Cell organization in soft media due to active mechanosensing : a review

MECHANICS OF THE CELL, PHY9805

YASAMIN MODABBER

Mechanosensing process in cells

Adhering cells can sense the mechanical properties of their local environment by actively pulling on it, and they use the information to position and orient themselves

They align:

- In the direction of external tensile strain
- Parallel to free and normal to clamped boundaries
- Along other cells to form strings

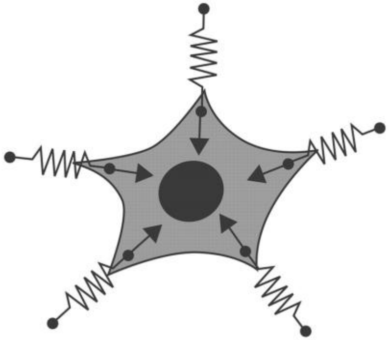
Goal:

Propose an optimization mechanism which finds the optimal orientation and positioning for cells with respect to the **external strain, boundary** and **other cells in the system**

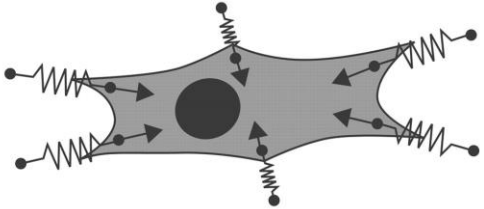
Extraction of Information through contractile motion

Suggested quantity:

- The work the cell has to perform in order to build up a certain level of force against the elastic environment.
- We model the extra-cellular matrix (ECM) using linear elasticity theory.
- $W = \frac{F^2}{2K}$
- $t = \frac{F^2}{2KP}$



Isotropic elasticity



anisotropic elasticity

Source: Bischofs, Ilka & Schwarz, Ulrich. (2003).

Introducing local effective stiffness instead of K

The deformation work required to build up an arbitrary force F is given by

$$W_0 = \frac{1}{2}\int d^3r\, C_{ijkl} u^{\mathrm{c}}_{ij}(\vec{r}) u^{\mathrm{c}}_{kl}(\vec{r}) = \frac{1}{2}\vec{F}\cdot\vec{u}_{\mathrm{c}}(\vec{r}_{\mathrm{c}}),$$

- $C_{ijkl} = Elastic\ constant\ tensor$
- $u_{ij}^{c} = strain\ tensor$
- $u_{i}^{c} = displacment\ tensor$ caused by the cell

In an elastic anisotropic medium w_0 varies with the direction of force application, creating a preferred orientation for cell.

The effect of external strain

The change in work for a prestrained medium is

$$\Delta W = \int d^3 r C_{ijkl} u^{\mathrm{c}}_{ij}(\vec{r}) u^{\mathrm{e}}_{kl}(\vec{r})$$

- $C_{ijkl} = Elastic\ constant\ tensor$
- $u^e_{ij} = tensile\ prestrain$
- $u^e_i = displacment\ tensor\ caused\ by\ external\ strain$

$\Delta W^e = P_{ij} u^e_{ij}(r)$

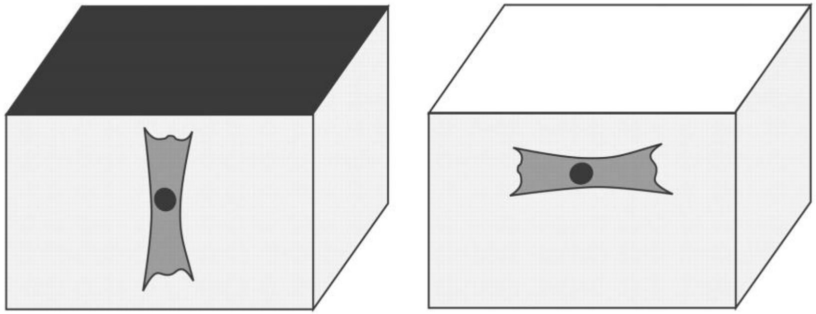
Due to the contractile activity (P_{ij} <0), tensile strain $\left(u^e_{ij} > 0\right)$ is favorable.

The effect of boundary

$$\Delta W^b = \frac{P^2}{Ed^3}\left(a_\nu + b_\nu \cos^2\theta + c_\nu \cos^4\theta\right)$$

- P: dipole strength
- θ: angle of orientation relative to the surface normal
- d: distance from surface
- E: rigidity

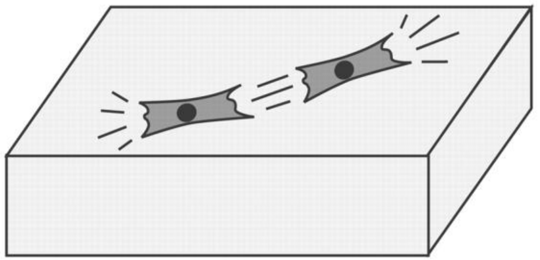
- For a free boundary
  - The coefficients are positive
  - Optimal configuration for $\theta = \frac{\pi}{2}$
- For a clamped boundary
  - The coefficients are negative
  - Optimal configuration for $\theta = 0$



Source: Bischofs, Ilka & Schwarz, Ulrich. (2003).

Cooperative cell effects

- For two interacting cells:
- $$\Delta W^{P_1 P_2} = \frac{P_1 P_2}{E r^3} g_\nu(\theta_1, \theta_2, \theta)$$
- P_1: dipole strength of cell 1
- P_1: dipole strength of cell 1
- r: distance
- E:rigidity



- ΔW is minimum for aligned cells
- Maximal strain stiffening along the axis of contraction
- We have a positive feedback loop which forms a string of cells

Source: Bischofs, Ilka & Schwarz, Ulrich. (2003).

Our optimization model was able to successfully account for cell alignment

- Alignment in the direction of external strain
  => minimizing ΔW^{e}

- Alignment parallel to free and normal to clamped boundaries
  => minimizing ΔW^{b}

- Alignment along other cells
  => minimizing ΔW^{PP}

Importance and Applications

- This model provides an optimization principle that allows us to predict cell organization in soft media.
- It is In excellent agreement with a great number of experiments.

Since cell response to the local rigidity affects the large scale organization of the tissue, a better understanding of the mechanism behind this phenomenon could lead to invaluable applications in tissue engineering, regenerative medicine and cancer therapy.

References

[1] Bischofs, Ilka & Schwarz, Ulrich. (2003). Cell organization in soft media due to active mechanosensing. Proceedings of the National Academy of Sciences of the United States of America. 100. 9274-9. 10.1073/pnas.1233544100.

[2] Bischofs, Ilka B., Samuel A. Safran, U. S. Schwarz Mpi Colloids, Interfaces, Germany, Weizmann Institute, Israel and University of Leipzig. “Elastic interactions of active cells with soft materials.” Physical review. E, Statistical, nonlinear, and soft matter physics 69 2 Pt 1 (2003): 021911 .