Modelling competition between cancer cells and healthy cells

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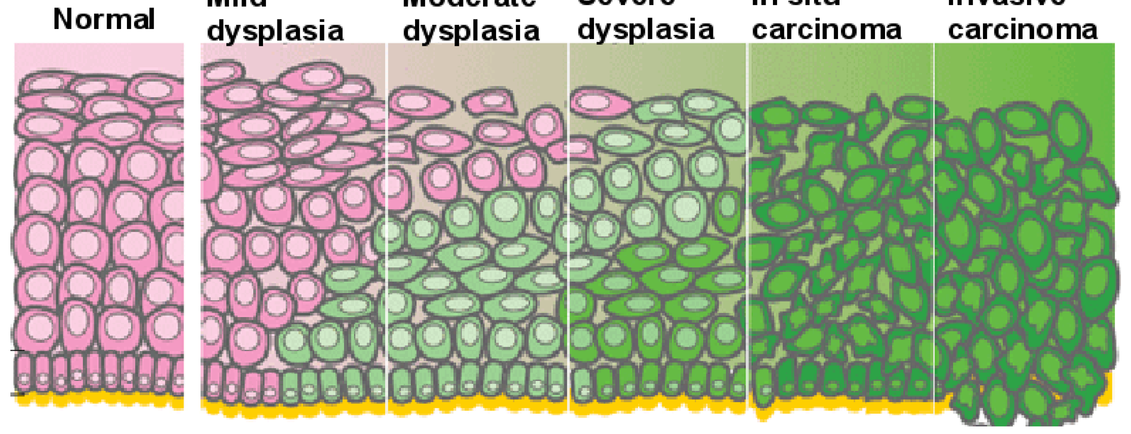
Background

- Study **cancer** cells and **normal** cells in one tissue
- At some point cancer cells may take over the normal cells by **competition**
- Question: which physical **properties** of cells influence competition between cell types?
- Highly relevant for **initial stages** of cancer
- Main **properties** of interest:
  - Cellular **rigidity** (λ)
  - Cellular **adhesion** (J):
    Homogeneous ($J_{g,g}$): to cells of the same type
    Heterogeneous ($J_{g,b}$): to cells of the other type
    A low J means high adhesion

Aim:

To gain insight in which physical **properties** of cells influence **competition** and make one cell type take over at cost of the other



Source: Gius et al (2007). *Cancer Res.* **67**: 7113:23

Approach

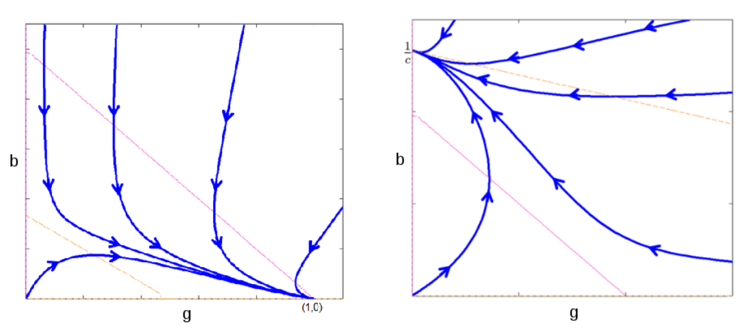
Use **two** different **models**:
1. Model of ODEs
2. Cellular Potts Model (CPM)

These models are used for:
1. **Comparison**: advantages of the more advanced CPM over the simpler ODE model
2. **Insight**: essential parameters may be detectable by both models

Characteristics of both models:
- Two cell types (50% green and 50% blue initially)
- Individual cells or cells as a population **grow**, **die** and **compete** for space.
- The main properties of interest are defined by parameters that differ between cell types

