Mechanical Nanotomography of Cells invading 3D-Matrices

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Forces and mechanical properties play a central role in many biological processes covering a huge range of length and time scale: from the movement of whole organisms over the adhesion, migration, proliferation of cells, down to the mechanics and interactions of single molecules. For example cells are able to sense external forces (mechanosensing), translate these mechanical forces into biochemical signals (mechanotransduction) and react to these signals (mechanoresponse). Mechanics also plays an important role on the level of single biomolecules. For example, forces act between ligands and receptors, forces induce conformational changes in biomolecules, and the mechanical properties of biomolecules are often related to their function.

In this talk I will focus on recent work in my lab related to mechanical interactions between cells and the extracellular matrix (ECM) critical to the metastasis of cancer cells. To assess the mechanical interplay between the cells and ECM during invasion, we created a model using bovine collagen I hydrogels ranging from 0.1-5 kPa in Young's modulus that were seeded with highly metastatic MDA-MB-231 breast cancer cells. Significant population fractions invaded the matrices either partially or fully within 24 h. We then combined confocal fluorescence microscopy and AFM indentation to determine the Young's moduli of individual embedded cells and the pericellular matrix using novel analysis methods for heterogeneous samples. In partially embedded cells, we observe a statistically significant correlation between the degree of invasion and the Young's modulus, which was up to a factor of two greater than that of the same cells measured in 2D. ROCK inhibition returned the cells' Young's moduli to values similar to 2D and reduced but did not abrogate invasion. This provides evidence that Rho/ROCK-dependent acto-myosin contractility is employed for matrix reorganization during initial invasion, and suggests the observed cell stiffening is due to an increase in actin stress fibers.