Tissue Competition: Role of Cross-adhesion

Tobias Büscher[1], **Nirmalendu Ganai**[1,2], **Gerhard Gompper**[1] **and Jens Elgeti**[1]

[1]Theoretical Soft Matter and Biophysics, Institute of Complex Systems, Forschungszentrum Jülich, 52428 Jülich, Germany

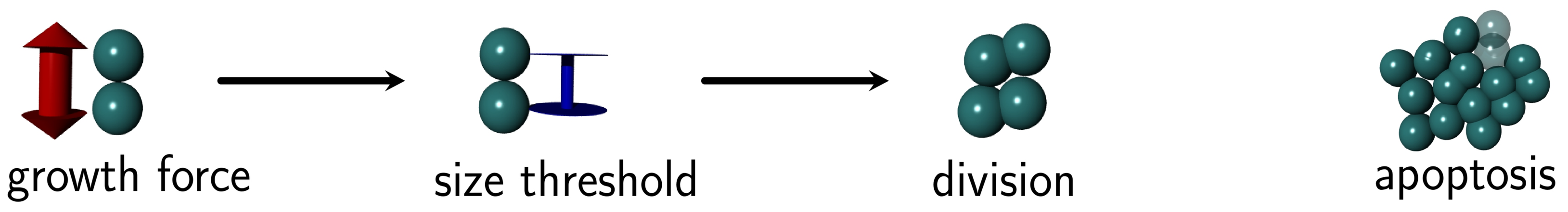
[2]Department of Physics, Nabadwip Vidyasagar College, Nabadwip, Nadia 741302, India

E-mail: t.buescher@fz-juelich.de

Introduction

During growth, a tissue changes its volume. The conjugate force to this is, in physical terms, a pressure. Thus, the tissue exerts mechanical pressure onto its surrounding. In turn, mechanical stress plays a role in growth, displayed by a reduce in proliferation rate of a cancer cell line when grown under pressure [2]. During cancer development a competition for space between the healthy host tissue and the malignant cells takes place. Mechanical forces can drive this competition. In the simplest case, the tissue with the higher homeostatic pressure, i.e. the pressure at which division and apoptosis balance, wins the competition [1-4].
Here, we focus on the influence of the cross adhesion between the two tissues. A cross adhesion lower than the self adhesion results in an enhanced growth rate at the interface, which can stabilize coexisting phases between the two tissues.

Simulation model



- Cells represented by two point particles
- Particles constituting a cell repel each other by a growth force

$$\mathbf{F}^g_{ij} = \frac{G}{(r_{ij}+r_0)^2}\hat{\mathbf{r}}_{ij}$$

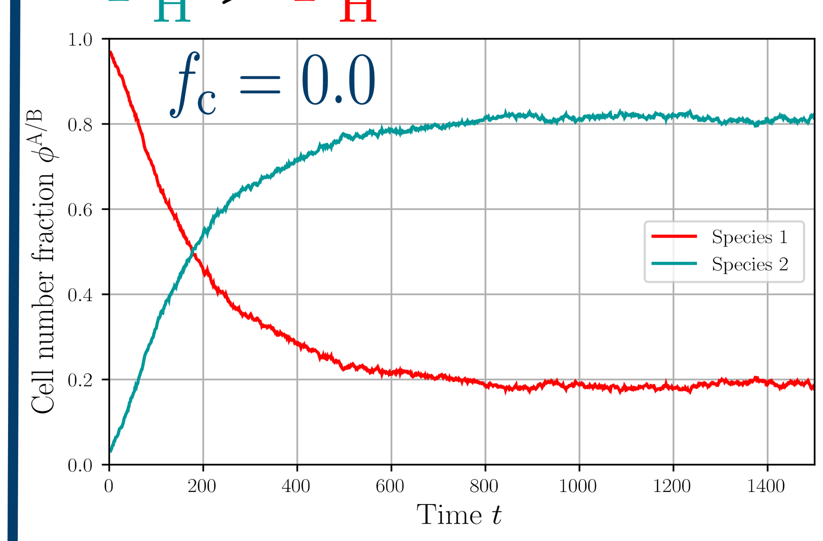
- Division when distance between the particles reaches the size threshold
- Apoptosis is implemented by removing cells at constant rate
- Volume exclusion force and cell-cell adhesion