Results - ODE Model

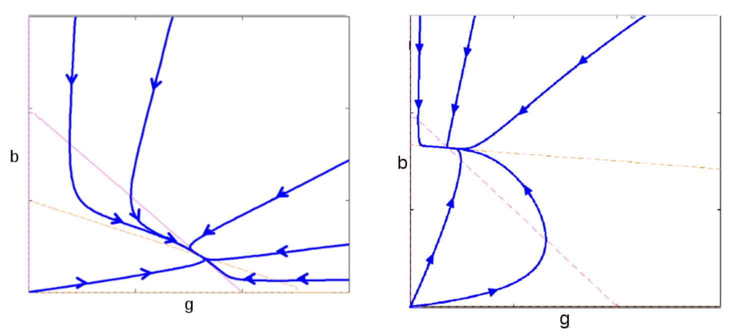
Cellular rigidity



Cellular rigidity ↑:
- $\beta_1 < \alpha_2 = \alpha_1 < \beta_2$
- Green wins (Left)

Cellular rigidity ↓:
- $\beta_1 > \alpha_2 = \alpha_1 > \beta_2$
- Blue wins (Right)

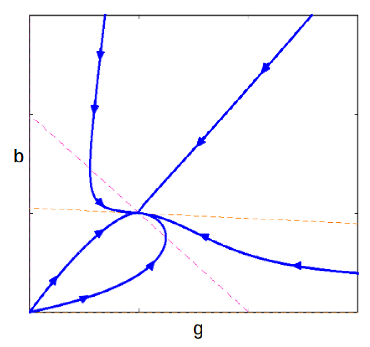
Homogeneous adhesion



Homogeneous adhesion ↑:
- $\alpha_1 > \alpha_2 > \beta_1 = \beta_2$
- Coexistence (Left)

Homogeneous adhesion ↓:
- $\alpha_2 > \alpha_1 < \beta_1 = \beta_2$
- Coexistence (Right)

Heterogeneous adhesion

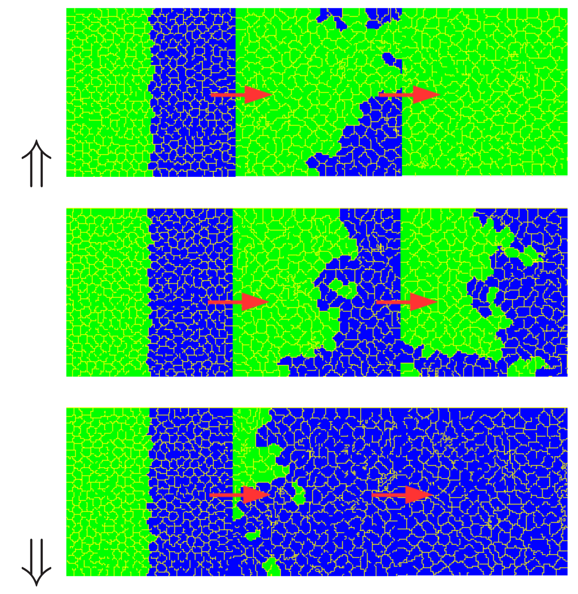


Heterogeneous adhesion ↑:
- $\alpha_1 = \alpha_2 > \beta_1 = \beta_2$
- Coexistence

Heterogeneous adhesion ↓:
- $\alpha_1 = \alpha_2 > \beta_1 = \beta_2$
- Coexistence

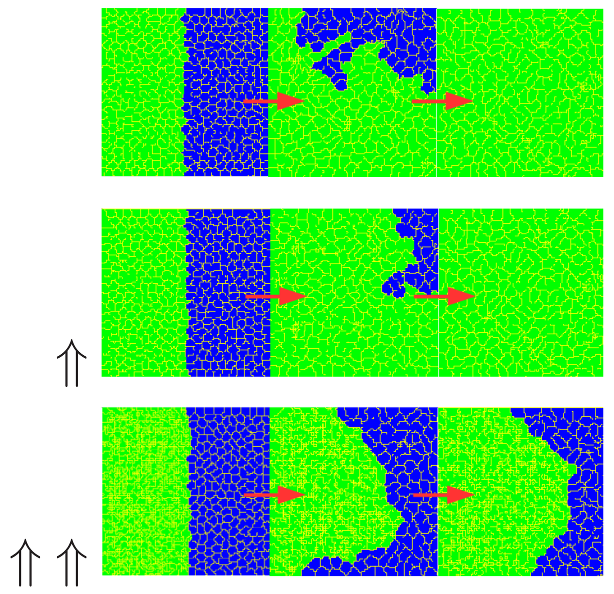
Results - Cellular Potts Model - Time Lapse

