In this thematic minireview series, the JBC presents five provocative articles on Enzyme Evolution. The reviews discuss stimulating concepts that include the emergence of primordial catalysts at temperatures that were considerably warmer than present day ones and the impact of the cooling environment on the evolution of catalytic fitness and the preservation of catalysis-promoting conformational dynamics. They also discuss the use of Urzymes or invariant modules in enzyme superfamilies as paradigms for understanding the evolution of catalytic efficiency and specificity, the use of bioinformatics approaches to understand the roles of substrate ambiguity and catalytic promiscuity as drivers of evolution, and the challenges associated with assigning catalytic function as the number of superfamily members grows rapidly.

How did enzymes evolve to speed up reactions moving them from geological to biological timescales that required lowering of formidable kinetic barriers? In the first article in the series (1), Wolfenden explains that Arrhenius analyses indicate that the temperature sensitivity of a reaction increases with its sluggishness to an extent not previously suspected. A corollary is that the emergence of life at high temperatures would have provided substantial acceleration of chemical reactions, hastening evolution. And if primordial catalysts, like modern enzymes, operated primarily by decreasing the enthalpic barrier ($\Delta H^\ddagger$) rather than by increasing $T\Delta S^\ddagger$, a selective advantage would have been conferred as the earth cooled. Enhanced mutation rates at high temperatures would have further accelerated the pace of evolution during earth’s early history.

In the second article in the series (2), Klinman and Kohen discuss the role of protein dynamics on hydride transfer catalysis. The prototype selected to illustrate the principle of coevolution of catalytically important amino acid networks is dihydrofolate reductase (DHFR) and of preserving catalytic fitness during adaptation to different environmental niches, is alcohol dehydrogenase (ADH). Residues in coevolving networks in DHFR identified by computational and genetic approaches and evaluated by biochemical ones, can couple protein dynamics to the reaction coordinate suggesting that evolutionary pressure has played a role in preserving conformational fluctuations important for catalyzing the chemical step. Similarly, adaptation of thermophilic ADH to cooler climes in psychrophilic and mesophilic organisms appears to have been accompanied by preservation of an optimal conformational landscape for catalyzing hydride transfer.

In the third article in the series (3), Carter discusses Urzymes, models of primordial catalysts constructed from the invariant cores of enzyme superfamilies. The class I and II aminoacyl tRNA synthetase Urzymes tested the hypothesis that ancestral members of each class were derived from opposite strands of the same gene. Significant catalytic activity and reduced specificity make these Urzymes novel experimental systems for understanding the evolution of modern enzymes and for examining how addition of modules might influence catalytic and allosteric functionalities related to catalytic efficiency and specificity.

In the fourth article in the series (4), Brown and Babbitt describe insights derived from large-scale studies on sequence-structure relationships, into the evolution of enzyme superfamilies. The
review examines how a relatively small number of architectural scaffolds have been repurposed to expand the repertoire of catalytic functions across diverse superfamilies. The review also discusses the challenges associated with making functional assignments as the number of newly sequenced family members grows at an ever-increasing pace and since a significant proportion of these sequences encode domains of unknown function. The authors proffer that protein similarity network analysis will be an important approach for generating hypotheses about structure-function relationships, which can be tested experimentally and perhaps even exploited to guide natural evolution of new functions in a laboratory setting.

In the fifth article in the series (5), Dunaway-Mariano, Allen and coworkers discuss catalytic promiscuity and substrate ambiguity as engines of evolutionary innovation. The potential advantages of substrate ambiguity, estimated to be a property of some 37% of metabolic enzymes in *Escherichia coli*, include disposing antimetabolites and xenobiotics, engendering redundancy and balancing metabolite pools. Using as examples the phosphatases in the haloalkanoate dehalogenase and thioesterases in the hotdog-fold superfamilies, the authors illustrate how promiscuity can be achieved via domain insertion or by varying the volume and accessibility of the active site pocket.

This collection of reviews is a sequel to an earlier set of minireviews on Enzyme Evolution in the Post-genomic Era (6).

Acknowledgement
This work was supported by grants from the National Institutes of Health (DK45776, HL58984, GM112455).

References

Introduction to the Thematic Minireview Series Enzyme Evolution
Ruma Banerjee

J. Biol. Chem. published online September 10, 2014

Access the most updated version of this article at doi: 10.1074/jbc.R114.610766

Alerts:
  • When this article is cited
  • When a correction for this article is posted

Click here to choose from all of JBC’s e-mail alerts