Phase-field modeling and isogeometric analysis of amoeboid motion: 3D simulation of obstacle-mediated chemotaxis

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A fascinating feature of eukaryotic cells is their ability to move. Cellular motility controls crucial biological processes such as, e.g., cellular nourishment, wound healing, tissue growth, pathogen removal, or metastatic disease. An outstanding feature of motile cells is their ability to perceive external stimuli that can direct their motion. Here, we study chemotaxis, which is the movement of cells guided by chemical cues. In particular, we focus on Dictyostelium Discoideum, an amoeboid cell that migrates spontaneously but also undergoes chemotaxis when subject to extracellular chemotactic factors. Amoeboid cell motility results from a balance between myosin-induced contraction and rapid membrane protrusions caused by the emergence of dense actin networks, called pseudopods. Pseudopod extension is driven by actin polymerization, which is regulated by several intracellular pathways affected by extracellular signals (i.e., chemoattractants in case of chemotaxis).

Here, we extend the model of spontaneous amoeboid motion presented in [1, 2] and propose a three-dimensional model for chemotactic motion of amoeboid cells.

The model accounts for the interactions between the cytosolic, membrane, and extracellular compounds involved in cell motility. The motion of the cell is driven by the actin filament network, which is assumed to be a Newtonian fluid subject to forces caused by the cell motion machinery (membrane surface tension, cell-substrate adhesion, actin-driven protrusion, myosin contraction, and a repulsive force accounting for the interaction with obstacles or fibers). The model is grounded on the phase-field method [3], which permits to solve the partial-differential equations posed on the different domains (i.e., the cytosol, the membrane, and the extracellular medium) by using a fixed mesh only. The solution of the higher-order equations derived from the phase-field theory entails a number of challenges. To overcome those challenges, we develop a numerical methodology based on isogeometric analysis [4], a generalization of the finite element method. For the spatial discretization we employ B-splines as basis functions, which possess higher-order continuity. We propose a time integration algorithm based on the generalized-α method.

We show two- and three-dimensional simulations of cell migration on planar substrates, flat surfaces with obstacles, and fibrous networks. The results show that our model reproduces the main features of chemotactic amoeboid motion. Our simulations unveil a complicated interplay between the geometry of the cell’s environment and the chemoattractant dynamics that tightly regulates cell motion. We also show three-dimensional simulations of chemotactic cells moving on planar substrates and fibrous networks. These examples may constitute a first approach to simulate cell migration through biological tissues.

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References


