

From raspberry flavor to addressing antibiotic resistance: learning how biocatalysis works, and teaching nature's catalysts new tricks

Enzymes collectively display a great breadth of catalytic properties yet are individually confined to one or a few specific catalytic tasks. We first present recent efforts in engineering enzymes to enable non-native recognition and thereby transform non-native substrates into useful products. We examine the cytochrome P450 BM3 oxidase that we have engineered to facilitate oxidation of non-natural substrates, using computational approaches and accelerated evolution. We then investigate the evolutionary origin of an emerging antibiotic resistance enzyme and track its modern context in multi-drug resistance contexts carried in pathogenic microbes. Biophysical characterization using native MS and electron microscopy provide insights into catalysis. We also demonstrate the application of engineered enzymes to biosensing for clinical applications.