Decoding information in cell shape — the role of membrane curvature

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Cell shape is critical to cellular function — this is a widely acknowledged fact. But how can we characterize the different aspects of cell shape? Local changes to cell shape are characterized by changes to the membrane curvature both at the plasma membrane and within organelle membranes. One of the open challenges in understanding how cell shape couples cellular function is the dynamic nature of the coupling between membrane curvature, biochemical signal transduction, and the actin cytoskeleton remodeling.

First, how does cell shape regulate signaling? Previously, we showed that cell shape regulates the spatiotemporal temporal dynamics of MAPK activation, as a function of local curvature-induced receptor densities. We now extend this work to show how cell shape changes organelle location and the impact of organelle location on signaling in contractile phenotype of vascular smooth muscle cells.

Second, how do proteins regulate cell shape? In clathrin-mediated endocytosis (CME), clathrin and various adaptor proteins coat a patch of the plasma membrane, which is reshaped to form a budded vesicle. Experimental studies have demonstrated that elevated membrane tension can inhibit bud formation by a clathrin coat. I will first discuss recent results that show that membrane tension can be heterogeneous along the surface of the membrane and depend on protein concentration. Then I will discuss the mechanics of membrane budding across a range of membrane tensions by simulating clathrin coats that either grow in area or progressively induce greater curvature.

And finally, how do signaling, cytoskeletal dynamics, and membrane physics regulate volume? We use a systems biology approach to construct a mathematical model of biochemical signaling and actin-mediated transient spine expansion in response to calcium-influx due to NMDA receptor activation. We have identified that a key feature of this signaling network is the paradoxical signaling loop that acts not only during signaling but also during cytoskeletal remodeling of the spine volume. Our model is able to capture the experimentally observed dynamics of transient spine volume and able to identify sources of robustness of spine volume dynamics. I will conclude with some perspectives on what modeling, the combination of mechanics with biochemistry in particular, can do for `Building the Cell'.

Padmini Rangamani is an assistant professor in Mechanical Engineering at the University of California, San Diego. She joined the department in July 2014. Earlier, she was a UC Berkeley Chancellor's Postdoctoral Fellow, where she worked on lipid bilayer mechanics. She obtained her Ph.D. in biological sciences from the Icahn School of Medicine at Mount Sinai. She received her B.S. and M.S. in Chemical Engineering from Osmania University (Hyderabad, India) and Georgia Institute of Technology respectively. She is the recipient of ARO, AFOSR, and ONR Young Investigator Awards, and a Sloan Research Fellowship for Computational and Molecular Evolutionary Biology. She is also the lead PI for a MURI award on Bioinspired low energy information processing from the AFOSR.

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