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Measurements and models of cytoskeletal rheology

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Much attention has recently focused on understanding the rheology of living cells and reconstituted actin gels using a variety of experimental methods (e.g., single- and multi-particle tracking, magnetic twisting cytometry, AFM indentation) and several different models or descriptors (e.g., biopolymer models, tensegrity, cellular solids, power-law rheology), but the debate continues regarding the fundamental basis for the experimental observations. Our recent studies examine the time-dependent behavior of neutrophils as they deform to enter a narrow channel with capillary-scale dimensions. A sudden drop in the shear modulus is observed, followed by recovery to pre-deformation values in < 1 minute. These rheological changes coincide with a reduction in f-actin content and a transient increase in calcium ion concentration $[Ca^{++}]$, and the change in storage modulus can be prevented by calcium chelation, suggesting that these observations are causally linked. Cells lacking the ability to increase $[Ca^{++}]$ also become activated more rapidly following deformation, and the time to activation is independent of intracellular strain rates, contrary to experiments lacking the chelating agent. To better understand these processes and the nature of cytoskeletal rheology in general, we have developed a Brownian dynamics model for cytoskeletal self-assembly and subsequent rheological measurement by single particle tracking. Cross-linking proteins are included possessing a range of properties that lead to a variety of cytoskeletal structures from a fine, homogeneous mesh to a structure containing large stress fibers of varying thickness. These results are described in a multi-dimensional phase space that takes into account the geometry, dimensions and stiffness of the cross-linkers.