Modeling tissues: numerical simulations and continuum mechanics

Part II - Numerical Simulations

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A rough taxonomy of tissue models

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This courses relies a lot on Carlos Tamulonis' PhD Thesis (2013)

Population dynamics

Population dynamics

- Only concerned with $N(t)$
- Focus on **signaling** and growth / death rates
- Main use is **mathematical oncology**: predict cancer growth in response to treatment

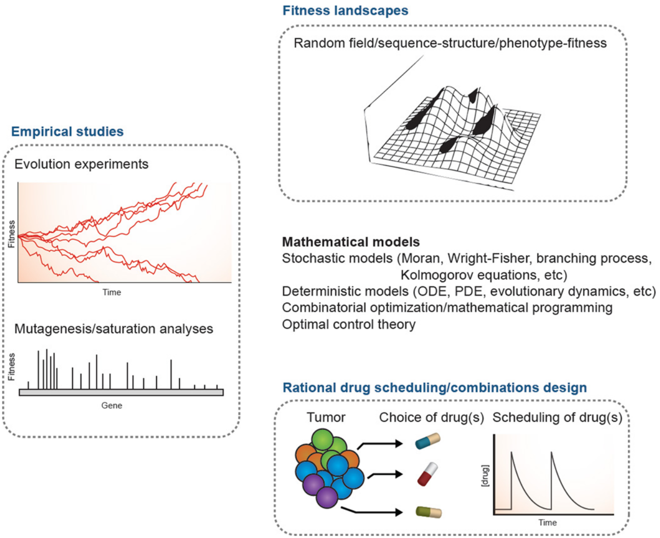


Figure 1: (Zhao, Hemann, and Lauffenburger 2016)

Agent based modelling

Agent based modelling

- Cells are **agents**: they *act*
- Follow each cell behavior
- Broad range of problems:
  - cancer
  - morphogenesis

Lattice based models

Lattice based models

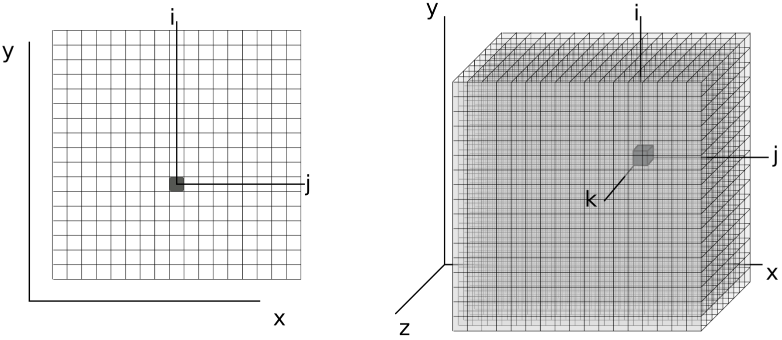


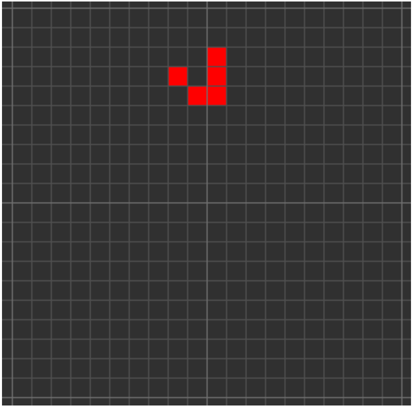
Figure 2: Discrete space in 2 and 3D

Game of life

Game of life

(James Conway)

- Not really cells, but Cellular Automata
- Classical 'emergent behavior' system



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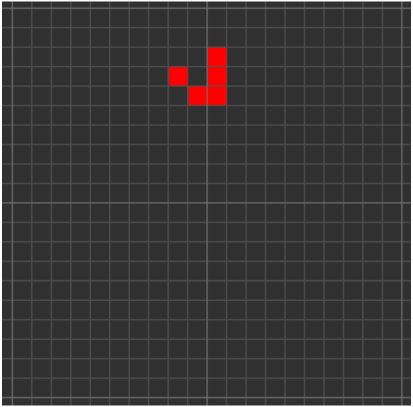

Figure 3: Game of life

Follow this link for a fun example of cellular automata

The Graner Glazier Hogeweg model

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- The world is a fixed grid
- Each cell α occupies a set of pixels
- Pixels at the interface can swap cells

