1993 PROGRAM

A.M.

9:00 Registration and Coffee - Room 137, Chemistry-Physics Building

9:30 Welcome by Dr. Lee Magid, Vice President for Research and Graduate Studies, University of Kentucky - Room 139, Chemistry-Physics Building

9:40 Introductory Remarks - Tina Amyes, University of Kentucky

9:45 Dr. William P. Jencks, Brandeis University
Sources of the Catalytic Activity of Ezymes

Enzymes have the ability to increase reaction rates by factors of 10^{12} or more for their specific substrates. A small fraction of this catalysis can usually be accounted for by well-understood chemistry, such as nucleophilic catalysis and acid or base catalysis by proton donors and acceptors at the active site. The source of the greater part of the observed catalysis is obscure, but it is clear that much of this catalysis arises from noncovalent interactions of the substrate(s) with the active site. Strain, distortion and desolvation in the enzyme-substrate complex can decrease the activation energy for reaction but require the expenditure of a large amount of binding energy. A fraction of our limited knowledge of the mechanisms of how catalysis of chemical reactions and of movement is mediated will be reviewed.

10:45 Discussion

10:55 Dr. Stephen J. Benkovic, The Pennsylvania State University
Catalytic Antibodies

The field of catalytic antibodies continues to envelop different reaction types and with particular emphasis on the stereochemical control of the course of the reaction. I will focus on two issues: i) the mechanism of action of several of these antibodies and ii) methods for improving their catalytic efficiency. Mechanistic analysis based on structure reactivity correlations, pre- and steady-state kinetics, and other reaction probes suggests that the most effective antibodies possess segments of the catalytic processes found in enzymes. Efforts to further improve upon the active site framework or to integrate additional functions into the antibody binding site through mutagenesis and combinatorial libraries will be described.

11:55 Discussion

P.M.

12:15 Buffet Lunch, Faculty Club. (Please return card by April 1, 1993 for reservations. Cost $8.00 to be paid at registration.)

1:40 Dr. Perry A. Frey, University of Wisconsin-Madison
Substrate Binding and Catalysis by UDP-Galactose 4-Epimerase

The most important problem in mechanistic enzymology is the elucidation of how enzymes use the substrate binding process to enhance the rates of reactions. The question of how UDP-galactose 4-epimerase uses binding interactions to nonreacting portions of the substrate to catalyze hydride transfer from the substrate to the cofactor, NAD, will be presented. The results of kinetic measurements, NMR and Raman spectroscopy, and x-ray crystallography will be fused into a coherent hypothesis that explains how the enzyme uses binding interactions to the uridine 5'-diphosphoryl moiety of substrates to enhance the intrinsic chemical reactivity of NAD at the active site. The simplest interpretation of the results will be shown to indicate that the enzyme reduces the energy of activation for hydride transfer in part by electronically destabilizing the nicotinamide ring of NAD.

2:40 Discussion

2:50 Dr. Gregory A. Petsko, Brandeis University
The Structural Enzymology of Proton-Transfer Reactions

The simplest chemical transformations in metabolism are the proton transfer reactions exemplified by certain isomerases and racemases. We have been studying three such enzymes to understand the structural features that lead to efficient proton transfer. All of these enzymes face the common problem of abstracting a hydrogen from a carbon acid of high pK_a with an enzymic base of low pK_a. We have used X-ray crystallography, site-directed mutagenesis, and molecular dynamics simulations to arrive at a set of principles for optimal catalysis of this simple reaction.

3:50 Discussion

4:00 Mixer - Room 137, Chemistry-Physics Building

UK Department of Chemistry
University of Kentucky
Lexington, KY 40506-0055

Nineteenth Annual
Symposium on

Chemistry & Molecular Biology

established in the memory of
Anna S. Naff

ENZYME CATALYSIS - MECHANISM, STRUCTURE AND DESIGN

SPEAKERS
Stephen J. Benkovic
Perry A. Frey
William P. Jencks
Gregory A. Petsko

Monday April 5, 1993

Department of Chemistry
University of Kentucky
Lexington, Kentucky 40506-0055