Engineering protein catalysts for synthetic applications

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Chemical synthesis of small molecules can be profitably complemented by enzymatic catalysis. In optimal settings, enzymes can facilitate complex reactions with extraordinary specificity and selectivity. However, practical reality usually differs from this ideal as wildtype enzymes are often just marginally stable in the selected reaction conditions and perform at scales well below what is required to drive an industrial process. However, as enzymes are combinatorically composed from a limited set of simple building blocks, improved catalysts can be constructed in the laboratory by applying enzyme engineering strategies, among them the directed evolution of proteins. Consequently, engineered enzymes are harnessed in many industrial fields ranging from the fine chemical to the pharmaceutical sectors.[1] Accelerating implementation, advances in computational protein structure and property prediction are increasingly informing enzyme engineers. By predicting how protein sequence encodes function, researchers aim to leverage the computational models to select a reduced number of optimized sequences for laboratory measurement with the aim to lower costs and shorten timelines of enzyme engineering campaigns.[2] In this presentation, successful engineering examples and *in silico* methods from our laboratory will be highlighted, including work carried out on Fe(II)/α-ketoglutarate dioxygenases,[3-4] as well as on additional enzyme families of synthetic interest.[5-6]

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