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Computational models for feedback between cell shape, cell signaling and extracellular matrix

Cell shape changes and cell migration in mammalian cells are regulated by many signaling proteins. Cells also interact with a meshwork of protein fibers, called the extracellular matrix (ECM), that affects signaling proteins that regulate cell motility, Rac and Rho. The feedback between Rac-Rho-ECM affects invasiveness of melanoma cancer cells. In our models, we expand on a previous 2-compartment model that describes Rac-Rho mutual inhibition, self-activation, the effect of each protein on the amount of contact with the ECM, and ECM activation of Rho. We study the full spatial dynamics in 1D and in static 2D domains, demonstrating oscillations and static/dynamic waves. These results give insight into how distinct types of cell migration emerge. By simulating the set of PDEs in a fully deformable 2D cell using a Cellular Potts model, we predict how spatially distributed signaling is coupled to cell motility. Predicted cell shapes and behavior resemble experimental observations. This full 2D model reveals how ECM anisotropy, cell stiffness, and other cell parameters affect cell migration, leading to experimentally testable predictions. Our computational models suggests insights into how the invasiveness of melanoma cells is regulated.