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Single-molecule analysis of collagen's metastability

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Collagen has been evolutionarily selected as the preferred building block of extracellular structures, where it constitutes approximately 20% of the body's protein mass. Despite the inherent and surprising thermodynamic instability of individual proteins at body temperature, collagen manages to assemble into higher-order structures that provide mechanical support to tissues. We have been working to unravel the mystery of this dichotomy, by characterizing how different compositional features in collagen proteins influence their thermal metastability.

In this presentation, I'll describe our use of AFM imaging and analysis to investigate the response of different types of collagen to changes in temperature. We observed structural changes including a time-dependent loss of these triple-helically structured proteins at body temperature. We found very few intermediate structures: in the absence of stabilizing interchain crosslinks, the thermally induced unfolding of collagen appears highly cooperative, leading to either apparently intact or unfolded structures. We identified a stabilizing feature in type IV collagen: interchain disulfide bonds (a "cystine knot") that enhance protein metastability. This cystine knot is evolutionarily conserved in collagen IV, suggesting an important role for such a feature in preventing –or at least slowing –irreversible denaturation of metastable proteins.

Keyword-1

single molecule

Keyword-2

Atomic Force Microscopy (AFM)

Keyword-3

collagen

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