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Multiscale computational modeling of chemical and mechanical signaling in collective cell migration

Single and collective cell migration involves both chemical and mechanical signaling between cells and the extracellular matrix (ECM, a fibrous network surrounding cells). Regulatory proteins (Rho GTPases) coordinate cell shape changes and migration. Adhesive forces between cells and physical stresses from the ECM allow cells to coordinate their behavior with neighbouring cells. To study how force interactions between cells and the ECM may drive tissue organization, I previously developed a multiscale model. This model couples the Cellular Potts Model, an agent-based model that describes cell movement to a Finite Element Method that is used to calculate ECM stresses. In this model, 1) cells pull on the ECM, 2) strains are generated in the ECM, and 3) cells move along ECM strains. This model was used to study cell shape changes in response to matrix stiffness, vascular-like tissue patterns on compliant substrates and tissue orientation along ECM stresses. My next step is to study how feedback between Rho GTPases and physical forces drives cell migration. Rho GTPases are upregulated under force and in turn higher GTPase levels are associated with higher cell traction forces. I will discuss how such dynamics may be included in my modeling framework. I will model Rho GTPase dynamics by solving PDE descriptions of reaction-diffusion systems on a deforming domain (the cell). Finally, I will discuss next research directions with respect to single and collective cell migration.