Modules of Cell Polarization/Motility Initiation

Alex Mogilner

Department of Math, University of California, Davis, CA 95616, and Courant Institute and Department of Biology, New York University, NY , 10012 USA

Maintenance and breaking of structural symmetry in cells has long been a puzzling problem. In animal epitheliocytes, two networks – branched and bundled actin networks – are intrinsic activators and inhibitors of cell polarity. We find experimentally and computationally that these networks are engaged in a winner-takes-all competition controlled by myosin. Myosin pulls branched actin filaments into bundles along the entire cell periphery, rendering cell shape symmetric. Suppression of myosin activity releases the filaments from bundling. Myosin-free filaments, displaying inherently non-uniform growth, can locally propel the cell membrane forward which triggers symmetry breaking. This phenomenon establishes a simple mechanical switch for cell polarization mediated by myosin that does not rely on complex biochemical interactions. On the other hand, in fish keratocytes, stochastic fluctuations in adhesion strength and myosin activity in isotropic uniform actin network trigger an actin flow-dependent, non-linear switch in adhesion strength, resulting in spontaneous symmetry-breaking and persistent motility. In this case, the nonlinear dynamics of two opposing mechanical forces, contractility and cell-substrate adhesion at the future rear of the cell trigger the polarization. Though the detailed molecular processes underlying these two polarization pathways are different, mechanics of both modules rely on free boundary of the cell movement of which is an essential component of the positive feedback of polarization. I will discuss how computational modeling of the cell as a free boundary domain helped to solve experimental puzzles. I will conclude with showing experimental results on transient polarization and motility of keratocytes in an electric field.