Mathematics and biomodelling of cellular competition

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Background

- Bachelor's and master's degree in Biopharmaceutical Sciences at Leiden University
- Internships at the laboratories of LACDR, LUMC and DKFZ
- Courses in biology, chemistry, pharmacology, but also mathematical biology
- Now PhD at Mathematical Institute of Leiden University in Mathematical Pharmacology

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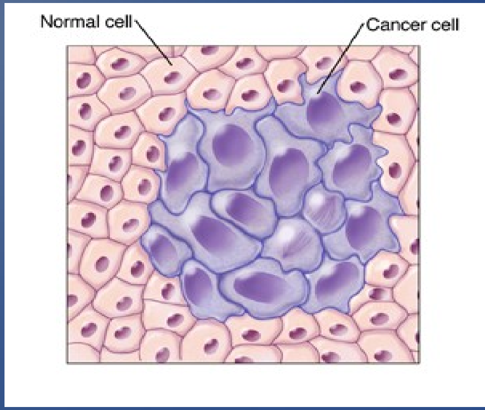
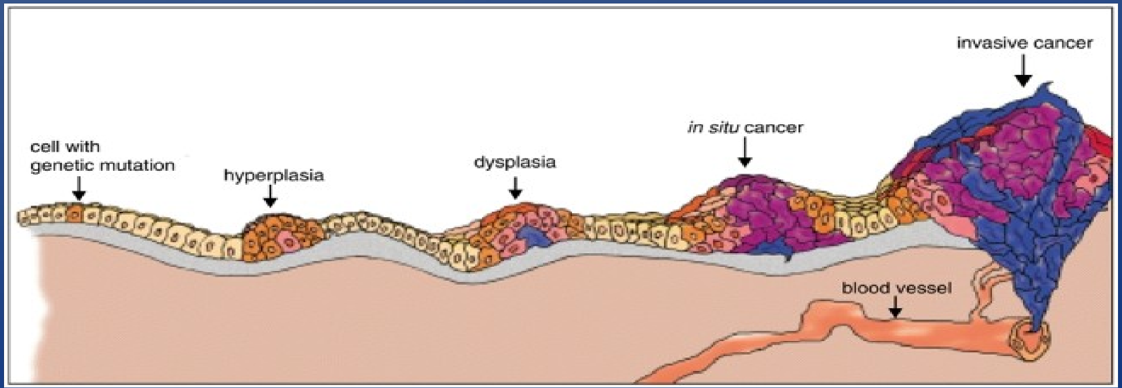
Modelling cancer cell competition

- Cancer cells in homeostatic tissue
- Which physical properties make one cell type take over the other cell type?

Main parameters of interest:
- Cellular adhesion
- Cellular compressibility
- Cellular flexibility





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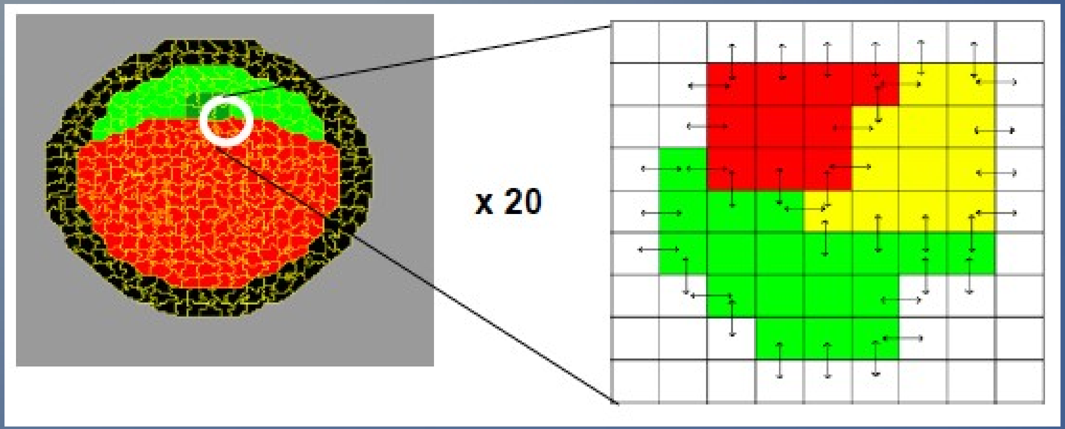
Stochastic vs deterministic model

