Cells respond to and are regulated by the mechanical properties of the substrate to which they are attached. Previous studies have shown that cells can generate larger forces on stiffer substrates, driving extracellular matrix assembly and increasing the substrate stiffness. In vitro models of fibrotic tissue focus on increasing the elastic modulus of the polymer substrate. However, this approach ignores the viscoelastic nature of fibrotic tissue. Recent research has suggested that as fibrotic tissue matures, the matrix transition from one with a high viscosity to one that is more purely elastic. In this work, we investigate mechanosensitive effects of viscoelasticity using single and dual blends of poly (dimethyl siloxane) (PDMS) formulations with tunable viscous and elastic properties.

We found that 3T3 fibroblast cells on a substrate with higher viscosity have larger cell area, but assemble less fibronectin. To elucidate the mechanism of altered viscosity, we simulated a modification of the Chan-Odde motor-clutch model, representing the substrate as viscoelastic spring-dashpot system instead of a purely spring element. The viscoelastic model shows that cells are sensitive to changes in substrate viscosity, switching from a “frictional slippage” to “load and fail” regime. Our experiments and simulations demonstrate that the viscous component of underlying substrates plays a larger role in cell functionality than previously expected. This may be key in exploring the dynamics of and potential treatments for fibrosis.