Multiscale cell-based modeling of mechanical cell-matrix feedback during collective cell behavior

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Apart from molecular signals, mechanical cell-cell communication is key to explaining collective cell behavior biological morphogenesis. Yet, most computational models of collective cell behavior focus on chemical signaling. Endothelial cell cultures on compliant substrates are a good model system of mechanical signaling during morphogenesis. Depending on the stiffness and other biophysical and chemical properties of the substrates, the endothelial cells can form blood vessel-like structures, including vascular networks and sprouts. Here we discuss a hybrid Cellular Potts and finite element computational model, in which a limited set of biologically plausible rules describing the mechanical cell-ECM interactions suffices for reproducing aspects of endothelial cell behavior at the single cell, pairwise and collective scale. The model includes the contractile forces that endothelial cells exert on the ECM, the resulting strains in the extracellular matrix, and the cellular response to the strains.
The simulations reproduce the behavior of individual endothelial cells, the interactions of endothelial cell pairs in compliant matrices, and network formation and sprouting from endothelial spheroids. We will conclude by showing how the mechanical interactions between cells and the extracellular matrix amplify the dynamic response of tissue organization to external strain. This response offers a potential route by which large scale strains in growing embryos can control the cellular structure of tissues.