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Phase-field model of cellular migration: Three-dimensional simulations in fibrous networks

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Abstract

Cell motion plays a key role in many biological processes. Computational models are gaining momentum as a tool that allows a quantitative understanding of the main biological mechanisms of cell motility and produce testable hypotheses. Here, we present a phase-field model of the spontaneous motion of a single cell. The model, which uses a single fixed mesh only, accounts for a generic membrane-bound activator as well as actin and myosin inside the cell. The biochemical interactions between the cellular agents are described through dynamic, nonlinear partial-differential equations. These equations are coupled with a momentum balance law that accounts for the forces involved in cell motion. We propose a computational method based on isogeometric analysis. We show numerical examples corresponding to stationary states of *keratocytes* and dynamic motion of *Dictyostelium* with and without obstacles. We present a three-dimensional example of cell motion within a fibrous network of obstacles. This simulation is seen as a preliminary step for the computational study of cellular migration in the extracellular matrix.

Keywords: Isogeometric analysis, Phase-field method, Cell motility, Amoeboid motion

1. Introduction

1.1. Cell motility

Cell motion is a prerequisite for life. Motion manifests itself at different scales, e.g., subcellular, cellular, and tissue scales. There are cells that swim using cilia or flagella, but most eukaryotic cells produce motion using filaments that constitute the so-called cytoskeleton. Cellular motion is a tightly regulated action that plays a crucial role in several biological processes such as tissue formation, wound healing, and immune response. Thus, it is not surprising that an abnormal behavior of motile cells may lead to serious conditions, including vascular disease and cancer metastasis. For example, metastatic disease is usually preceded by the so-called epithelial-to-mesenchymal transition, whereby an epithelial cell acquires a migratory phenotype. In this process, the migratory cell has to move through the extracellular matrix, interacting with numerous collagen fibers. This process is exceedingly complex and is by no means well understood. However, a new super-resolved fluorescence microscopy has recently permitted to image a neutrophilic HL-60 cell migrating through a three-dimensional collagen matrix [1]. This discovery led to a Nobel Prize in 2014.

A key ingredient for cellular motility is actin, a family of globular proteins. These proteins have the ability to assemble into filaments through a process called polymerization. Actin filaments exert forces on the cell's membrane, producing protrusions mostly in its front part. Another key element of the motion process is myosin. The main function of myosin is the conversion of energy into mechanical force. Myosins comprise a large family of motor proteins. We are primarily interested in non-muscle myosin II, which is the most relevant myosin isoform for cell motility. Myosin II is usually located in the back of the cell and propels itself along actin filaments producing contractile stresses.

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