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Mathematical models of mechanical aspects of cell motility and cell-substrate interaction

Mechanical interactions between a cell and the substrate are vital for cell migration and signaling. It has been shown experimentally that cell-substrate mechanical interactions affect signal transduction in processes such as focal adhesion growth and shrinkage, stress fiber formation, and the cyclic extension and contraction phases of certain motile cells, such as *Dictyostelium discoidium*.

In the talk, I will present two mathematical models aimed at understanding the mechanical stresses that occur during cell motility and the effect of cell-substrate interaction on these intracellular stresses. The first model treats the cell as a two-dimensional hypoelastic continuum that is moving over a two-dimensional elastic substrate. Focal adhesions are modeled as collections of discrete elastic springs that can break and reform, and cytoskeletal organizations driving cell movement are captured by an empirical active deformation tensor. A finite element implementation of the model of cell and substrate deformation is coupled to the equations governing the dynamics of the adhesions. The resulting simulations are used to better understand the oscillatory nature of amoeboid cell motility. In a slightly different context, we also couple the model for the intracellular mechanical interactions to a reaction diffusion model of the transport of plaque proteins that are required for dynamic reorganization of focal adhesions. The goal here is to illustrate how mechanics can affect biochemical kinetics within the cell, and in particular how mechanical interactions lead to the formation of observed focal adhesion patterns on the cell-substrate interface.

In the second mathematical model, we consider a cell moving through a two-dimensional slice of a three dimensional collagen network. In this case, based on the work of Yang and coworkers (2008), the cell is modeled as a fluid enclosed in an elastic membrane, and the collagen network is modeled as series of deformable beams. Governing equations for an elastica (an inextensible, highly deformable rod) are used to model collagen fiber deformation, and the deformation of the cell membrane as well as cell-collagen interaction is tracked using the level set method. Preliminary numerical implementation of this model are used to understand how the mechanical properties of the collagen affect the morphology of the cell moving through it. While the two models presented in this talk are qualitatively different, their overall purpose is to allow us to gain a better understanding of how mechanical interaction with the environment through which a single cell moves affects its movement.

Liu Yang, Janet C. Effler, Brett L. Kutscher, Sarah E. Sullivan, Douglas N. Robinson, and Pablo A. Iglesias. "Modeling cellular deformations using the level set formalism." *BMC Systems Biology*, vol. 2, 2008.