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Steele 006

"Decoding Repetitive Proteins to Design Stimuli-responsive Biopolymers"

Abstract: Evolution allows organisms to adapt to their environments, yet some molecular patterns stay constant through billions of years of evolution. These patterns encode the secrets of biological materials, such that similar patterns often emerge in different materials with similar functions. For example, a family of elastin proteins form stretchable fibers, which allow the constant movement of human skin, blood vessels, and lungs. We aim to decode the secrets of biological materials by investigating sequence patterns in repetitive proteins, towards establishing systematic protein sequence–biomaterial property relationships.

Here, we explore two classes of repetitive proteins as stimuli-responsive biopolymers. First, we investigate bacterial proteins that undergo conformational changes in response to calcium ions. We modify hydrophobicity, electrostatics, and sequence heterogeneity to demonstrate sequence-dependent, reversible folding and domain size changes in response to calcium ions. We also identify structural features that give rise to ion selectivity, which is not yet well-predicted by AI/ML tools. Second, we introduce enzymatic stimuli to drive isothermal phase separation of elastin-like polypeptides (ELPs). ELPs have drawn interest as heat-responsive biopolymers, such that ELPs undergo reversible phase separation from water upon heating. However, temperature is not always a convenient trigger, especially in biological environments that maintain near-constant temperature, pH, and ionic composition. To expand ELP function, we program a mechanism for isothermal phase separation upon proteolytic cleavage of a di-block ELP. This mechanism presents a new opportunity to exploit biological triggers for ELP phase behavior and self-assembly processes. Overall, we demonstrate repetitive proteins as tunable and modular building blocks for functional biomaterials.

Bio: Danielle J. Mai is an Assistant Professor of Chemical Engineering at Stanford University. She earned her B.S.E. in Chemical Engineering from the University of Michigan and her M.S. and Ph.D. in Chemical Engineering from the University of Illinois. Dr. Mai conducted postdoctoral research at MIT as an Arnold O. Beckman Postdoctoral Fellow. The Mai Lab engineers biopolymers, which are the building blocks of life. Specifically, the group integrates precise biopolymer engineering with multi-scale experimental characterization to advance biomaterials development and to enhance fundamental understanding of soft matter physics. Dr. Mai's work has been recognized through the AIChE 35 Under 35 Award (2020), APS DPOLY/UKPPG Lecture Exchange (2021), Air Force Office of Scientific Research Young Investigator Program Award (2022), ACS PMSE Arthur K. Doolittle Award (2023), and MIT Technology Review List of 35 Innovators Under 35 (2023).