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Electron Transfer Bifurcation: A Mechanism for Energy Conservation at the level of Electrons.

Electron transfer bifurcation ('bifurcation') enables enzymes to produce a more potent reductant at the expense of a weaker one, in apparent defiance of thermodynamics. However no rules are broken, because only one super-reducing electron is produced from each pair of electrons consumed. In-effect, exergonic transfer of the second electron pays for endergonic transfer of the first. Thus, along with the valuable increased-potency reduced electron carrier, an energy-depleted product is also formed. The potent reduced ferredoxin or flavodoxin product supports biological fixation of Nsub2/sub or COsub2/sub, two reactions we would like to be able to facilitate in man-made materials. Hence our interest in understanding the mechanism of bifurcation. A central problem is to understand how bifurcating enzymes provide an exergonic path to allow the favorable electron transfer required to 'pay the bills', but limit its use to a single electron of each pair. Somehow, one electron can (and must) use this path, but the other one is prevented from doing so, being transferred instead to a less favorable acceptor. Successful direction of this electron (and most of the energy) to the unfavorable acceptor is the process that captures energy released from the favorable transfer, making it available for future use.

Working with bifurcating Electron Transfer Flavoprotein (BfETF), we are assessing the applicability of several possible mechanisms that could bar the high-energy electron from exploiting the exergonic path and dissipating energy. Our work demonstrates that thermodynamic considerations may prevent a second electron from using to the endergonic path, but this presentation will focus on possible significance of an enormous domain-scale conformational change that is documented in structural studies and proposed to gate electron transfer. Accelerated molecular dynamics (MD) trajectories and quantum mechanical (QM) calculations are underway to understand what motions may be coupled to catalytic events (as opposed to reflecting fluctuations inherent in the protein structure). These approaches enable us to assess the significance of redox-coupled movements of individual protons and reorganization of crucial hydrogen bond networks in the interfaces between domains proposed to move relative to one-another. Meanwhile, we are using Small Angle Neutron Scattering (SANS) and Nuclear Magnetic Resonance (NMR) to learn what conformations may be present under conditions of catalytic activity. SANS and NMR are ideally suited to the task because they do not perturb the oxidation states of flavins, which constitute key steps in BfETF turnover. Unfortunately, the common X-ray and FRET-related methods can cause photoreduction of flavins and therefore could trigger the conformational change we seek to control and characterize. Indeed, our new data reveal subtle but consistent changes in the SANS profiles in response to reduction of the BfETF. Thus we have evidence that a conformational event is indeed coupled to step(s) in bifurcation, in BfETF.

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Topic

Biological Energy Transfer

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