Cellular rigidity ↑↓



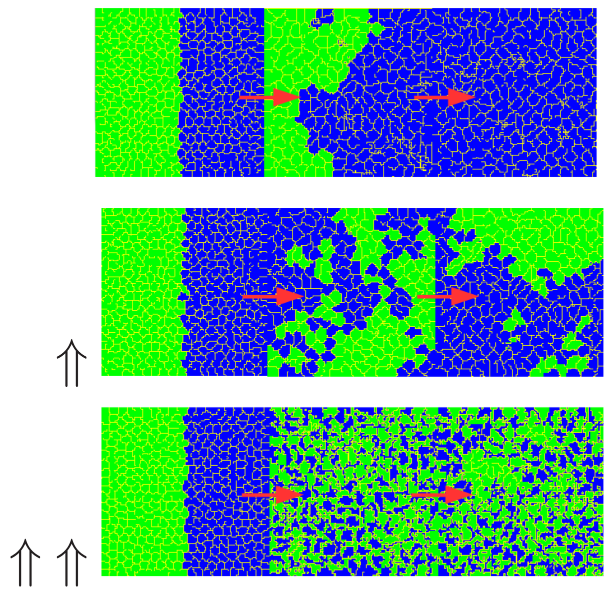
Timesteps 0 2000 5000

Homogeneous adhesion ↑



Timesteps 0 2*10 [4] 1*10[5]

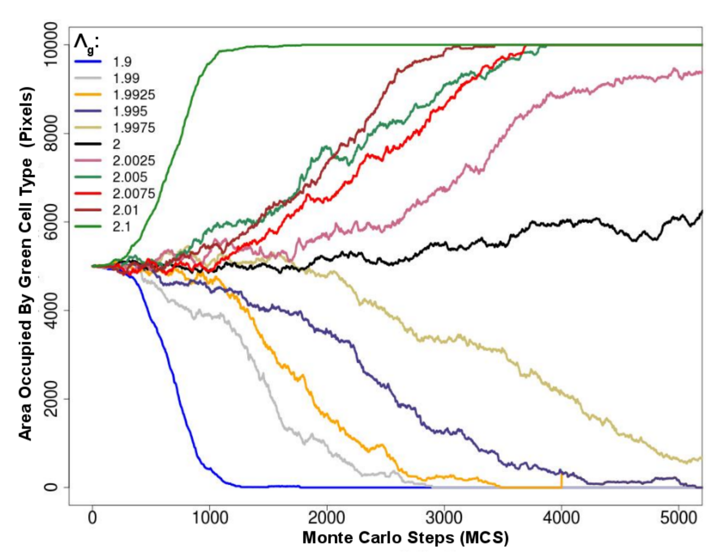
Heterogeneous adhesion ↑



Timesteps 0 2*10 [4] 1*10[5]

