

Modeling tissues: numerical simulations and continuum mechanics

Part II - Numerical Simulations

Guillaume Gay, CENTURI multi-engineering platform, Marseille

Abstract

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In this second part of the course, we will go over the various methods used to simulate tissues.

We will start by showing a rough taxonomy of cell models in general and we'll briefly discuss the general framework of agent-based modelling. Then we will see in some details the three big classes of tissue modeling strategies:

1. Lattice based models rely on a discretized space to simulate cells. Each cell here occupies a set of pixels, and the physics of the system is solved locally. Those models are adapted to rapid assessment of tissue dynamics with mixed cell types, proliferation and differentiation models.
2. Cell-center based models. Here each cell is an individual sphere (maybe deformable) interacting in free space with its immediate neighbours. This class of model is adapted to problems in cancer biology, involving high cell numbers.
3. Vertex-based models. Here cells are delimited by polygons or polyhedron, and the physics is applied at the polygon vertices. This class of models is widely used for morphogenesis modeling.

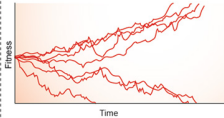
A rough taxonomy of tissue models

Population dynamics

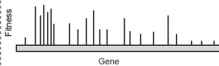
- ▶ Only concerned with $N(t)$
- ▶ Focus on **signaling** and growth / death rates
- ▶ Main use is **mathematical oncology**: predict cancer growth in response to treatment

Empirical studies

Evolution experiments

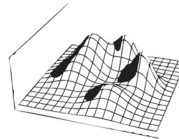


Mutagenesis/saturation analyses



Fitness landscapes

Random field/sequence-structure/phenotype-fitness



Mathematical models

Stochastic models (Moran, Wright-Fisher, branching process, Kolmogorov equations, etc)

Deterministic models (ODE, PDE, evolutionary dynamics, etc)

Combinatorial optimization/mathematical programming

Optimal control theory

Rational drug scheduling/combinations design

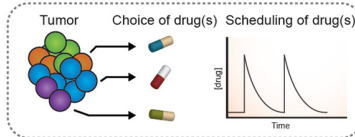


Figure 1: (Zhao, Hemann, and Lauffenburger 2016)

Agent based modelling

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

Lattice based models

Lattice based models

Models are defined on a fixed grid

Game of life

(James Conway)

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

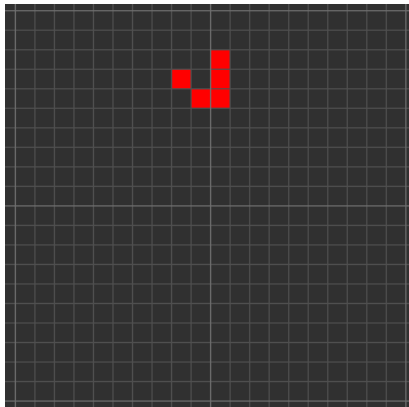


Figure 2: Game of life

The Graner Glazier Hogeweg model

The Modified Metropolis Algorithm

Cellular Potts Model Hamiltonian

Extending the CPM: the example of Chemotaxis

Existing Software

Cells as spheres

The work of Dirk Drasdo et al.

JF. Joanny

PhysiCell (Mathematical Oncology)

Cells as polygons

Topology of epithelium

Voronoi 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>.