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MODELING THE MECHANICS OF CELL LOCOMOTION

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Cell migration individually or collectively is crucial for all morphogenetic and regenerative processes, also contributing to the development of numerous diseases, including cancer. For individual cell migration, cell movement starts with protrusion of the cell membrane followed by the formation of new adhesions at the cell front that link the actin cytoskeleton to the extracellular matrix of the tissues, generation of traction forces that move the cell forwards and disassembly of adhesions at the cell rear. Therefore, cell locomotion is a multiscale process that results from the integrated effect of five main mechanical events that cells exert on the tissue matrix: cell polarization, protrusion, attachment to the matrix (adhesion), internal contraction, and detachment from the matrix at the cell rear.

All these processes are regulated by environmental signals from the surrounding microenvironment that allow cells to guide and regulate their directional movement. Unraveling the intrinsic mechanisms that cells use to define their migration is an essential element for advancing the development of new technologies in regenerative medicine.

Due to the complexity of all these mechanisms, computational simulations are a relevant tool for providing deeper insight and quantitative predictions of the mechanical interplay between cells and tissue matrix during cell migration. Different numerical strategies are being developed in order to simulate individual cell migration in 3D [1], mainly focused on the contractile characteristics of the cytoskeleton as a mechano-sensor system [2]. Now, we are developing novel numerical approaches to couple multiple mechanisms (protrusion, contraction and cell-matrix adhesion) that regulate cell migration. These numerical simulations will combine discrete and continuous approaches that enable design of effective strategies for each particular event. In addition, we will compare our numerical results with experiments, which provide experimental information to define the main assumptions of our models.

Therefore, in this work, I will present the main elements that are necessary to consider for correct modelling of individual cell migration in 3D. In addition, I will show recent progress that we have made in the development of different integrative numerical strategies for advancing in the simulation of cell movement in 3D.

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