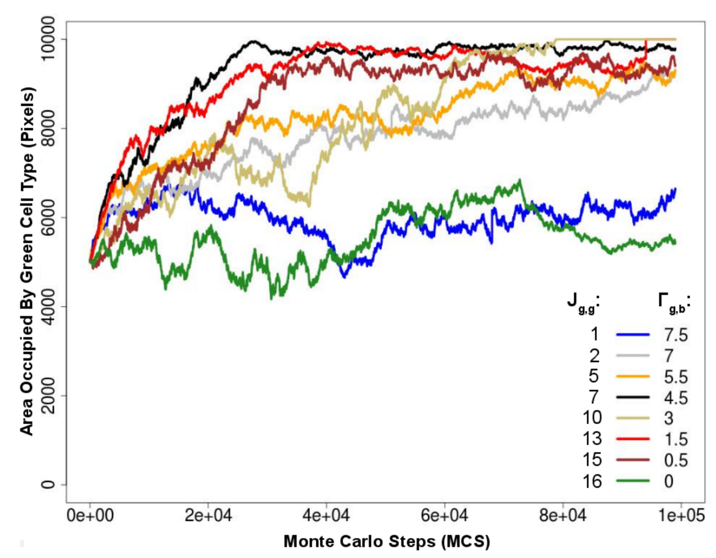
Results - Cellular Potts Model - Graphs

Cellular rigidity



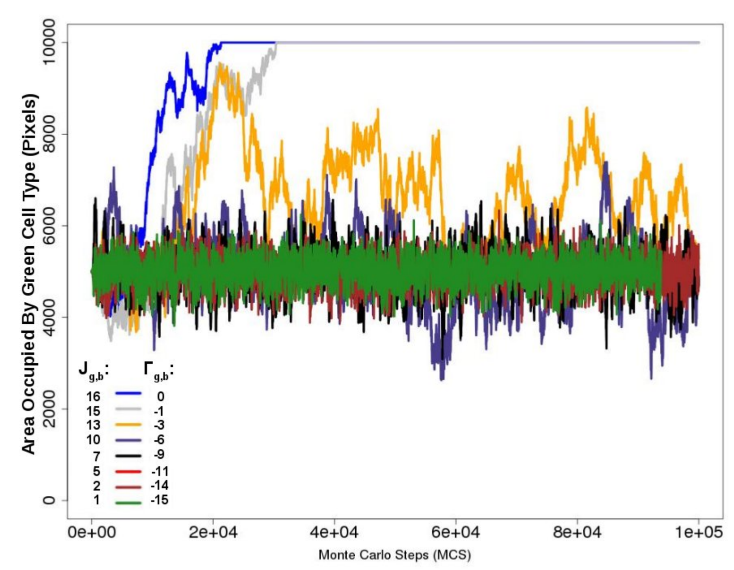
Most rigid cell type wins.

Homogeneous adhesion



(Not too) low $J_{g,g}$ favoured

Heterogeneous adhesion



Low $J_{g,b}$ inhibits the competition

Graphs represent the area occupied by the green cell type over time for different parameters.

ODE Model

- Model of Ordinary Differential Equations(ODEs)
- Deterministic
- Population as a whole (g and b)
- Populations **grow**, **shrink** and **compete** with eachother.

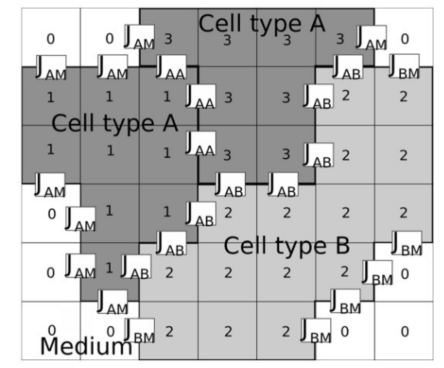
Lotka-Volterra based model with logistic growth and interaction term.

$$\frac{dg}{d\tau} = \Gamma_1(1 - \alpha_1 g - \beta_1 b)g$$
$$\frac{db}{d\tau} = \Gamma_2(1 - \alpha_2 b - \beta_2 g)b.$$

α = how much are cells hindered by own cell type
β = how much are cells hindered by other cell type

Cellular Potts Model

- Stochastic: as in biological systems
- Cell-based: cells modelled as set pixels on a grid
- Individual cells grow, divide, die and compete
- Several dimensions: volume, shape and rigidity of individual cells can be incorporated



Source: Voss-Böhme A (2012). *PLoS ONE* 7(9): e42852

- Energy (H) is minimized
- $H = H_{\text{adhesion}} + H_{\text{volume}}$

Conclusions

- Both models show that increasing **rigidity** of cells is an advantage in cellular competition
- Increasing **homogeneous adhesion** is generally a competitive advantage
- However, when homogeneous adhesion is **too strong**, competition is hindered because the two different cell types hardly **interact**
- Increasing **heterogeneous adhesion** inhibits the **coherence** of cells of the same type and thereby also hinders competition
- Both types of adhesion are important to induce and to win the competition.