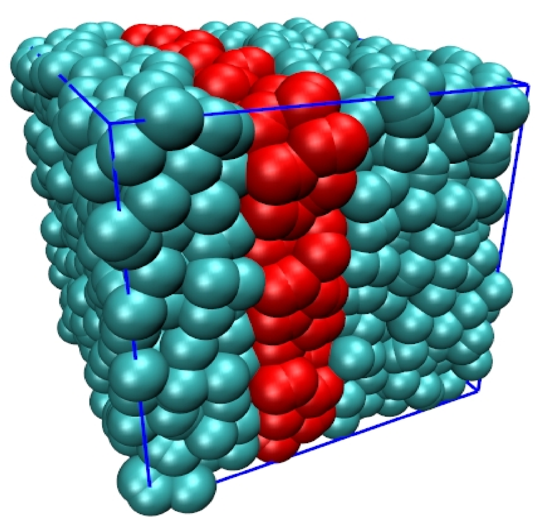
$$\mathbf{F}^v_{ij} = f_0\left(\frac{R^5_{\mathrm{pp}}}{r^5_{ij}} - 1\right)\hat{\mathbf{r}}_{ij} \text{ and } \mathbf{F}^a_{ij} = -f_1\hat{\mathbf{r}}_{ij}$$

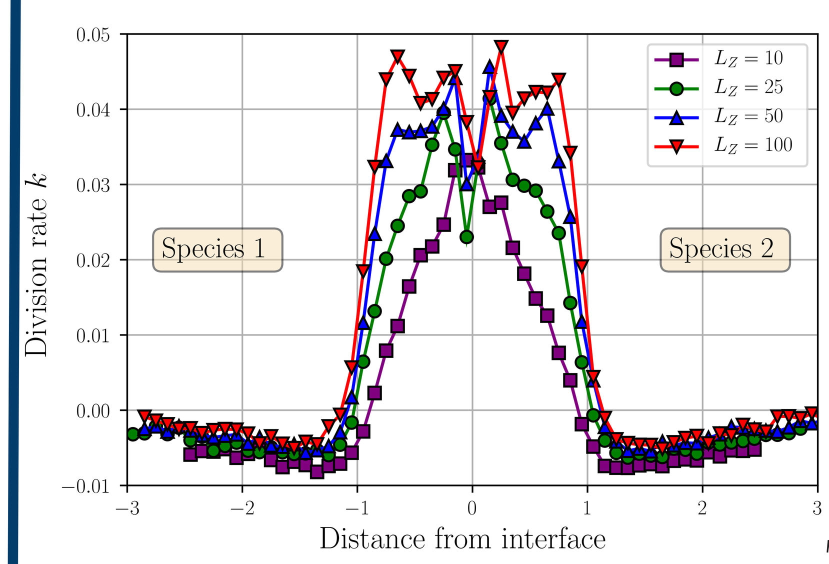
- Dissipative particle dynamics (DPD) -type thermostat accounts for dissipation and random fluctuations

