



## VABILO NA INŠTITUTSKO PREDAVANJE / INVITATION TO THE INSTITUTE LECTURE

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Velika predavalnica Kemijskega inštituta /  
Lecture Hall at the National Institute of Chemistry  
Hajdrihova 19, Ljubljana

### **Looking for key factors in enzyme catalysis; Some Recent Confirmation of the Electrostatic idea**

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 mechanisms. A significant part of this difficulty is associated with the ill-defined nature of some proposals and with the slow realization that computer simulation approaches provide perhaps the best way for defining and examining the issues in a unique way (1-3). This talk focuses on examination of several proposals including the dynamical proposal and, idea that correlated motions play a key role in catalysis and the relationship between KIE and catalysis. A wide range of simulation techniques are used to examine the magnitude of the dynamical effects. It is found that these effects do not contribute to catalysis, regardless of the definition used (2). Next, it is illustrated that enzymes work by using their preorganized polar environment to stabilize the transition state of the reacting substrates. This is demonstrated by analyzing the effects of mutations in DHFR (4), which has been used as an evidence for the importance of dynamical effects. Additional demonstration is provided by analyzing the preorganization effect in KSI (5), which provided perhaps the best example of the key role of the preorganization effect.

#### **References:**

- 1) Computer Simulations of Chemical Reactions in Enzymes and Solutions, A. Warshel, John Wiley & Sons, (1991).
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- 3) Electrostatic Basis for Enzyme Catalysis; A. Warshel, P. K. Sharma, M. Kato, Y. Xiang, H. Liu, and M. H. M. Olsson, Chem. Rev., 106,3210-3235 (2006).
- 4) The Catalytic Effect of Dihydrofolate Reductase and its mutants is determined by Reorganization Energies Hanbin Liu and Arie Warshel, Biochemistry (ASAP).
- 5) Electrostatic Contributions to Binding of Transition State Analogues Can Be Very Different from the Corresponding Contributions to Catalysis: Phenolates Binding to the Oxyanion Hole of Ketosteroid Isomerase, A. Warshel, P. K. Sharma, Z. T. Chu and J. Aqvist, Biochemistry 46, 1466-1476 (2007).

Kindly invited!

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