Pre-Fracture Softening in Intermediate Filament Networks

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The cytoskeleton is impressively versatile, manifesting the ability to either stiffen[1] or soften[2] in different stress regimes. A major challenge in cell mechanics has been to identify the mechanical and structural origin of this behaviour.

Of the various predominant cytoskeletal components, intermediate filaments are of particular interest as they have a complex hierarchical structure spanning multiple length scales from the alpha-helical secondary structure of monomers, to rope-like filaments and fully crosslinked networks. Each stage of this structural hierarchy contributes a different mechanism of stress response. While much has been revealed from single filament[3] and simulation studies[4] a comprehensive understanding requires us to consider the structural hierarchies beyond the single filament level. Our motivation is to disentangle the different structural and mechanical regimes of intermediate filaments through probing the rheology of minimal intermediate filament networks using a range of applied stresses.

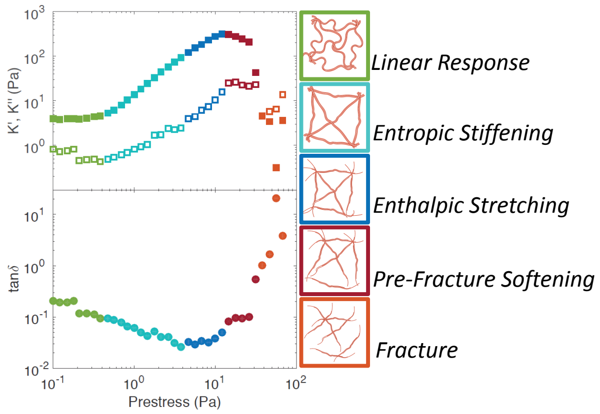

FIG. 1. Non-linear rheological response of Vimentin Intermediate Filament networks. By increasing the stress incrementally, a range of different mechanical regimes are revealed.

Transiently crosslinked intermediate filaments networks are probed with a prestress rheology protocol[5] to increase mechanical load, with long increments of constant stress, allowing the cytoskeletal network to creep and reach a steady state between each subsequent stress step. This not only allows us to access higher applied stress and strain regimes than have previously been reported but also allows network remodelling to be measured from the viscoelastic creep and analysed using a nonlinear generalisation of the Kelvin-Voigt model.

Our approach reveals a rich diversity of mechanical responses over different force regimes, arising from the structural hierarchy within the network (Fig. 1). Filaments exhibit entropic stiffening at low forces and enthalpic backbone stretching at intermediate forces. Significantly, we reveal a regime of pre-fracture softening regime, not previously observed. From the creep response we directly link this softening to network remodelling and compare different crosslinking agents to infer that the remodelling is driven by crosslinker unbinding, leading to loss of network connectivity. This provides intriguing new insights into how intermediate filaments contribute to the cells ability to store and dissipate applied mechanical loads.

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