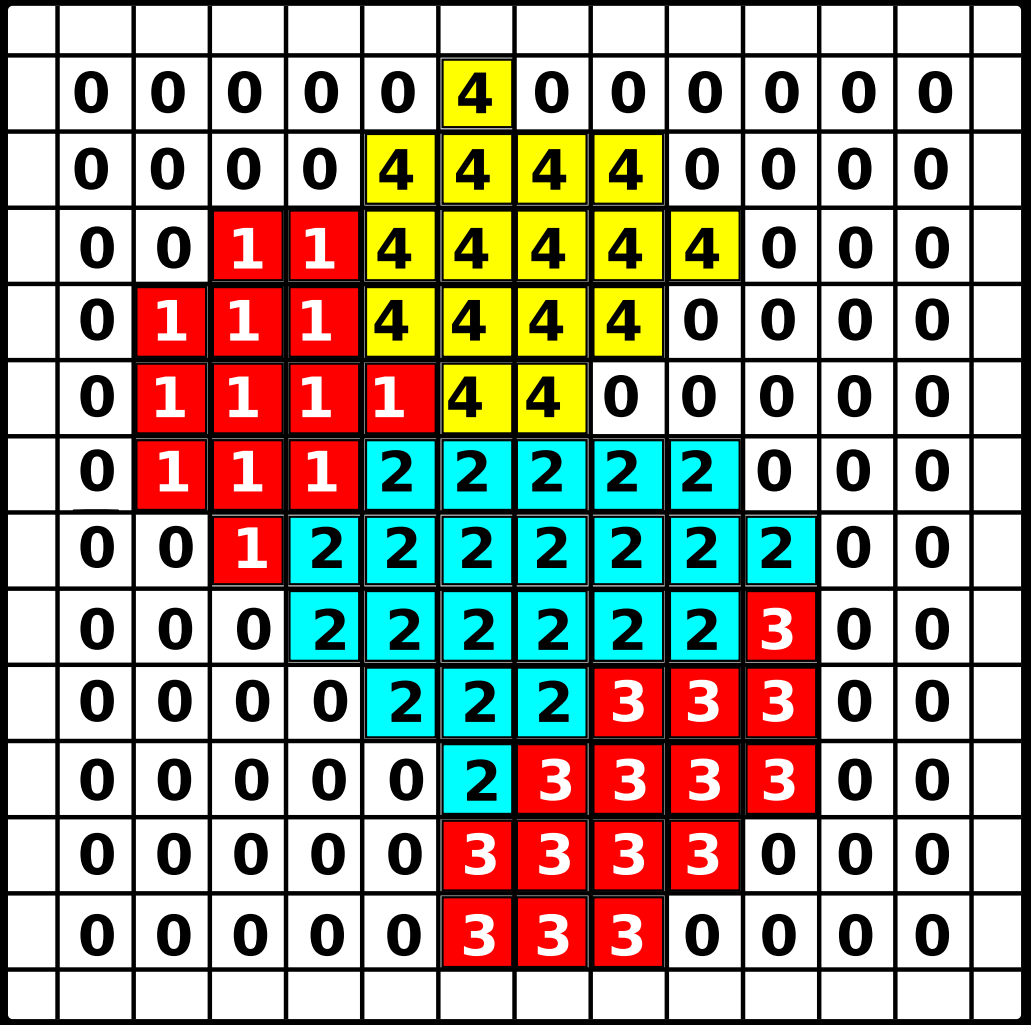


taken from http://pathmicro.med.sc.edu/lecture/hiv7.htm

divide or cleave, grow and die
They have a gene expression state



