Cell-Matrix Interactions in Fibrosis and Cancer: Multiscale mechano-chemical models

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Much of our understanding of the biological mechanisms that underlie cellular functions, such as migration, differentiation and force sensing has been garnered from studying cells cultured on two-dimensional (2D) substrates. In the recent years there has been intense interest and effort to understand cell mechanics in three-dimensional (3D) cultures, which more closely resemble the in vivo microenvironment. However, a major challenge unique to 3D settings is the dynamic feedback between cells and their surroundings. In many 3D matrices, cells remodel and reorient local extracellular microenvironment, which in turn alters the active mechanics and in many cases, the cell phenotype. Most models for matrices to date do not account for such positive feedback. Such models, validated by experiments, can provide a quantitative framework to study how injury related factors (in pathological conditions such as fibrosis and cancer metastasis) alter extracellular matrix (ECM) mechanics. They can also be used to analyze tissue morphology in complex 3D environments such as during morphogenesis and organogenesis, and guide such processes in engineered 3D tissues. In this talk, I will present discrete network simulations to study how cells remodel matrices and how this remodeling can lead to force transmission over large distances in cells. I will also discuss an active tissue model to quantitatively study the influence of mechanical constraints and matrix stiffness on contractility and stability of micropatterned tissues.

BIO: Vivek Shenoy is a Professor in the School of Engineering and Applied Sciences at the University of Pennsylvania with appointments in the Departments of Materials Science and Engineering, Bioengineering and Mechanical Engineering. Dr. Shenoy's research focuses on developing theoretical concepts and numerical methods to understand the basic principles that control the behavior of both engineering and biological systems. He has used rigorous analytical methods and multiscale modeling techniques, ranging from atomistic density functional theory to continuum methods, to gain physical insight into a myriad of problems in materials science and mechanics. He has authored over 150 research publications, with papers in *Science*, *Proceedings of the National Academy of Sciences*, *Nature, Nature Materials, Physical Review Letters* and *Nano Letters*. Dr. Shenoy's honors include a National Science Foundation CAREER Award (2000), the Richard and Edna Solomon Assistant Professorship (2002-2005) and the Rosenbaum Visiting Fellowship from the Isaac Newton Institute of Mathematical Science, University of Cambridge. Shenoy is the principal investigator and program director of the NSF-funded Center for Engineering Mechnobiology established in 2016.