

Proton-Coupled Electron Transfer in Soybean Lipoxygenase: Dynamical Behavior and Kinetic Isotope Effects

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Theoretical studies of the proton-coupled electron transfer reaction catalyzed by the enzyme soybean lipoxygenase will be presented. The calculations are based on a vibronically nonadiabatic formulation that includes the quantum mechanical effects of the active electrons and the transferring proton, as well as the motions of all atoms in the complete solvated enzyme system. The rate is strongly influenced by the proton donor-acceptor frequency, the vibronic coupling, and the protein/solvent reorganization energy. The calculations reproduce the experimentally observed magnitude and temperature dependence of the kinetic isotope effect (KIE) without fitting any parameters directly to the experimental kinetic data. They also provide insights into the physical basis for the large magnitude and weak temperature dependence of the KIE. The large magnitude of the KIE arises mainly from the dominance of ground state tunneling and the relatively large ratio of overlaps for the hydrogen and deuterium vibrational wavefunctions. The weak temperature dependence of the KIE is due in part to the dominance of the local component of the proton donor-acceptor motion. The impact of mutations on the enzyme motions coupled to catalysis and the relation between these motions and the experimentally observed rates and KIEs will be discussed.