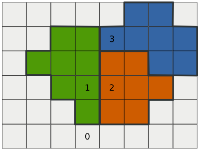

Figure 4: step n

The Modified Metropolis Algorithm

The behavior is governed by the definition of a **Hamiltonian** H governing the energy of the cells

Changes follow a simple local algorithm:

1. Choose randomly a site (i, j)

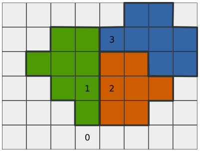

Figure 5: step n

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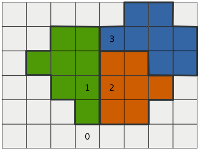

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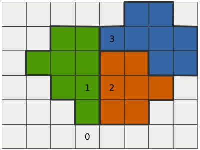

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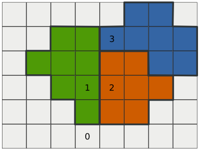

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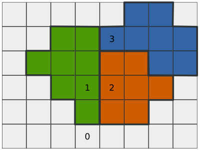

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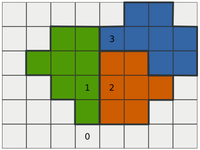

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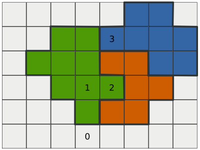

Figure 6: step n+1

Cellular Potts Model Hamiltonian

Now the whole game is now to define the Hamiltonian to better reflect our problem!

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The simplest model: volume conservation and adhesion:

$$
\begin{aligned}
H &= H_V + H_i \\
H_V &= \frac{\lambda}{2} \sum_{\alpha} (V_\alpha - V_0)^2 \\
H_i &= \sum_{ij,i'j'} J(\tau(ij), \tau(i'j'))
\end{aligned}
$$

$\tau(ij)$ type of cell at ij

$J(\tau(ij), \tau(i'j'))$: bond energy

Cell sorting

A classical problem:
2 cell types $(1,2)$ — 0 is the medium

$$
\begin{aligned}
J(1,1) &= 0 \\
J(1,1) &= 1 \\
J(2,2) &= 8 \\
J(2,1) &= 16 \\
J(1,0) &= J(2,0) = 32
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Cells prefer their own kind, 1 more than 2

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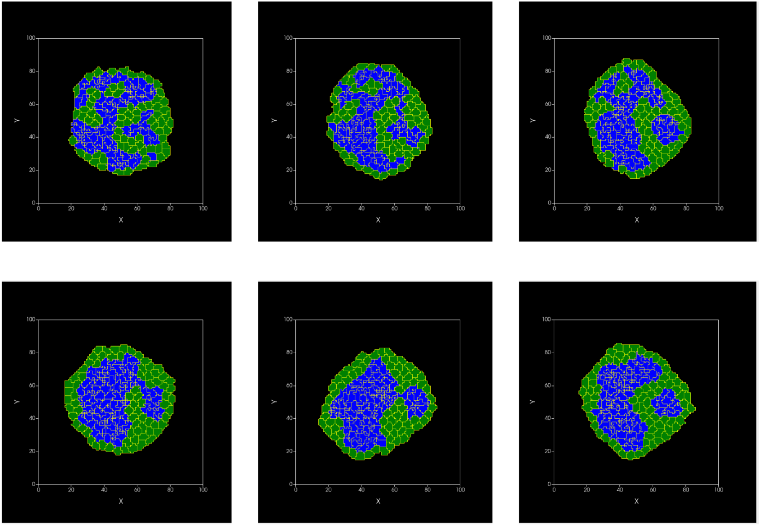

Extending the CPM: the example of Chemotaxis

Existing Software

- Chaste
- CompuCell3D

Cells as spheres

The work of Dirk Drasdo et al.

JF. Joanny

PhysiCell (Mathematical Oncology)

Cells as polygons

Topology of epithelium

Voronoï tessalation (Honda et al.)

Topology changes in 2D & 3D

Active vertex model

Rosettes

Mechanical Model formulations

Work by Farhadifar et al.

Work by Lisa Manning et al.

Towards rheological models

Existing implementations

Zhao, Boyang, Michael T. Hemann, and Douglas A. Lauffenburger. 2016. "Modeling Tumor Clonal Evolution for Drug Combinations Design." *Trends Cancer* 2 (3): 144–58. https://doi.org/10.1016/j.trecan.2016.02.001.