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Computational Study of Electron Tunneling in Proteins

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Electron transfer (ET) processes in proteins are characterized by the motion of a single electron between centers of localization (such as the chlorophyll dimer in photosynthetic reaction centers). An electronic donor state D is created by the injection of an electron or by photo-excitation, after which the system makes a radiationless transition to an acceptor state A , resulting in the effective transfer of an electron over several angstroms. The experimental and theoretical understanding of the rate of this process has been the focus of much attention in physics, chemistry and biology.

Electron Transfer Tubes

The initial work funded by the grant included the development and computational testing of the electron transfer *tube* model of electron transfer. This model is based on the idea that the detailed arrangement of atoms and bonds in protein media can be a primary determinant of electron transfer rates.

Electron transfer tubes are made up of specific sequences of bonding orbitals. A given donor and acceptor pair in a molecular system can be connected by more than one ET tube. Each tube is associated with a specific coupling factor that contributes to the overall electron transfer coupling between the donor and acceptor. Moreover, these different couplings interfere in quantum mechanical fashion; adding more tubes does not always enhance electronic coupling, it can also degrade it.

Tubes are a useful concept in that they can be created or disrupted by protein mutation, thus offering a way to not only test the theory, but feed experimental numbers into the theory.

The attached reprint "*Electron Transfer Tubes*"

by J.J. Regan and J.N. Onuchic (from *Electron Transfer: From isolated Molecules to Biomolecules*, 1999 John Wiley & Sons — see attached) contains a detailed discussion of the theory and its application to the interpretation of a series of electron transfer experiments performed in the protein Azurin.

Cytochrome c Oxidase

Cytochrome c oxidase, a membrane-based enzyme, is a terminal component in the respiratory chain in mitochondria and many bacteria. It catalyses the reduction of molecular oxygen to water, while at the same time pumping protons across the membrane to establish a voltage across it. The central question is how does the protein arrange to deliver electrons and protons to their various destinations? The mechanism of this process is still not fully understood, despite the fact that the enzyme has been crystallized and subjected to X-ray studies.

In *Pathways for Electron Tunneling in Cytochrome c Oxidase* by J.J. Regan, B.E. Ramirez, J.R. Winkler, H.B. Gray and B.G. Malmström (*J. Bioenergetics and Biomembranes*, v30:1, p35, 1998 — see attached), the electron transfer part of the question is studied using the tube model on the structure obtained from crystallography.

The paper offers a wiring diagram for the enzyme that can be tested experimentally through the use of site-directed mutagenesis, and suggests ways in which the electron transfer can gate the proton transfer and vice versa.

Papers attached

Two papers describing these results in more detail are attached.

reprints separated for later processing

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