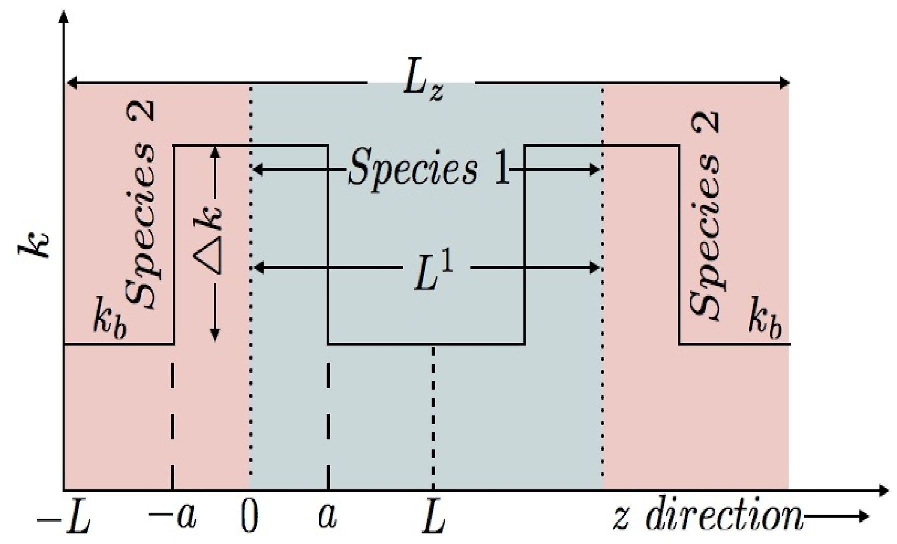
Enhanced growth at interface

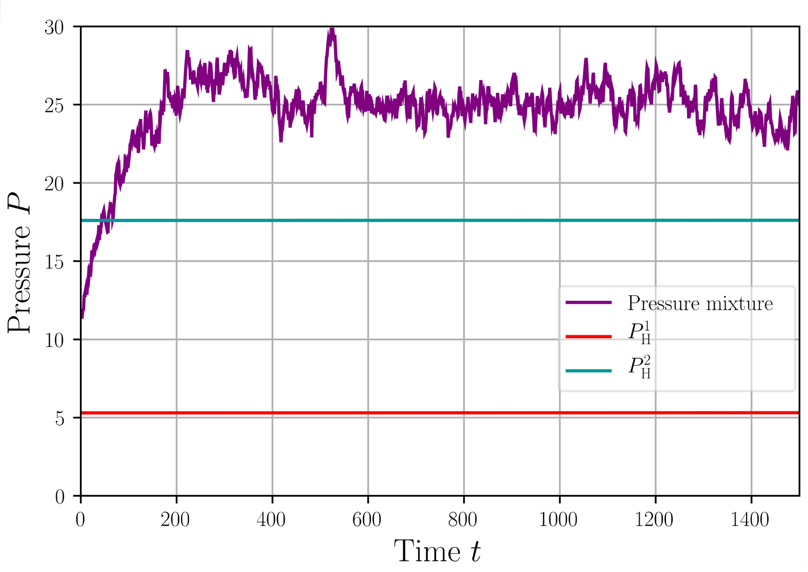
$P^2_{\mathrm{H}} > P^1_{\mathrm{H}}$











Two rate model:

$$\frac{\partial\phi^i}{\partial t} = k^i_{\mathrm{b}}\phi^i_{\mathrm{b}} + k^i_{\mathrm{s}}\phi^i_{\mathrm{s}} = k^i_{\mathrm{b}}\phi^i + \Delta k^i\phi^i_{\mathrm{s}}$$

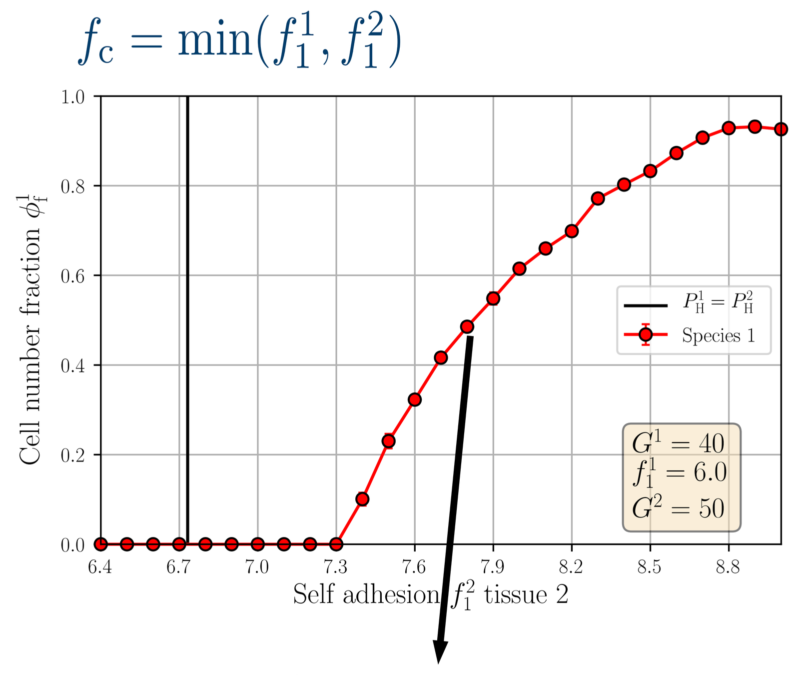
$$k^i_{\mathrm{b}} = \gamma^i(P^i_{\mathrm{H}} - P)$$