- **Stochastic model:**
  - Cellular Potts model
  - *Chance* to get different properties changes by adjusting the parameters
  - Outcome differs per simulation
  - Model behavior of individual cells

- **Deterministic model:**
  - Ordinary Differential Equation-based model
  - Outcome depends on initial conditions
  - Outcome is fixed
  - Model cell-type as a whole

Cellular Potts/Glazier-Graner-Hogeweg Model

Monte Carlo Simulation



1 MCS

Each MCS:

$$P(\sigma(\mathbf{x}) \to \sigma(\mathbf{x}'))(t) = \begin{cases} e^{-\Delta H|_{\sigma(\mathbf{x})\to\sigma(\mathbf{x}')}/T} & \Delta H|_{\sigma(\mathbf{x})\to\sigma(\mathbf{x}')} > 0\,; \\ 1 & \Delta H|_{\sigma(\mathbf{x})\to\sigma(\mathbf{x}')} \le 0\,, \end{cases}$$

General formula:

$$H = \sum_{i,j \text{ neighbors}} J\left(\tau(\sigma(i)),\tau(\sigma(j))\right)\left(1-\delta(\sigma(i),\sigma(j))\right) + \sum_i \lambda_{\text{volume}}[V(\sigma(i)) - V_{\text{target}}(\sigma(i))]^2$$

Modelled with CompuCell3D software (Python, XML-based)

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The ODE Model

Two cellular populations (x and y) are simulated in which the growth of each population is modeled.

After rescaling and reducing parameters:

$$\frac{dx}{dt} = x(1 - x - y)$$

$$\frac{dy}{dt} = Ry(1 - \frac{\alpha_2}{\beta_1}y - \frac{\beta_2}{\alpha_1}x)$$

$$c = \frac{\alpha_2}{\beta_1} \text{ and } d = \frac{\beta_2}{\alpha_1}$$

In which:
R = growth rate (birth – death) of y relative to x
α_1 = related to carrying capacity and fitness x
α_2 = related to carrying capacity and fitness y
β_1 = influence of y on x
β_2 = influence of x on y

Essentially only 3 parameters: R, c and d

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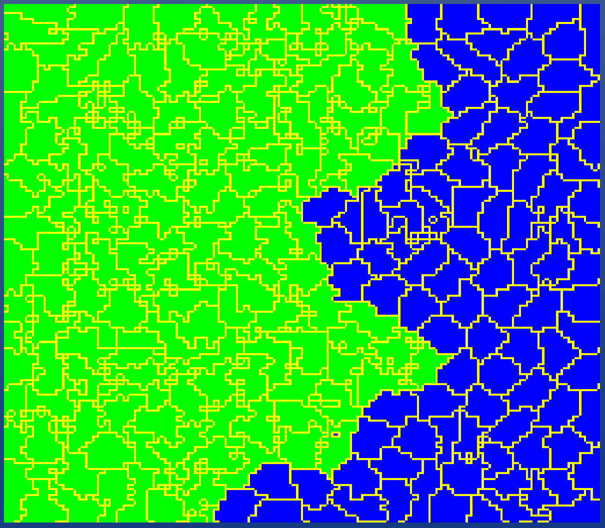
(Some) results

- Increasing adhesion of one cell to cells of its own type increased cellular growth.

- However, the effect decreased when adhesion energies were too strong, as cells tended to stick together instead of interacting with the other cells

- Cells with higher adhesion showed an higher surface area and seemed more flexible

- Nice interplay between adhesion, volume and compressibility



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