8:30 Coffee-CP Room 137

9:00 Welcome and Introduction — CP Room 139

9:15 INTRODUCTION-REGULATION OF ENZYME ACTIVITY
— Dr. W. N. Lipscomb —

9:30 INDUCED FIT AND ALLOSTERIC INTERACTIONS IN THE STRUCTURE AND FUNCTION OF YEAST HEXOKINASE
— Dr. T. A. Steitz —

High resolution structures of monomeric and dimeric yeast hexokinase and their substrate complexes provide important clues to the specificity and mechanism of this kinase and suggest models for its activation. The binding of glucose results in a dramatic structural change; one domain of the monomer (40% of the atoms) rotates 12° relative to the other domain, thereby closing off the deep cleft into which the sugar binds. The energy for this induced fit mechanism of enzyme specificity comes from a change in the molecular surface area. The subunits of the dimer associate in an asymmetric fashion forming a unique activator binding site between the subunits.

10:30 Discussion and Coffee Break

10:45 ASPARTATE TRANSCARBAMYLASE, AN EXAMPLE OF ENZYME REGULATION
— Dr. W. N. Lipscomb —

From two three-dimensional structures at 3 Å resolution, and from a large body of biochemical data, some remarks can be made about the assembly, the active site and the regulatory processes in the allosteric enzyme, aspartate transcarbamylase. The enzyme $C_6R_6$ has six catalytic polypeptide chains (C) and six regulatory chains (R) in $D_3$ symmetry. A Zn site of the regulatory chain shows four cysteines as ligands, just at the boundary between C and R chains. Cytidine triphosphate, the allosteric inhibitor, is located on the R chain some 40 Å from the catalytic site. Progress toward a three-dimensional structure in which a substrate analogue is bound will also be described. Kinetics for a fragment $C_6R_4$ indicate that about half of the inhibition by cytidine triphosphate remains, in some disagreement with a symmetry model but supporting a sequential model for regulatory processes. The question of the minimum structure required for regulation will be discussed in terms of the three-dimensional x-ray diffraction results.

11:45 Discussion

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Fourth Annual Symposium on

# CHEMISTRY and MOLECULAR BIOLOGY

established in memory of
ANNA S. NAFF

## *Regulation of Enzyme Activity*

Speakers
Professor William N. Lipscomb
Professor Thomas A. Steitz

## MARCH 31, 1978

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