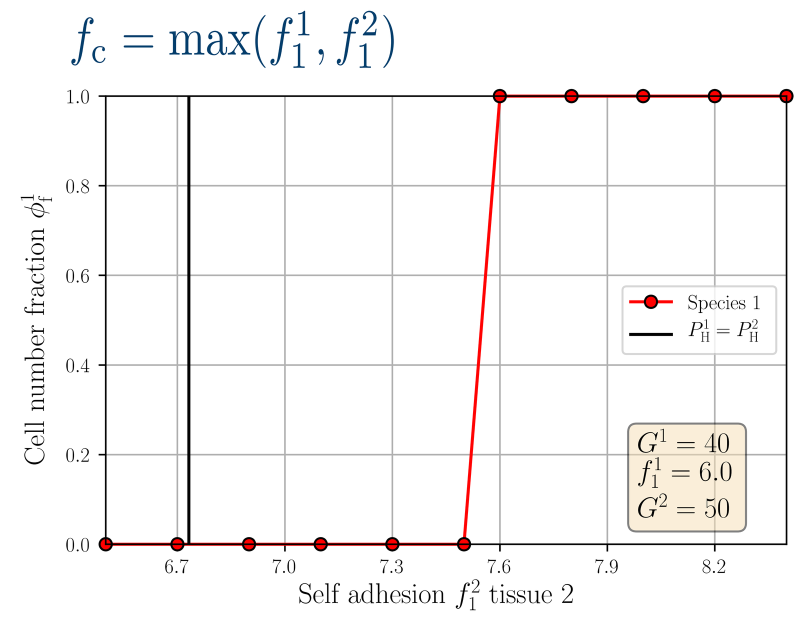
$$\Delta k^i = \Delta k^i_0 + \Delta k^i_1(P^i_{\mathrm{H}} - P)$$

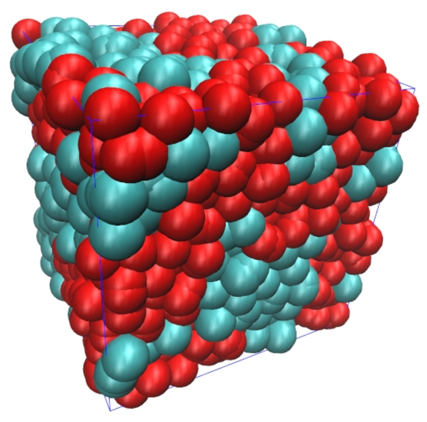
$$P^i = P^i_{\mathrm{H}} + \frac{2a\Delta k^i_0}{2a\Delta k^i_1 + \gamma^i L^i}$$

