Live cell motility under the FBLM-FEM prism: from single cell migration properties to the first steps of tissue formation

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The lamellipodium is a thin, sheet-like structure that is found in the propagating front of fast moving cells such as fibroblasts, keratocytes, cancer cells, and more. It is a dense network of linear biopolymers of the protein actin, termed actin-filaments. These actin-filaments are highly dynamic structures that participate in a plethora of cellular processes, e.g. they constantly polymerize by addition of new monomers on their one end, depolymerize on their other end, get fragmented, resist to bending, adhere to the substrate, and many more.

These processes are important for the structure and functionality of the lamellipodium and for the motility of the cell. They are affected to a large extent by the extracellular environment. For example, the chemical landscape in which the cell resides, and the local composition and the architecture of the Extracellular Matrix (ECM), lead to biased motility responses of the cell.

We develop a model, termed Filament Based Lamellipodium Model (FBLM), that describes these processes and has the motility of the cell as an emergent property. It is an anisotropic, two-phase, two-dimensional, continuum model that describes the dynamics of the lamellipodium at the level of actin-filaments. It distinguishes between two families (phases) of filaments and includes the interactions between them, as well as between the network of the filaments and the extracellular environment. When endowed with a problem specific Finite Element Method (FEM), that we have previously developed, the combined FBLM-FEM is able to reproduce realistic, crawling-like moving cells.

In this talk we statr with the presentation of the basic components of the FBLM and the FEM and focus on a series of numerical simulations that illustrate the motility properties of the FBLM-FEM combination. We exhibit the numerical convergence of the FEM and perform sensitivity analysis on the parameters that control its development. We then embed the FBLM in a complex

extracellular environment with multiple chemical sources, and a non-uniform and adaptive ECM, and study its response to variations of the chemical and adhesion environment. We present some of our results in cell-cell communication, collision, and cell-cell adhesion. And close by considering a larger number of cells and make the first steps in the direction of tissue formation.

This presentation is based mostly on materials extracts of joint works with Christian Schmeiser, Dietmar Oelz, Angelika Manhart, Diane Perichaurd, Vic Small, and Aaron Brunk.

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