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Uncovering the molecular basis for collagen mechanics and self-assembly

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Collagen is the fundamental structural protein in vertebrates and is widely used as biomaterial, for example as a substrate for tissue engineering. Assembled from individual triple-helical proteins to make strong fibres, collagen is a beautiful example of a hierarchical self-assembling system. Using a combination of biophysical and biochemical techniques, we are investigating how its composition relates to its mechanics at the single-molecule level, and to the interactions driving self-assembly into fibrillar structures. In this talk, I will focus on our optical-tweezers-based microrheology studies, which investigated dynamics of interactions between collagen proteins and the development of heterogeneous microscale mechanics during self-assembly into fibrillar gels.

Telopeptides, short non-helical regions that flank collagen's triple helix, have long been known to facilitate fibril self-assembly. Our studies show that their removal not only slows down fibril nucleation but also results in a significant frequency-dependent reduction in the elastic modulus of collagens in solution. We interpret these results in terms of a polymer association model, in which telopeptides facilitate transient intermolecular interactions that enhance network connectivity in solution and lead to more rapid assembly in fibril-forming conditions. Furthermore, by measuring the evolving viscoelastic properties of collagen solutions as telopeptides are cleaved, we demonstrate the ability to read out the progress of enzymatic reactions with microrheology. These findings enhance our ability to rationally engineer the self-assembly process.

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