Flat interface $\Rightarrow P^1 = P^2$

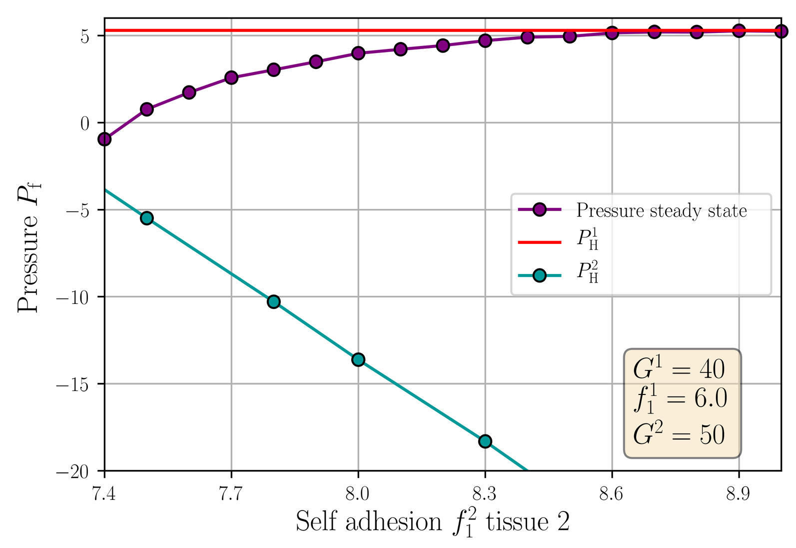
Role of cross-adhesion







- $f_c \approx f^i_1$ causes mixed state
- Negative $\Delta k^i(\sim f^i_1 - f_c)$ yields unstable state
- Tissue with smaller P_{H} can win competition due to higher self adhesion $\Rightarrow$ harder to push away



Two rate model for mixed state:

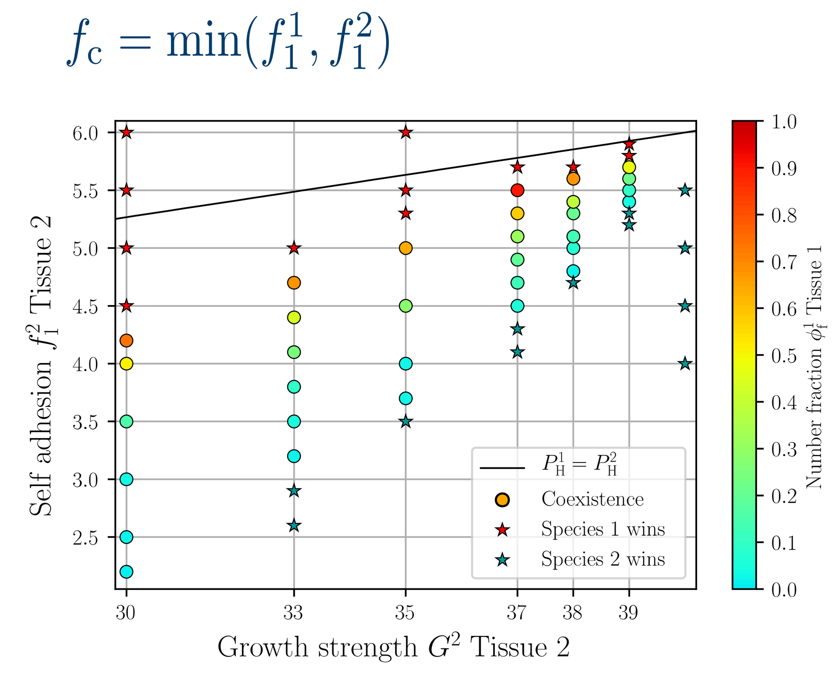
$$\frac{\partial\phi^i}{\partial t} = k^i_{\mathrm{b}}\phi^i + \Delta k^i\phi^i_{\mathrm{s}};\ k^i_{\mathrm{b}} = \gamma^i(P^i_{\mathrm{H}} - P)$$

$$\phi_{\mathrm{s}} \sim \phi^1\phi^2 = c\phi^1(1-\phi^1);\ \gamma^1 = \gamma^2 := \gamma$$

$$P = P^2_{\mathrm{H}} - \Delta P_{\mathrm{H}}\phi^1 + \frac{c\Delta k^1 + c\Delta k^2}{\gamma}\phi^1(1-\phi^1)$$