The CPM as a mesoscale cell model



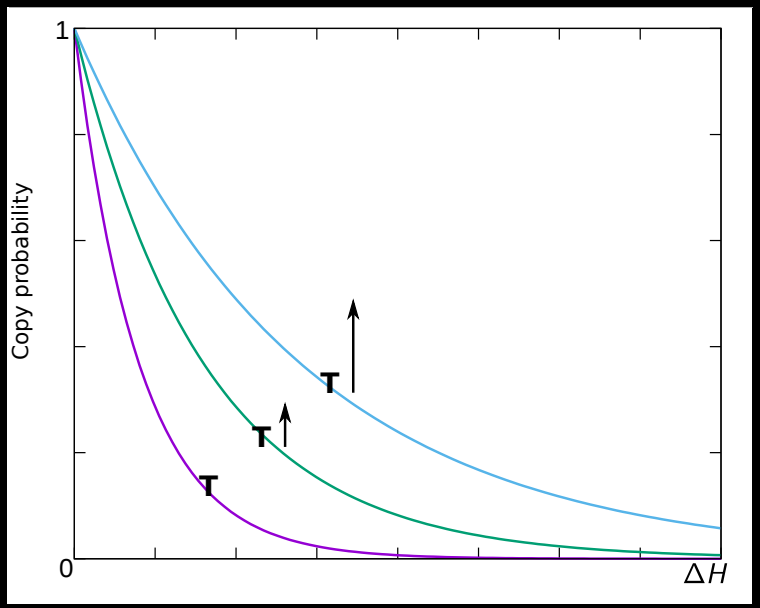
Each cell is a distinct unit –> cell id σ

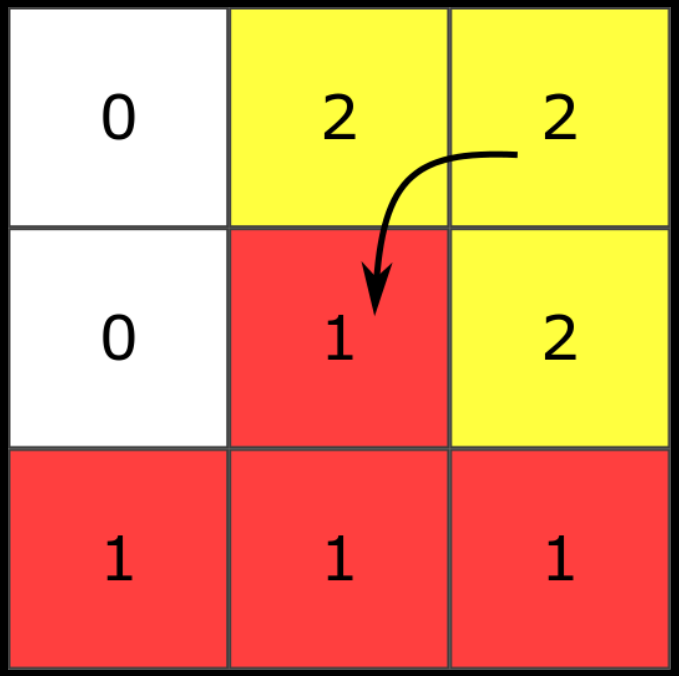
Cells can have a type (τ)

