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Mechanics plays a significant role in cellular behavior; cells exert forces on their surroundings and sense mechanical properties of the extracellular matrix (ECM). Subcellular processes such as protrusion formation, cell-ECM adhesion, and actomyosin contraction are mechanically regulated through signaling pathways. To improve our understanding of the role of mechanics in cell behavior, we developed multiscale mechanical models of single cells in 2D and 3D.

Methods

Two separate models were developed that capture a mechanically active cell in either a 2D or 3D environment. The discrete element method is used to describe the actin cortex mechanics (viscoelasticity and bending rigidity) of the cell[1].

The first model describes a three-dimensional cell on a plane (Fig. 1a). Retrograde flow is modeled as actin diffusion along the cell surface; outward forces proportional to this flow are modeled along a protrusive front, behind which force sensitive discrete focal adhesions can form. Stress fibers can connect adhesions, generating the largest traction forces.

The second model describes a 2D representation of a mechanically active cell embedded in a viscoelastic ECM (Fig. 1b). The ECM is modeled by means of smoothed particle hydrodynamics, which allows for large deformations and ECM degradation[2]. Protrusions are modeled by local reduction of actin cortex stiffness and application of small outward forces, followed by adhesion formation. Curvature-dependent cortex contractility then leads to traction generation.

Results

The models comprise three sets of parameters: Cell mechanical properties, ECM mechanical properties, and traction exertion dynamics. By quantifying parameter sensitivity, we described each set's effect on the ability of cells to exert tractions. We specifically vary protrusion, adhesion, actomyosin contraction, ECM stiffness, and ECM degradation. We quantify the effect on traction polarization, morphology, and cellular traction magnitude.

Simulations are compared to experimental results obtained by means of traction force microscopy for cells interacting with a homogeneous matrix, i.e. 2D culture on polyacrylamide and 3D culture in polyethylene glycol. The models generate realistic traction distributions.
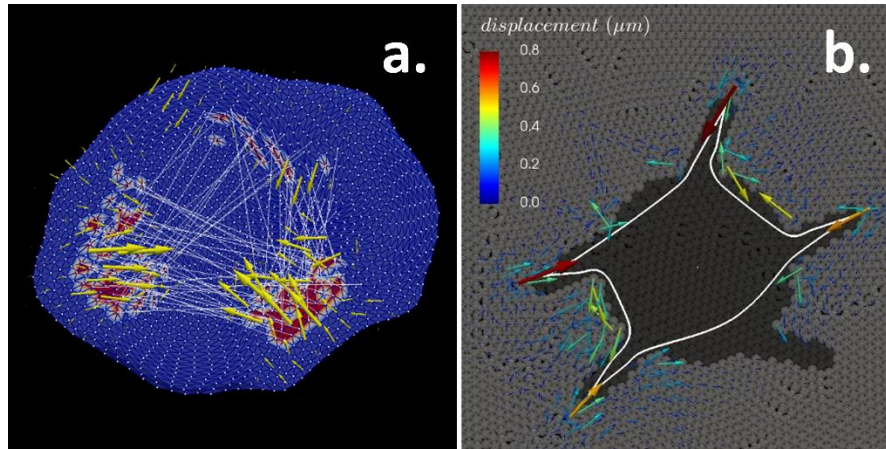
Fig. 1: (a) Bottom view of simulated cell on a substrate: Arrows indicate traction forces, red areas on cell surface represent focal adhesions, and white lines represent stress fibers. (b) Displacement field for a contractile cell model after protrusion formation in a degradable viscoelastic ECM model.

Discussion

Experimental measurements at the subcellular scale can be technically difficult to obtain. Our models allow to investigate the role of various cellular processes and ECM mechanical properties and therefore can lead to a better understanding of the role of mechanics in cell behavior.

Acknowledgements

References

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2. Heck *et al.,* (2017). *Comput Methods in Appl Mech Eng,* 322 p515