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Differential cellular response to linear and strain-stiffening hydrogel substrates JESSAMINE P. WINER, SHAINA A. OAKE, BETHANY C. BAUMANN, PAUL A. JANMEY, University of Pennsylvania — Many cell types act as tensiometers, modulating their spread area, motility, and protein expression in response to the substrate stiffness. Studies of stiffness sensing typically employ linear elastic materials whose stiffness is independent of the applied strain. Biological gels, however, often stiffen in response to increasing strain. Fibroblasts and mesenchymal stem cells adherent to linearly elastic gels typically display a small, round phenotype on soft substrates and increase spread area as the elastic modulus of their substrate increases. On the strain-stiffening biopolymer gel fibrin, the same cell types are maximally spread even when the gel's low strain elastic modulus would predict a round morphology. Traction microscopy reveals that cells apply active displacements of several microns up to five cell lengths away, and atomic force microscopy shows that these displacements locally stiffen the gel by deforming it beyond its linear range. The magnitude of cell-applied strains is inversely related to the gel's low strain elastic modulus and results in long distance cell-cell communication and alignment.

Jessamine Winer
University of Pennsylvania

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