The heart of CPM: the Hamiltonian

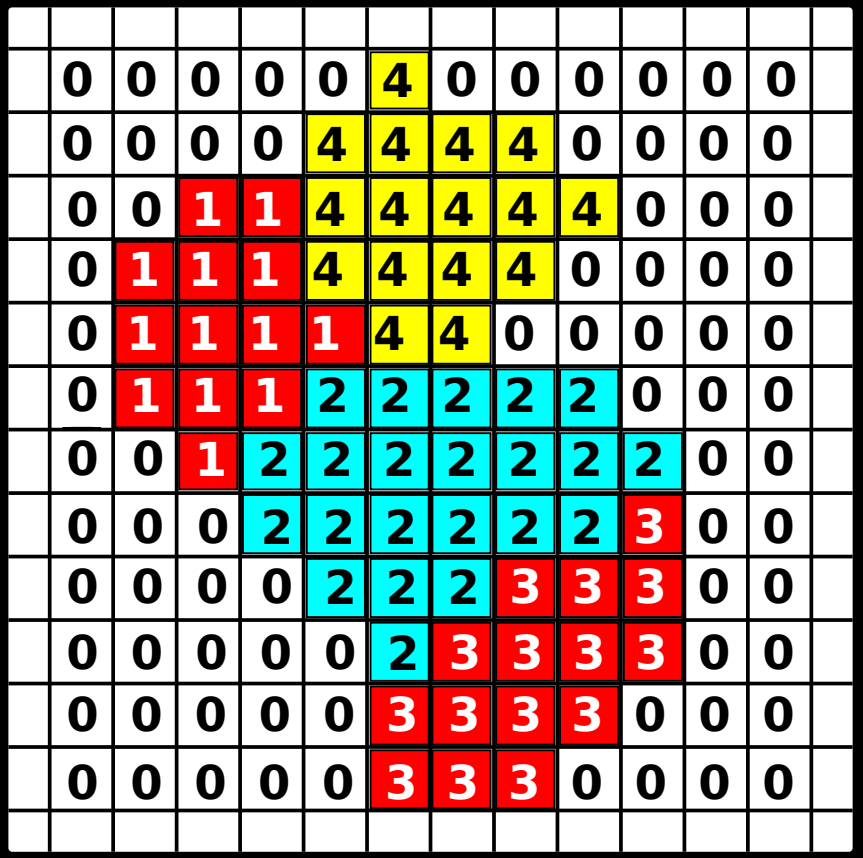
Dynamics due to energy minimisation and random fluctuations
The Hamiltonian, H, describes the total energy of the system
Monte Carlo step: consider for each pixel whether a neighbour will copy into it: probability determined by change in H

$$P_{1->2} = \begin{cases} 1, & \text{if } \Delta H \leq 0. \\ e^{\frac{-\Delta H}{T}}, & \text{if } \Delta H > 0. \end{cases} \quad (1)$$





The energies in basic CPM



intracellular pressure: deviations from resting volume
energy from the interface between cells: adhesion-driven membrane tension

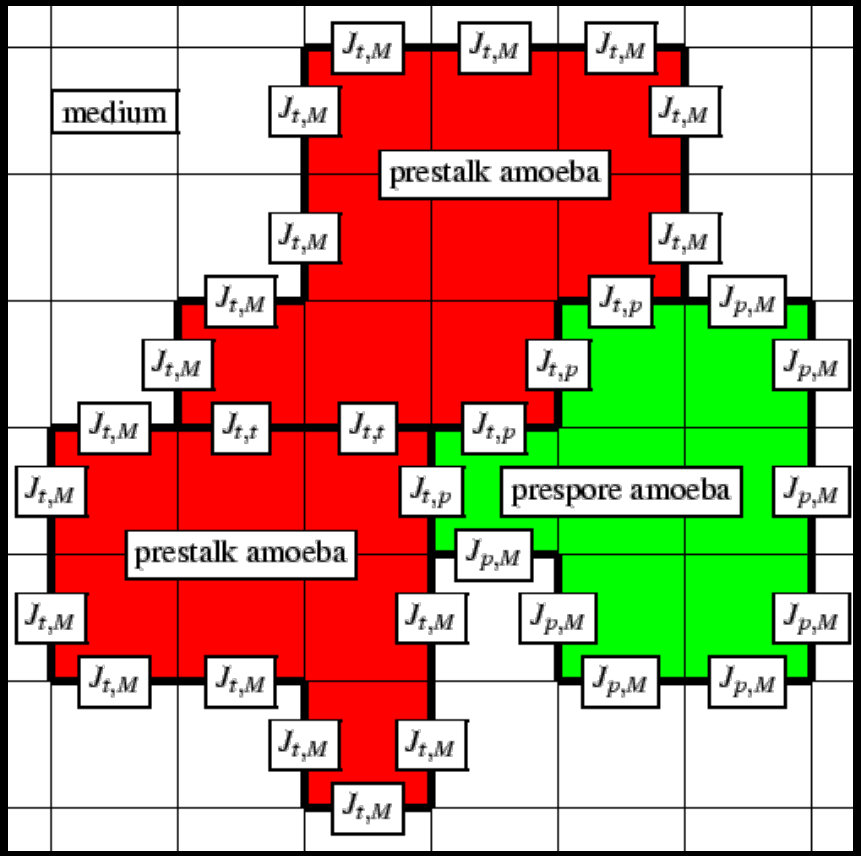
Capturing cell volume preservation in CPM

