

Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes

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Abstract

A hybrid quantum-classical approach for the simulation of proton and hydride transfer reactions in enzymes will be presented. This approach includes electronic and nuclear quantum effects, as well as the motion of the entire solvated enzyme. It allows the calculation of rates and kinetic isotope effects for comparison to experiment and elucidates the fundamental nature of the nuclear quantum effects such as zero point energy and hydrogen tunneling. This approach also provides insight into the relation between specific enzyme motions and catalytic activity. It distinguishes between thermally averaged motions that influence the activation free energy barrier and dynamical motions that influence the barrier recrossings. Applications to the biochemically important enzymes liver alcohol dehydrogenase and dihydrofolate reductase will be discussed.