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CELL-BASED MODELING OF TISSUE-LEVEL RESPONSES TO MECHANICAL STRAIN

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Apart from molecular signals, mechanical cell-cell communication is key to explaining collective cell behavior during biological morphogenesis. Using a novel, hybrid Cellular Potts and finite element computational framework [1], we study how mechanical interactions between cells and the extracellular matrix (ECM) can regulate single cell behavior and collective cell behavior during biological morphogenesis. Our model describes the contractile forces that cells exert on the ECM, the resulting strains fields in the ECM, and the cellular response to local strains. The model simulations reproduce the behavior of individual endothelial cells on compliant matrices, and show that local cell-ECM interactions suffice for explaining interactions of endothelial cell pairs (Fig. 1A) and collective cell behavior, including network formation (Fig. 1B) and sprouting from spheroids [1]. If an external strain is exerted on the ECM, the cells rapidly align with the strain field (Fig. 1C), even in response to very subtle strain cues [2]. We will also present unpublished simulation results on chick somitogenesis under external strain. Altogether, our models suggest simple mechanisms by which local, mechanical cell-ECM interactions can assist in integrating morphological information across organization levels.

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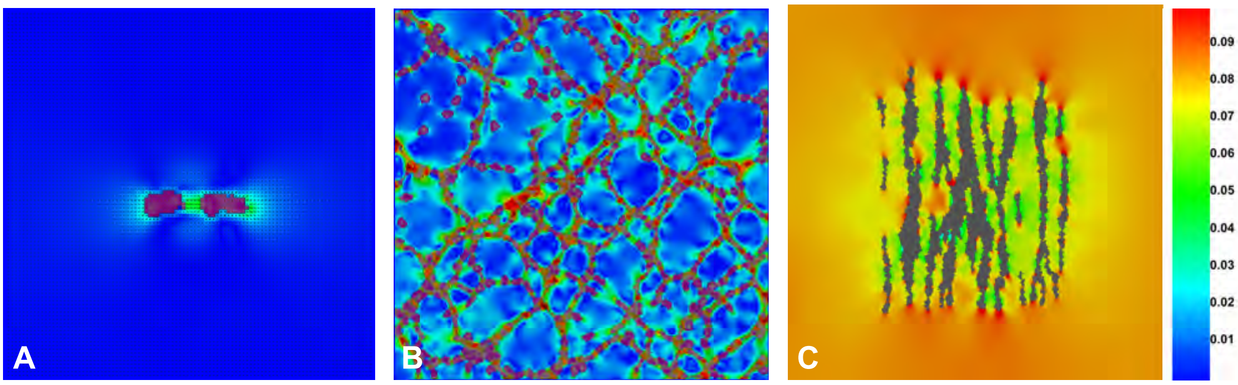

Figure 1: Simulations of mechanical cell-matrix interactions (after Ref. [1] and Ref. [2]; panels A and B taken from Ref. [3]) (A) simulation of a cell pair on a 12 kPa substrate at 500 MCS on a 100×100 lattice; (B) collective cell behavior on a 12kPA substrate at 1000 MCS on a 300×300 lattice. (C) collective cell behavior under mechanical strain on a 12 kPa substrate at 3000 MCS on a 400×400 lattice; the substrate was uniaxially stretched along the vertical axis. Color bar: magnitude of largest principal strain (unitless)

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