Cell traction forces serve as an amplifier for mechanical cues

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Cells respond to mechanical cues in the extracellular matrix

ECM supports tissue cells adhere to ECM ECM guide cell migration

cells: migrate to stiffer areas spread more on stiff substrates more stable focal adhesions on stiff substrates elongate along stretch orientation

Figure: Copied from http://www.osteopata.it

Figure: [van der Schaft et al., 2011]
Cells deform the ECM

Cells apply a traction force to the ECM → local ECM deformations

Q: How do traction forces affect response to mechanical cue in the ECM?
A: try to find out by mathematical modeling

Figure: Copied from [Califano and Reinhart-King, 2010]
Cellular Potts Model

Cells are modelled as a collection of lattice sites
[Glazier and Graner, 1993]

Monte Carlo Step:
- Move: extension/retraction of one lattice site
- Accept or decline move

System behavior based on balance of forces

Surface
Contact
Connectivity

Accept move with Boltzmann probability
Traction forces and mechanotaxis

Cell traction forces: cell nodes pull on cell nodes

\[ F_i = \mu \sum_j d_{ij} \quad [\text{Lemmon and Romer, 2010}] \]

Substrate: Linear elastic, isotropic, infinitesimal strain

\[ Ku = f, \quad \epsilon = (\epsilon_{xx}, \epsilon_{yy}, 2\epsilon_{xy}) = \left( \frac{\partial u_x}{\partial x}, \frac{\partial u_y}{\partial y}, \frac{\partial u_x}{\partial x} + \frac{\partial u_y}{\partial y} \right) \]

Mechanotaxis: Cells prefer to adhere to higher strained areas and in the strain orientation.
Static stretch

single cell
no cellular traction forces
Static stretch

single cell

cellular traction forces
Cell forces amplify and speed up single cell response to static stretch
Static stretch

group of cells
no cellular traction forces
Static stretch

group of cells
cellular traction forces
Cell forces induce self organization

[Eastwood et al., 1998]
Conclusion

Cell traction forces can amplify response to mechanical cues and promote self-organization
Substrate Stiffness and Cell Area Predict Cellular Traction Stresses in Single Cells and Cells in Contact. 

Effect of precise mechanical loading on fibroblast populated collagen lattices: morphological changes. 

Simulation of the differential adhesion driven rearrangement of biological cells. 

A Predictive Model of Cell Traction Forces Based on Cell Geometry. 


Between molecules and morphology. Extracellular matrix and creation of vascular form. 
Hamiltonian

\[ H = \sum_{(\vec{x}, \vec{x}')}(\tau(\sigma_{\vec{x}}), \tau(\sigma_{\vec{x}'}) (1 - \delta(\sigma_{\vec{x}}, \sigma_{\vec{x}'}) + \lambda_A \sum_{\sigma} (a(\sigma) - A)^2 \]  

(1)

\[ P(\Delta H) = \begin{cases} 1 & \text{if } \Delta H < 0 \\ e^{-\frac{\Delta H}{T}} & \text{if } \Delta H \geq 0. \end{cases} \]  

(2)
Mechanotaxis

To incorporate cell response to strains in the substrate, another term is added to the Hamiltonian:

\[
\Delta H_{\text{mech}} = -g(\vec{x}, \vec{x}') \lambda_{\text{mech}} \left[ f(E(\epsilon_1))(\vec{v}_1 \cdot \vec{v}_m)^2 + f(E(\epsilon_2))(\vec{v}_2 \cdot \vec{v}_m)^2 \right]
\]

- \(g\): ±1 extensions/retractions
- \(\lambda_{\text{dur}}\): durotaxis parameter
- \(\vec{v}_1, \vec{v}_2, \epsilon_1, \epsilon_2\): principal directions and strains
- \(\vec{v}_m\): copy direction
- \(E(\epsilon)\): \(E_0(1 + \frac{\epsilon}{\epsilon_{\text{st}}})\) modelling strain-stiffening
- \(f(E)\): sigmoid function “A certain level of stiffness is needed to cause a cell to spread, and there is a maximum of response”
Order parameter

Orientational order parameter

\[ \vec{v}(\sigma(\vec{x})) \] direction of long axis of cell at \( \vec{x} \).

\( \vec{n} \) local director, the weighted local average of cell orientations, within a radius \( r \) around \( \vec{x} \), such that

\[ \vec{n}(\vec{x}, r) = \langle \vec{v}(\sigma(\vec{y})) \rangle \{ \vec{y} \in \mathbb{Z} : |\vec{x} - \vec{y}| < r \} . \]

\( \theta(\vec{x}, r) \) angle between \( \vec{v}(\sigma(\vec{x})) \) and \( \vec{n} \)

\( S \) order parameter, defined as

\[ S(r) = \left\langle \frac{3 \cos^2 \theta(\vec{X}(\sigma), r) - 1}{2} \right\rangle_\sigma \]

where \( \vec{X}(\sigma) \) is the center of mass of cell \( \sigma \).