Particle-based modelling and simulation in cell mechanics: from adhesion and contraction to cell migration

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ABSTRACT

Mechanics is acquiring a crucial role in biology as a tool to understand fundamental processes in physiology and pathology and for the development of novel technologies associated to the improvement of our health. In fact, mechanics is relevant in many different aspects of biology, depending on the specific spatial scale size under analysis: molecular scale (i.e. DNA transcription, protein folding, chemical cascades and mechanotransduction); cellular scale (i.e. motility, aggregation, morphogenesis and mechanobiology); tissue scale (growth and remodelling); and finally organ scale. Numerical simulation is especially appropriate for this kind of analyses, opening new possibilities for research in this field. In particular, particle-based simulations are very useful, because they are able to capture the large-scale dynamics of multiple components simultaneously incorporating their interactions.

In this work, we focus our modelling strategy on two fundamental processes, which are crucial for defining cell motility: cell contractility and cell-matrix adhesion. Actually, cell locomotion is a multiscale process that results from the integrated effect of three main mechanical events that cells exert on the matrix: cell attachment to the matrix (adhesion) in the cell front, internal contraction, and detachment from the matrix at the cell rear. So, initially, we present two particle-based approaches to simulate cell contractility [1] and cell-matrix adhesion [2].

Both models constitute the base of a hybrid computational model for the 1D simulation of individual and collective cell migration regulated by the stiffness gradient of the matrix, a process known as durotaxis [3].

Despite this model is very interesting to simulate collective cell migration, mainly regulated by adhesion dynamics, it presents some limitations to simulate more complex phenomena associated to collective migration of epithelial monolayers. Therefore, to solve these problems we present a novel hybrid computational modelling strategy that combines particle-based and finite element approaches. We show that this hybrid method can be used to model and simulate topological changes on proliferating epithelial tissue driven by cell mechanics [4]. Also, it has been successfully applied to reproduce collective cell migration in epithelial monolayers following stiffness gradients of the substrate and in wound healing and gap closing phenomena.

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