CROSSLINKING ENABLES LONG-RANGED CELL-MATRIX MECHANICS IN A HYBRID CELLULAR POTTS AND MOLECULAR DYNAMICS MODEL

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Hybrid model of cell-matrix mechanics

Mechanical interactions between cells and the extracellular matrix (ECM) are fundamental for tissue patterning and homeostasis. The major structural and load-bearing ECM components are fibrous proteins or proteoglycans such as collagen that assemble into complex networks, which cells realign and remodel. Cell traction forces can deform fibrous ECM over distances of multiple cell diameters [1-4], which has been implicated in long-ranged cell alignment and tissue morphogenesis [3-7].

Relating individual cell-level mechanics to tissue-scale behavior is an outstanding challenge which cell-based models such as the cellular Potts model (CPM) are well-positioned to address. These models are very good at representing realistic cell behavior, but generally coarse-grain the ECM as a uniform isotropic material (e.g. simulated with a finite element method). This type of ECM model fails to capture phenomena such as fiber accumulation near contractile cells and long-ranged force transmission. To address this limitation, we hybridized a CPM model of cells with a bead-spring model of fibrous ECM networks simulated with molecular dynamics methods (Figure 1).

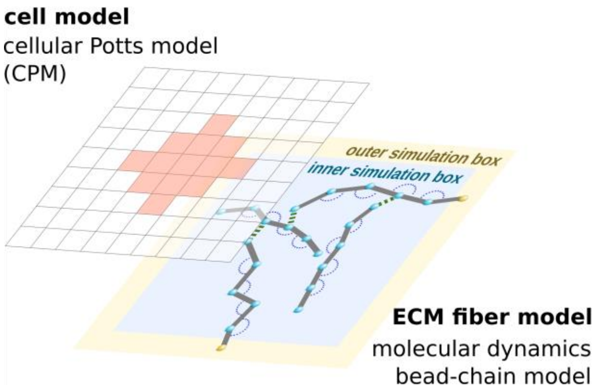

Figure 1: We model cell and ECM using two different formalisms.

Model captures cell-ECM dynamics

We model a contractile cell pulling with discrete focal adhesion-like sites on the ECM fiber network, and demonstrate how network parameters affect cellular contractility (Figure 2). Our model shows agreement with experimentally measured dynamics of fiber densification and displacement [8]. Further, we show that contractile cell forces propagate over multiple cell radii scaling with power law exponent of -0.5 typical of viscoelastic ECM [1, 3]. Our model lays the foundation to investigate how local and long-ranged cell-ECM mechanobiology contributes to multicellular morphogenesis.

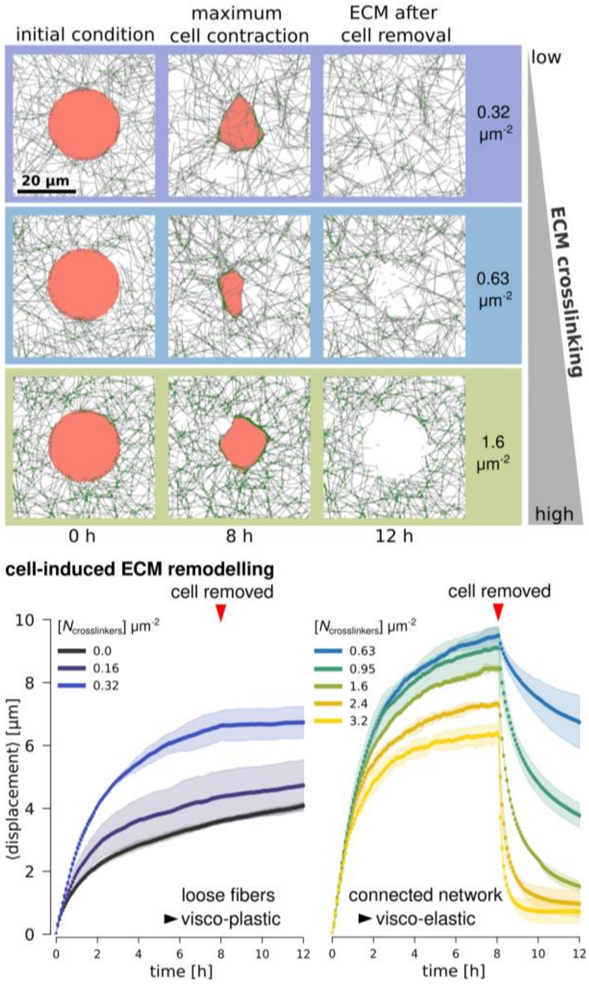

Figure 2: ECM crosslinking affects material properties and the extent of cell contractility.

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