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Building dynamic, functional proteins to understand and treat disease

Natural proteins have evolved to perform functions that enable life. To perform their functions, proteins often form complexes with other biomolecules and undergo structural changes in response to distal perturbations, termed allostery. How can we engineer new proteins for artificial functions in cells and tissues? In this talk, I will describe three ways that we can build new functions in proteins. First, I’ll discuss the de novo design of a versatile protein-based sense/response system. In this project, we computationally designed a new small molecule binding site in a protein-protein interface to couple small molecule detection to several outputs: fluorescence, luminescence, and cell survival. Next, I will share ongoing work using biophysical characterization techniques and computational protein design to understand the intramolecular signal transduction mechanism of a model transcription factor, which opens the door to a deeper understanding of the molecular underpinnings of allostery and the design of new allosteric proteins. Finally, I will describe our recent project to combine computational and experimental protein engineering methods to rapidly build potent SARS-CoV-2-neutralizing biotherapeutics. These projects introduce a platform for future work in characterizing complex disease mechanisms, building new antiviral therapeutics, and engineering protein systems with dynamic components.