Computational Exploration of Promiscuous Enzyme Function

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Enzymes are exceptional catalytic machines with an active site that selectively facilitates one reaction pathway over others to perform the reactions needed to sustain our vital processes at breathtaking rates. Owing to their extraordinary catalytic power under mild conditions and ease of preparation using environmentally benign techniques, enzymes gain popularity as sustainable catalysts in industrial scale processes [1]. An important strategy for the development of biocatalytic methods in industrial applications is to use the ability of enzymes to catalyze different substrates and different reactions (substrate promiscuity and catalytic promiscuity) besides their substantial catalytic activity for their natural substrates [2]. These promiscuous enzymes can further be improved and tailored to specific needs via protein engineering [3]. Identification of enzyme promiscuity as well as information on the binding site and catalytic elements for the promiscuous catalytic function to repurpose these enzymes is central to develop successful biocatalysts. This work describes a computational approach that combines state-of-the-art methods to identify promiscuous enzymes for C–C coupling reactions commonly used in the synthesis of pharmaceutically important products [4], and to elucidate the origins of their promiscuous catalytic activity [5].

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