The Johns Hopkins University

Whiting School of Engineering

Department of Electrical and Computer Engineering

Mathematical Models of Mechanosensory Feedback

Dissertation Defense by

Krithika Mohan

Graduate Research Assistant

Electrical and Computer Engineering

Abstract

Cells undergo controlled changes in morphology in response to intracellular and extracellular signals. These changes require a means for sensing and interpreting the signaling cues, for generating the forces that act on the cell's physical material, and a control system to regulate this process.

Experiments on *Dictyostelium* amoebae have shown that force-generating proteins can localize in response to external mechanical perturbations. This mechanosensing, and the ensuing mechanical feedback, is believed to play an important role in minimizing the effect of mechanical disturbances in the course of changes in cell shape, especially during cell division. Owing to the complexity of the feedback system, which couples mechanical and biochemical signals involved in shape regulation, theoretical approaches can guide further investigation by providing insights that are difficult to decipher experimentally.

In this dissertation, we develop and validate computational models to explain the different mechanosensory and mechanoresponsive behaviors observed in *Dictyostelium* cells. These models couple a molecular scale model that accounts for how the cell senses and responds to external forces to a partial differential equation model that describes protein localization in response to these forces. Furthermore the models presented identify the feedback mechanisms hidden in the observed mechanoresponsive behaviors of *Dictyostelium* cells during micropipette aspiration experiments. Through these feedback mechanisms, we provide a mechanistic explanation for cellular retraction and hence cell shape regulation. The complete multi-scale model is validated experimentally by comparing simulations of mechanosensory response to the observed experimental response for a number of different applied stresses.

Finally, we conclude by showing how the models developed in the context of *Dictyostelium* are applicable to mechanosensory behaviors of actin cytoskeletal proteins in mammalian cells. The models presented in this dissertation, represents the work done in collaboration with Tianzhi Luo and Doug Robinson of the Department of Cell Biology, Johns Hopkins School of Medicine.

Thursday, February 5, 2015

2:30 p.m.

Gilman 50

FOR DISABILITY INFORMATION CONTACT: Janel Johnson (410) 516-7031 janel.johnson@jhu.edu