DEPARTMENT OF COMPUTATIONAL BIOLOGY
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

SEMINAR SERIES

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Dynamical Contributions to Enzyme Catalysis: Critical Tests of A Problematic Hypothesis

Abstract: Biological systems were optimized by evolution to reach a maximum overall efficiency. However, the available structural, spectroscopical, and biochemical information do not allow one to determine what are the most important catalytic contributions. Apparently in many cases it is crucial to use computer simulation approaches in order to find out the actual contribution from different proposed catalytic factors (1-3). This talk focuses on the popular proposal that dynamical effects play a major role in enzyme catalysis. It will be pointed out that in order to have a catalytic advantage to dynamical effects they must behave in a different way in enzymes and solutions. It will be pointed out that a wide range of simulation techniques have been used to examine the magnitude of the dynamical effects and their functional role (4-6), and that it was found that these effects do not contribute to catalysis, regardless of the definition used (4-7). Among others , it will be demonstrated that the "solvent" contribution to catalysis involves similar dynamics in the enzyme and in solution and that the so-called nonequilibrium solvation effects are not dynamical effects but well defined free energy contributions. The discussion will then move to recent analysis of the relationship between flexibility and catalysis and correlated motions and catalysis (7,8) as well as tunneling and catalysis (6,9). In all cases it will be demonstrated that we do not have catalytic effects Finally, it will be illustrated that enzymes work by using their reorganized polar environment to stabilize the transition state of the reacting substrates. This means that enzyme catalysis is due to enzyme-enzyme interaction and not to enzyme-substrate interaction. Furthermore, this means that the reactive motions in enzymes are smaller rather than larger than the corresponding motions in solution.

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4:00 - 5:00 pm7
Room 6014, BST3

(Refreshments will be provided)