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EN.585.743.81.SP25 Modeling Approaches to Cell and Tissue Engineering
Modeling Project
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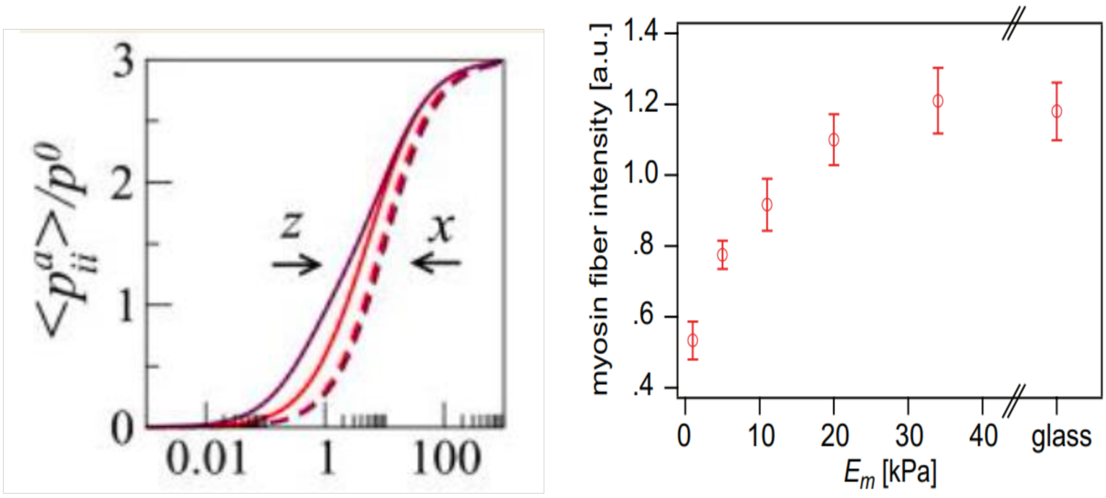
## Introduction

In Lecture 12, the polarization of the stem cell cytoskeleton as a function of the stiffness of ECM is considered. A number of characteristics of cell/ECM interaction, such as the modeling-predicted order parameter [1] (Figure 1(a)) or experiment-estimated myosin fiber intensity [1] (Figure 1(b)) demonstrate an increase–saturation pattern as functions of ECM stiffness. Use the 1-D model where the cell and ECM are presented by the active and elastic springs, respectively [1] (Figure 2) and show that the active force generated by the cell, f$_a$, as a function of the ECM stiffness, has the same increase saturation pattern of behavior.




(a) Normalized order parameter vs. $\frac{E_m}{E_c}$.

(b) Myosin fibre intensity vs. $E_m$.

Figure 1: (a) Order–parameter saturation. (b) Actomyosin-intensity saturation.

## Derivation

We want to show, using the 1D two-spring model of cell and matrix (Figure 2), that the cell's active force $f_a$ satisfies the equation:

$$\frac{f^a}{f^0} = \alpha \, \frac{k_m}{\tilde{k}_c + k_m}$$

Initially, the force balance equation is:

$$k_c(l_c - l_c^R) = k_m(l_m - l_m^R)$$

In the presence of an active force, the force balance becomes:

$$k_c(l_c - l_c^R) = k_m(l_m - l_m^R) + f_a$$

The active force is modeled as:

$$f^a = -\alpha \, k_c(l_c - l_c^R)$$

where $\alpha > 0$ is the cell polarizability parameter. From the spring model, the cellular strain satisfies:

$$\frac{\Delta l_c}{l_c^0} = \frac{\tilde{k}_c}{\tilde{k}_c + k_m} \frac{\Delta l_c^0}{l_c^0}$$

where $\tilde{k}_c = (1+\alpha)k_c$ is the effective active stiffness.

Expanding this:

$$l_c - l_c^0 = \frac{\tilde{k}_c}{\tilde{k}_c + k_m}(-\Delta l_c^0)$$

Thus:

$$\begin{aligned} l_c - l_c^R &= (l_c - l_c^0) + (l_c^0 - l_c^R) \\ &= -\frac{\tilde{k}_c}{\tilde{k}_c + k_m}\Delta l_c^0 + \Delta l_c^0 \\ &= \left(1 - \frac{\tilde{k}_c}{\tilde{k}_c + k_m}\right)\Delta l_c^0 \\ &= \frac{k_m}{\tilde{k}_c + k_m}\Delta l_c^0 \end{aligned}$$

Substituting back into the active force:

$$f^a = -\alpha k_c(l_c - l_c^R) = -\alpha k_c\left(\frac{k_m}{\tilde{k}_c + k_m}\Delta l_c^0\right)$$

