Modelling cell-matrix mechanics with cellular Potts and molecular dynamics

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Cells surround themselves with extracellular matrix (ECM) to adjust the structure of their environment. In many animal tissues, the ECM takes the form of vast interconnected networks of protein fibers with non-trivial topology and bulk mechanics. Mechanical reciprocity between cells and the ECM plays a central role in fundamental biological processes such as cell migration and tissue morphogenesis [1]. Modelling this mechanical interplay is challenging. Many modelling approaches focus either on ECM fiber networks but simplify cells [2], or, vice-versa, they model cells in detail but average ECM structure [3].

We introduce a cell-based model using the cellular Potts formalism which we hybridize with a discrete ECM fiber model solved with methods from molecular dynamics [4]. We model ECM fibers as bead-spring chains with linear elastic potentials between consecutive beads and linear bending potentials between consecutive bead triplets. Fibers can be mechanically coupled via crosslinkers, and cells link to fibers via discrete focal adhesion-like sites.

We simulate a common experimental setup in the field of cellular biomechanics consisting of an isolated contractile cell embedded in a fiber network. We demonstrate how fiber crosslinks affect network strain, showing that the underlying dynamics of the model suffice to reproduce experimentally measured dynamics of fiber densification and displacement [5]. Further, we show that contractile cell forces propagate over multiple cell radii scaling with power law exponent ≈ 0.5 typical of viscoelastic ECM [2, 6]. We end by showing preliminary work on cell migration and discuss how the model can be used to study how ECM mechanics impact on cancer metastasis.

References

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