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Turning up the heat on enzyme design

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Enzymes are essential protein catalysts that regulate most important biological processes. Our ability to control the function of enzymes via rational design will significantly improve our understanding of protein structure-function relationships and transform our ability to control biological processes (e.g., creating temperature adaptive proteins for biomedical and bio-industrial applications). Our current inability to predict the role of the protein scaffold structure and corresponding feedback mechanisms upon mutation reflects a significant gap in our understanding of enzyme function beyond the catalytic-site structure and to design enzymes that function outside of standard physiological conditions. Our current effort has focused on developing a novel computational protein design strategy to rationally design temperature-adapted enzymes. This project is innovative, because it represents a new and substantive departure from fixed-backbone enzyme design. Namely, we developed a discrete multistate enzyme design cycle (i.e., iterative hypothesis-driven multi-state enzyme modeling and experimental validation) that accurately captures structural and thermodynamic scaffold feedback properties to explicitly design conditional (temperature-adapted) enzymatic catalysis. Furthermore, we gained significant new insights into thermodynamic properties of enzyme structure function relationships.

Biography

Corey J Wilson is the director of the Biomolecular Engineering program at Yale University. He holds a doctorate in Molecular Biophysics (2005) and continued his education as a Gordon E. Moore Postdoctoral Scholar at Caltech (2006-2008) before taking his position at Yale University where he is the Principal Investigator of a thriving research group. His group at Yale seeks to engineer novel, non-natural proteins of tailored function for high impact applications. Protein engineering applies the fundamental principles of biophysics and biochemistry toward design, and is best achieved through an integrated experimental/computational framework.

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