Since the baseline force $f^0$ is proportional to $k_c \Delta l_c^0$:

$$f^0 = k_c \Delta l_c^0$$

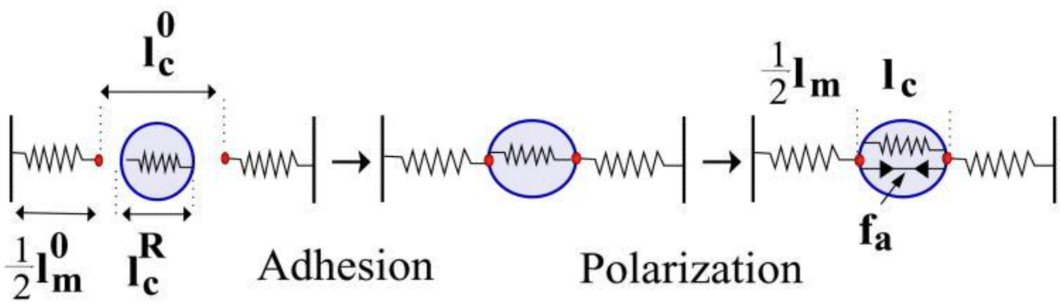
Thus, we have:

$$f^a = -\alpha\,\frac{k_m}{\tilde{k}_c + k_m} f^0$$

Depending on how you define the direction of the active force, we have, finally:

$$\boxed{\frac{f^a}{f^0} = \alpha\,\frac{k_m}{\tilde{k}_c + k_m}}$$

Figure 3




(Zemel et al., 2010 and Lecture 12)

Figure 2: 1D model: active cell spring (stiffness $k_c$) in series with ECM spring (stiffness $k_m$).

## Interpretation

The formal form of anisotropic polarized actomyosin force is:

$$\frac{f^a}{f^0} = \alpha\,\frac{k_m}{\tilde{k}_c + k_m}$$

- $\alpha$: polarizability factor
- $\tilde{k}_c = (1+\alpha)\,k_c$: effective stiffness of the cell
- $k_m$: matrix rigidity
- For very soft matrices ($k_m \ll \tilde{k}_c$):

$$\frac{f^a}{f^0} = \alpha\,\frac{k_m}{\tilde{k}_c + k_m} \quad\longrightarrow\; 0 \quad \text{as } k_m \to 0.$$

  If $k_m \ll \tilde{k}_c$, then $\tilde{k}_c + k_m \approx \tilde{k}_c$ and

$$\frac{f^a}{f^0} \approx \alpha\,\frac{k_m}{\tilde{k}_c} \approx \alpha^*\,k_m \quad\longrightarrow\; 0 \quad \text{as } k_m \to 0.$$

- For very stiff matrices ($k_m \gg \tilde{k}_c$):

$$\frac{f^a}{f^0} = \alpha\,\frac{k_m}{\tilde{k}_c + k_m} \approx \alpha\,\frac{k_m}{k_m} \quad\longrightarrow\; \alpha$$

Thus, the active force grows with matrix stiffness and saturates at a maximum value proportional to $\alpha$.

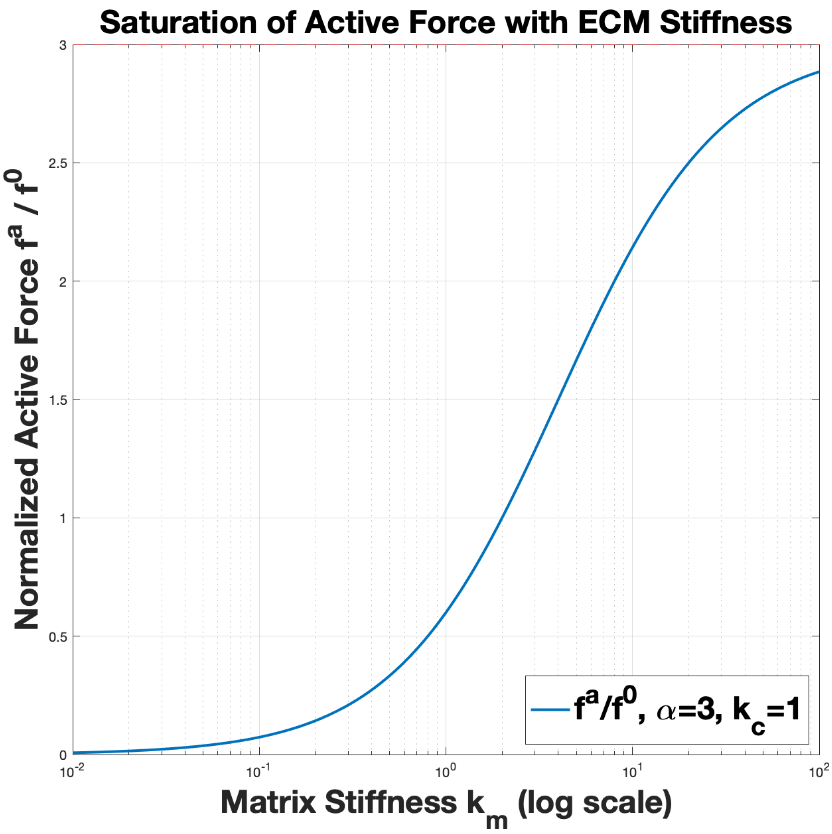



Figure 3: Active Force vs. Matrix stiffness.

# References

[1] Assaf Zemel, Florian Rehfeldt, Alexander E.X. Brown, Dennis E. Discher, and Samuel A. Safran. Optimal matrix rigidity for stress-fibre polarization in stem cells. *Nature Physics*, 6(6):468–473, 2010.