Tanny Lai
Biophysics Team, Fluid Dynamics, A*STAR Institute of High Performance Computing
e-mail: laitl@ihpc.a-star.edu.sg
Yukai Zeng
Mechanical Engineering, Carnegie Mellon University
Philip R. LeDuc
Mechanical Engineering, Carnegie Mellon University
K.-H. Chiam
Biophysics Team, Fluid Dynamics, A*STAR Institute of High Performance Computing

Combined experimental and mathematical modeling of circular dorsal ruffles

Circular dorsal ruffles (CDRs) are transient actin-based structures that are observed on the dorsal plasma membrane upon stimulation by receptor-tyrosine-kinase growth factors such as the platelet-derived growth factor (PDGF). While the function of CDRs has not been elucidated, it has been suggested that they are involved in cell migration and macropinocytosis. Here, we combine experiments with mathematical modeling to attempt to understand the regulation of CDRs. Experimentally, we find that lifetime of CDRs can be modified by varying the substrate stiffness, whereas their sizes are independent of substrate stiffness. To understand these results, we construct a mathematical model of the signaling pathways that regulate CDRs. By coupling such reactions to protein diffusion, we find that our reaction-diffusion system of equations can reproduce the ring-like structure of CDRs, and how substrate stiffness modifies their lifetime via the focal adhesion kinase (FAK). We also show that the low diffusion coefficient of membrane bound proteins relative to the high diffusion coefficient of cytosolic proteins is key to the generation of CDRs. Finally, we reduce the model to a coupled two-species model involving the proteins Rac (which has been shown to result in the generation of actin filaments) and Rho (which has been shown to be involved in cell-substrate adhesion), and their antagonism, and was able to explain the formation of the CDRs as an excitable system. Using this reduced model, we study the conditions for this excitability to occur, and therefore make predictions on when and where CDRs will appear.