

Seminar in Physical Chemistry

**Ben-Gurion University of the Negev
Department of Chemistry**

Wednesday, March 21, 2012

Time 16:00

Bldg. 29 Room 307

Enzyme Catalysis and Nano Chemistry from a Computational Perspective

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Enzymes are fascinating biological macromolecules which catalyze chemical reactions at rates which approach the encounter rate between the enzyme and substrate. Studying the nature of enzyme catalysis is of great importance in order to appreciate Nature's achievement, develop synthetic catalysts, and design new inhibitors. An increasingly important tool in understanding enzyme catalysis is molecular simulations based on hybrid quantum mechanics- molecular mechanics (QM/MM) potential energy surfaces. In the current presentation we describe the importance of nuclear quantum effects in three oxidoreductase enzymes studied in our group: (1) Nitroalkane Oxidase (NAO), Dihydrofolate Reductase (DHFR), and Formate Dehydrogenase (FDH). In NAO the overall rate limiting step is a proton transfer, while in DHFR and FDH the chemical step entails a stereospecific hydride transfer. In all of these enzymes we compute rate constants and kinetic isotope effects (KIE) using accurate hybrid QM/MM potential energy surfaces in conjunction with novel classical and quantum path-integral simulation methods developed in our group. For the NAO reaction we study the enzymatic reaction as well as an analogous proton abstraction in aqueous solution. Interestingly, we show that in NAO there is a small *catalyzing tunneling contribution*. This conclusion is based

on computationally predicted and experimental primary and secondary KIEs, as well as direct tunneling calculations. In the case of DHFR and FDH we present results indicating differential quantum delocalization in the reactant and transition states based on hydride momentum distribution functions obtained from novel open path-integral simulations.

I will also describe work on properties of self-assembled monolayers (SAMs). SAMs are excellent models for studying interfacial reactions and various properties of thin films. Carboxylic acid terminated SAMs (CATSAMs) are of special interest since their surface properties are highly pH-dependent. To elucidate the complicated pH-dependent structural properties of CATSAMs, we combine force field molecular dynamics simulations with hybrid QM/MM calculations of vibrational frequencies to elucidate structural features of the CATSAMs.