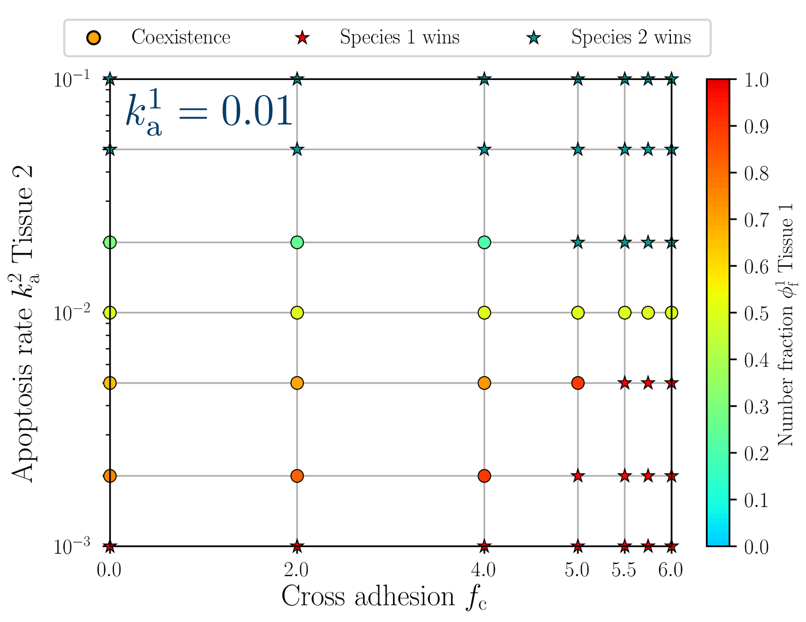
Fixed point: $\phi_{\mathrm{f}} = \frac{-\gamma\Delta P_{\mathrm{H}} + c\Delta k^1}{c\Delta k^1 + c\Delta k^2}$

Single cell mutation



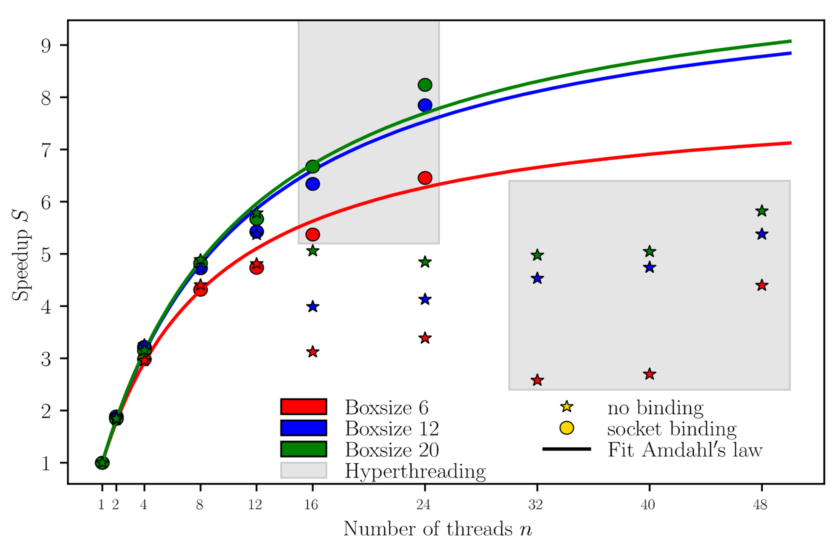
- Change parameters of a single cell (mutation)
- Lower self and cross adhesion, most cancer cells express less adhesion proteins
- Evolution to mixed state
- Chance of mutated species to die out before reaching steady state

Different apoptosis rate



- Apoptosis rate does not change homeostatic pressure
- Interfacial effects stabilize the competition (cross adhesion lower than self adhesion)
- Shift towards the tissue with lower apoptosis rate in cell number fraction

Scaling behaviour



- OpenMP parallelised code
- Memory-wise small simulations
- Communication between sockets causes overhead
- Running one simulation bound to each socket most efficient
- Hyperthreading gives up to 40 % speed up

References

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