

Enzyme Redesign: From Metal-Dependent to Metal-Independent, a Symphony Orchestra without Concertmasters

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Abstract : The design of enzymes is an extremely challenging task, and this is also true for metalloenzymes. In the case of naturally evolved enzymes, one may consider the active site residues as the musicians in the enzyme orchestra, while the metal can be considered as their concertmaster. Together they catalyze reactions as if they performed a masterpiece written by nature. The Lactonase can be thought as a member of the amidohydrolase family, with two concertmasters, Fe and Zn, at its active site. It catalyzes the quorum sensing signal- N-acyl homoserine lactones (AHLs or N-AHLs)- by hydrolyzing the lactone ring. This process, known as quorum quenching, provides a strategy in the treatment of infectious diseases without introducing selection pressure. However, the activity of lactonase is metal-dependent, and this dependence hampers the clinic usage. In our study, we use the empirical valence bond (EVB) approach to evaluate the catalytic contributions decomposing them to electrostatic and other components.

Keywords : enzyme redesign, empirical valence bond, lactonase, quorum quenching

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