$$H = \lambda(a - A)^2$$

For all cells:

$$H = \sum_{\sigma} \lambda(a_{\sigma} - A_{\tau(\sigma)})^2$$

Capturing adhesive cell interactions in CPM



Whether cells adhere depends on the interaction energy J, defined per unit contact length.

J values are typically defined between cell types

touching medium also has an associated energy

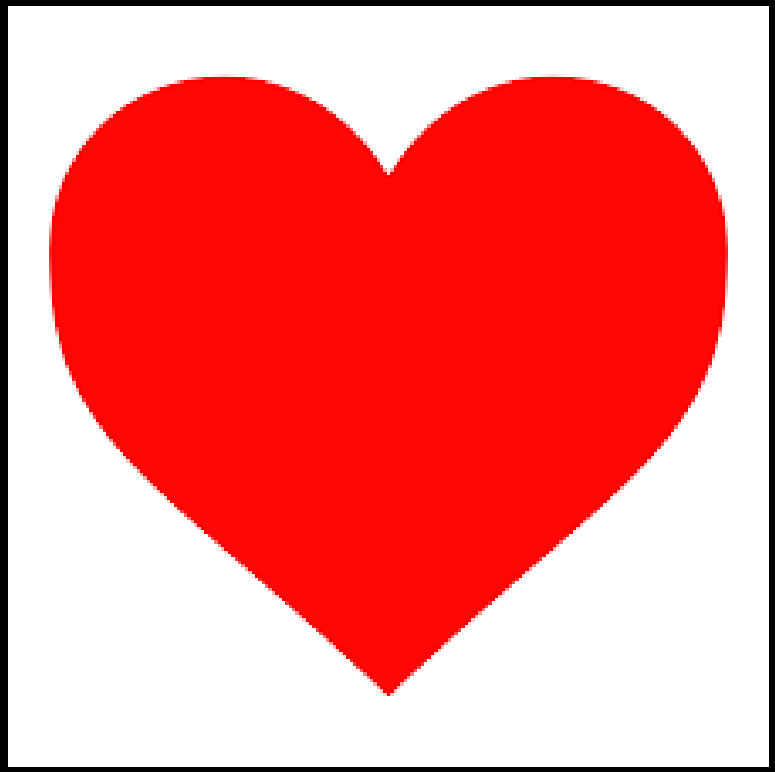
Capturing adhesive cell interactions in CPM

$$H = \sum_{\sigma} \lambda (a_\sigma - A_{\tau(\sigma)})^2 + \sum_{all\ \sigma,\sigma'} \frac{J_{\sigma,\sigma'}}{2} + \sum_{all\ \sigma,medium} J_{\sigma,medium} \quad (2)$$

To stick or not to stick

$J_{cell,med} < J_{cell,cell}$

$J_{cell,med} > J_{cell,cell}$



Energy minimisation leads to ball shape of entire tissue

Differential adhesion hypothesis

Hypothesis: tissues behave like immiscible fluids
How to test this with CPM?

Commands

```
sudo dpkg-reconfigure
keyboard-configuration
```

copy directory from USB stick to your home directory

```
cd practicum
evince exercises.pdf
```

Before starting the exercises:

```
cd pkgs
sudo dpkg -i *.deb
```
(this may take some time)

```
cd ../cpmcode
make
```

to run code:

```
./bin/CPM -d DIRNAME -s SEED parfile.cfg
```