**Thermal Response of Silk-Elastin-Like Protein Hydrogels: Integrating Experiments and Multiscale Computational Modeling**

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Protein polymers are crucial ingredients for the development of dynamically adaptable hydrogels as opposed to static designs that are predominant in current biomedical usage. An example is silk-elastin-like protein (SELP) hydrogels which are reversibly responsive to multiple stimuli. In particular, the thermal response of a SELP constructed from SE8Y repeats is investigated. Experimental results showed a reversible size transition as temperature increased beyond 294K with corresponding decreases in optical absorbance and pore sizes, while the mechanical stiffness increased. Through fully atomistic molecular dynamics (MD) modeling at two temperatures of 280K and 330K, the molecular origin of the SELP thermal response is determined to be a decrease in the end-to-end length and the solvent-accessible surface area (SASA) of a single SELP molecule. However, conformational sampling of proteins in conventional MD modeling is limited by rough potential energy landscapes. By sampling a smoother energy landscape through coarse-grained MD simulations at a range of temperatures from 277K to 330K, the experimental inverse temperature transition of silk-elastin-like proteins (SELPs) is effectively captured. Both the SASA and the radius of gyration of a single SELP molecule showed a steep decrease above a temperature of 297K, in good agreement with the experimental transition temperature of 294K. This CG model is extended with dityrosine crosslinking capabilities to enable future simulations of dynamic stimuli-responsive SELP hydrogels to guide the development of novel multi-stimuli responsive SELP hydrogels.