Effective strategies for unraveling microscopic energetics and dynamics of proton transport in complex systems: From QM/MM to Monte Carlo EVB based models

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Proton transport (PTR) plays a major role in many biological processes. The control of PTR by biological systems became a popular issue after the discovery of aquaporin and subsequent works. These studies illustrated that aquaporin transports water while preventing PTR. Most workers in the field have argued that PTR in proteins is controlled by the so-called Grotthuss mechanism, where the orientation of the water molecules plays a crucial role. Furthermore, simulation studies of the transport of neutral water through aquaporin were used to postulate how the PTR is controlled. However, it is not clear why simulations of neutral water molecules should be useful in studies of charge transport processes. Obviously, this and other related issues can only be explored by simulating the relevant PTR process.

This lecture will introduce reliable and effective methods for actual simulations of PTR in solutions and proteins. This will include QM/MM methods, the EVB method [1] and a simplified version of the EVB that will be used as our main tool in studies of multistep PTR. It will be demonstrated that PTR in proteins is controlled by the electrostatic free energy of the proton rather than the effect of water orientation. This point will be illustrated by studies using different levels of our model, ranging from the simplified modified Marcus' equation [2-4] to simplified EVB with Brownian Dynamics and / or Monte Carlo and finally fully atomistic EVB [3]. The use of our approach in probing key problems (such as the action of cytochrome c oxidase [3-7]) will be illustrated, emphasizing its ability to provide a molecular unpretending of fundamental pumping process

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