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Matrix elasticity: Why do cells “care”

Abstract:

Many experiments have shown that the substrates upon which cells are placed or the extracellular matrix (ECM) in which cells reside in 3D can regulate cellular structure and function. From fate “decision making” of mesenchymal stem cells to rigidity driven durotaxis, the contractile, active acto-myosin network plays a major role in the mechanosensing and transduction of elastic signals, which in turn depends on the elastic properties of the substrate or ECM.

Previous theoretical models of elastic interactions assumed that cells exert constant force or strain when interacting with other cells and that the energy cost of deformation of the substrate or matrix in the presence of other cells lies at the origin of elastically mediated interactions among cells. Similar ideas are used to predict cytoskeletal orientation and registry as a function of substrate rigidity as observed in experiments. Here, we present a new suggestion for why cells “care” about the elastic deformations of the substrate or matrix induced by their neighbors. Cells that maintain a homeostasis that governs the local stress or strain in their vicinity can actively adjust their contractility to complement strains or stresses induced by other cells or other mechanical perturbations. This active response can be modeled as an “ideal” induced force that cancels out the external fields so that stress or strain homeostasis in the cell neighborhood is maintained. We propose that by actively adjusting its force to complement those of its neighbors or external perturbations and thereby maintain homeostasis, the cell senses its environment and interacts with the neighboring cells. In particular, this predicts that even circularly (spherically) symmetric cells on isotropic substrates (in isotropic ECM) interact elastically, in contrast to the vanishing interactions for the case of “dead inclusions” under these situations. Furthermore, it is reasonable to assume that cells tend to minimize the energy cost associated with these induced forces by reorienting or otherwise modifying their cytoskeletal network and adhesions. Cells also “care” about the qualitative nature of the matrix or substrate elasticity as we show theoretically by contrasting cell deformations and interactions in linear vs. non-linear, shear-stiffening elastic

networks. The latter are characteristic of biopolymers such as actin, collagen, fibrin and fibronectin. For a cell modeled as an isotropically contractile sphere, the non-linearity leads to a highly amplified far-field strain. This effect also amplifies the interactions between two such cells in a non-linear elastic medium and can lead to a significantly larger interactions. The role of non-linear substrate elasticity has been the focus on recent experiments that show anomalously long-range cellular correlations in such systems.