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Controlling Cell Exploration and Oscillation Using Deposited Footprints

For eukaryotic cells to heal wounds, respond to immune signals, or metastasize, they must migrate, often by adhering to extracellular matrix. Cells may also deposit matrix, leaving behind a footprint that influences their crawling. Recent experiments showed that epithelial cells on micropatterned adhesive stripes move persistently in regions they have previously crawled on, where footprints have been formed, but barely advance into unexplored regions, creating an oscillatory migration of increasing amplitude. Here, we explore through mathematical modeling how footprint deposition and cell responses to footprint combine to allow cells to develop oscillation and other complex migratory motions. We simulate cell crawling with a phase field model coupled to a biochemical model of cell polarity, assuming local contact with the deposited footprint activates Rac1, a protein that establishes the cell's front. Depending on footprint deposition rate and response to the footprint, cells on micropatterned lines can display many types of motility, including confined, oscillatory, and persistent motion. On 2D substrates, we predict a transition between cells undergoing circular motion and cells developing an exploratory phenotype. Consistent with our computational predictions, we find in earlier experimental data evidence of cells undergoing both circular and exploratory motion.