Effect of substrate stiffness on balance of active cell-cell and cell-ECM forces studied through a computational model of a deformable cell pair

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Cells communicate with their environment and neighboring cells, transmitting forces. The interplay between cell-cell and cell-ECM adhesions is complex, with junction types being connected to one another via the cytoskeleton. Cell-pair studies on patterned substrates provide one of the simplest collective cell in vitro models. We developed a computational model of this setup in which subcellular force exertion mechanisms are taken into account. We compare simulated traction maps with those recovered in vitro through traction force microscopy. The discrete element method (DEM) is used to model the actin cortex mechanics [1]. We model two cells on a rectangular pattern; the cells forms an interface with the substrate and with each other. The discrete nature of the method is used to model focal adhesions and adherens junctions simultaneously. Stress fibers connect adhesions to one another and exerting a contractile force. Mechanosensing is incorporated in the form of force-dependent lifetime of adhesions and reinforcement of actomyosin contraction with fiber stalling. In agreement with experiments, the model shows decoupling of cells, increase in number of focal adhesions, and increase in contractile strength with increased substrate stiffness. Results suggest the stiffness of the cell-cell interface becomes a tipping point for substrate stiffness to define mechanosensing dynamics.

[1] Odenthal et al, PLoS Comp Biol, 9(10), 2013.