**310e Forced Unfolding of Protein Domains Determines Cytoskeletal Rheology**

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The importance of mechanics and force to biological processes is increasingly appreciated and has been shown to affect behaviors as distinct as cell motility, morphogenesis, and differentiation. Due to recent advances in microrheological experimental techniques a consensus picture of cellular mechanical properties has emerged. Most cells exhibit a power-law frequency dependence in both their shear modulus and creep response. The strength of these dependences can be controlled by drugs that alter cellular prestress or force generation. Cells exerting more prestress generally have a weaker frequency dependence, or more elastic behavior. However the physical origin of these behaviors is still unexplained. We have developed a model of cytoskeletal mechanics based on thermally activated, forced unfolding of protein cross-links in a stressed semi-flexible polymer gel capable of reproducing most of these behaviors. In simulated athermal networks and networks thermalized with a kinetic Monte Carlo based algorithm, unfolding events produce an emergent, nearly exponential distribution of cross-link tension. Such tension distributions readily lead to stress relaxation spectra that have a power-law tail, and reproduce the recently observed power-law form of cells' dynamic shear moduli as well as power-law creep response. Furthermore the primary determinant of the cellular mechanical response is the strength of the bonds holding together the cross-link domains. Weaker bonds give more liquid-like frequency response while stronger bonds give more elastic responses. This also suggests a natural explanation for the prestress dependence. In a system of mixed bond strengths, higher stresses should lead to unfolding of stronger bonds and a more elastic response, as is observed cellularly. Additionally unfolded domains should be readily detectable biochemically, suggesting a clear link to cellular signalling. Interestingly, the number of unfolded domains is a monotonic function of the strain and shows no hystersis. This suggests novel mechanisms of cell shape sensing, compliance sensing, and mechanotransduction as the cell might “measure” the number of these domains to infer the strain in its local environment.