

DESIGN AND EVOLUTION OF ARTIFICIAL ENZYMES

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Protein design is a challenging problem. We do not fully understand the rules of protein folding, and our knowledge of structure-function relationships in these macromolecules is at best incomplete. Nature has solved the problem of protein design through the mechanism of Darwinian evolution. From primitive precursors, recursive cycles of mutation, selection and amplification of molecules with favorable traits have given rise to all of the many thousands of gene products in every one of our cells. An analogous process of natural selection can be profitably exploited *in silico* and in the laboratory on a human time scale to create, characterize and optimize artificial catalysts for tasks unimagined by Nature. Recent progress in combining computational and evolutionary approaches for enzyme design will be discussed, together with insights into enzyme function gained from studies of the engineered catalysts.