THEORY AND SIMULATION OF BIOLOGICALLY - IMPORTANT CHARGE TRANSFER REACTIONS

R. I. Cukier, Department of Chemistry
Phone: 355-9715 x 263. E-mail: cukier@argus.cem.msu.edu.

The coupling of proton motion to charge separation is basic to mechanisms of biological energy conversion. The proteins and enzymes of photosynthesis and respiration have optimized structures that derive their function by utilizing energy gathered along a charge separating network to drive a proton pump, which in turn is manifested in a transmembrane chemical potential that provides the energy for the synthesis of complex biomolecules. From a bioenergetic standpoint, a crucial issue with respect to structure/function relations for the biological machinery of Photosystems I and II and cytochrome *c* oxidase is this coupling of the electron to the proton. As succinctly stated by Feher in the context of bacterial RCs "we do not know from experimental measurements whether electron transfer precedes or follows proton transfer, since these individual steps have not been kinetically resolved". Yet the role of protons in mediating electron transfer is not restricted to the processes of complex structures such as these. Recent studies on electron transfer proteins, such as cytochrome *c*, provide evidence that the conduction of electrons involve interchain hops through hydrogen-bonded peptide residues of the protein. Thus even in the simplest of proteins, function is derived from the coupling of electron transfer to proton motion.

Our approach (summarized in "*Proton-coupled electron transfer*" R. I. Cukier and D. G. Nocera, Ann. Rev. Phys. Chem. **49**, 337 (1998)) is to develop quantum mechanical (QM) and statistical mechanical (SM) theories and simulation methodologies to address the above and related problems. In essence, a solute (where the charge transfer (CT) will take place) is embedded in a solvent (e.g., a protein). The solute must be treated with QM, as charge transfer reactions of electrons and protons are tunneling reactions, and the solvent, by virtue of its less detailed role, and by current necessity computationally, is treated classically. That CT reactions move charge substantially implies that the coupling of solute to a polar solvent is essential to the energetics responsible for the transfer. Hence, SM methods must be used. We use QM schemes (solving Schrödinger's equation for wavefunctions and energies of electrons and protons in the solute) and SM theory, (continuum electrostatic description and/or integral equation methods) and/or methods of Molecular Dynamics (MD), for computational approaches to describe the solvent. We have integrated QM and MD in one simulation package to address *model* problems of proton-coupled electron transfer (PCET). Future plans are to simulate PCET in biologically relevant context. Also, to consider other intrinsically QM/MD problems such as proton chains involved in proton translocation for establishment of electrochemical gradients across a membrane.

What we need: Help with biology - systems of interest. Help with computational biology - doing MD for large-scale systems such as proteins/membranes. Help with computational methods. We recently migrated from FORTRAN to C++ and need help in improving algorithms for speed and reliability, and in parallelizing code. (A goal - assemble a multi-CPU linux/PC/PVM - based supercomputer.)

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