Abstract for an Invited Paper
for the MAR10 Meeting of
The American Physical Society

Resolving sub-cellular force dynamics using arrays of magnetic microposts[1]

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The biological response of cells to mechanical forces is integral to both normal cell function and the progression of many diseases, such as hypertensive vascular wall thickening. This likely results from the fact that mechanical stresses can directly affect many cellular processes, including signal transduction, gene expression, growth, differentiation, and survival. The need to understand the relationship between applied forces and the mechanical response of cells as a critical step towards understanding mechanotransduction calls for tools that can apply forces to cells while measuring their contractile response. This talk will describe an approach that simultaneously allows local mechanical stimulation of the adherent surface of a cell and spatially resolved measurement of the local force fields generated throughout the cell in response to this stimulation. Cells are cultured on the top surfaces of arrays of micrometer-scale posts made from a flexible elastomer (PDMS), and the contractile forces generated by an adherent cell bend the posts. Measurements of the displacement of each post allow the contractile force field of the cell to be mapped out with sub-cellular precision. To apply forces to cells, rod- shaped magnetic nanoparticles are embedded in some of the posts so that externally applied magnetic fields selectively deform these "magnetic posts," thereby exerting tunable local, mechanical stresses to the adherent surface of attached cells. Alternatively, magnetic particles bound to or internalized by the cell may be employed to apply forces and torques to the cell. With either approach, measuring the deflection of the surrounding non-magnetic posts probes the full mechanical response of the cell to these stresses. Results that illustrate the temporal dynamics and spatial distribution of the non-local response of fibroblasts and smooth muscle cells to local stresses will be discussed.

[1]In collaboration with Y.-C. Lin, C. Kramer, and C. S. Chen. Supported by NIH NHLBI 1R01HL090747.