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Introduction

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Electron transfer reactions play essential roles in numerous important biological processes, including photosynthesis, mitochondrial respiration, and intermediary metabolism. There are two general classes of biological electron transfer reactions: (1) oxidation and reduction reactions of organic metabolites that usually involve the short-range transfer of two or more electrons associated with covalent bond formation and breakage, and (2) long-range transfer of single electrons over distances of tens of Ångstroms. Electron transfer reactions in this second class are involved in the primary energy coupling mechanisms of photosynthesis and respiration. Marcus greatly simplified the conception of long-range electron transfer by recognizing that the reactants and products are weakly coupled, and can be described by two intersecting harmonic oscillator potentials. With this assumption the rate of electron transfer has a simple Gaussian dependence on the free energy of the reaction, with an optimum when the free energy is equal to the reorganization energy. This later parameter is a measure of the energy required to rearrange and repolarize the reactants and surrounding solvent before electron transfer can occur. Marcus also proposed that the rate of electron transfer would have a simple exponential dependence on the distance between the donor and acceptor centers.

The present minireview series describes extensive experimental and theoretical studies of the factors which control long-range biological electron transfer. The first review by Moser *et al.* presents a broad overview of the different classes of biological electron transfer reactions, and summarizes the development of the original Marcus theory as well as more recent theories of electron transfer. Detailed studies of the photosynthetic reaction centers from *Rps. viridis* and *Rb. sphaeroides* have revealed the primary importance of free energy, reorganization energy, and distance in controlling the rate of electron transfer. The second review by Allen and Williams describes a series of *Rb. sphaeroides* reaction center mutants in which the redox potential of the bacteriochlorophyll dimer is varied over a range of 355 mV. The resultant change in reaction free energy was found to significantly alter the rates of electron transfer to and from the dimer as predicted by Marcus theory. These studies indicate the primary role that the reorganization energy plays in facilitating the initial charge separation reaction and limiting the nonproductive charge recombination reaction to the ground state. Curry *et al.* describes further refinements in the widely used pathway model of electron transfer to include different protein structural elements and a treatment of the protein–protein interface. Bjerum *et al.* summarize the development of the ruthenium labeling technique to study intraprotein electron transfer, and describe recent experiments demonstrating the importance of reorganization energy and pathway in determining the rate of electron transfer. The review by Tollin describes the development of flash photolysis methods utilizing flavins to study both intraprotein and interprotein electron transfer reactions. Mauk *et al.* review the extensive experimental and theoretical studies of the binding interaction between cytochrome *c* and cytochrome b_5, and analyze the role that binding kinetics and specificity play in interprotein electron transfer. Durham *et al.* discuss the development of the ruthenium photoreduction technique to measure the actual rate of electron transfer within the 1:1 electrostatic complex between cytochrome b_5 and cytochrome *c*. Evidence is presented that complex formation lowers the reorganization energy by displacement of solvent, thus favoring electron transfer. The last review by Millett *et al.* describes rapid kinetic studies of electron transfer between cytochrome *c* and cytochrome *c* peroxidase. This is a very attractive system for investigating fundamental questions about interprotein electron transfer, especially in view of the X-ray crystal structure of the 1:1 complex between the two proteins determined by Pelletier and Kraut (*Science* **258**, 1748–1755, 1992; cover photograph). At the center of the binding domain, the exposed heme methyl group of cytochrome *c* is in van der Waals

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contact with the cytochrome *c* peroxidase residues Ala-193 and Ala-194. Pelletier and Kraut proposed an efficient electron transfer pathway that extends from the cytochrome *c* heme methyl group through Ala-194, Ala-193, and Gly-192 to the indolyl radical cation on Trp-191 (cover photograph). Kinetics studies utilizing a covalently attached ruthenium complex demonstrate that cytochrome *c* rapidly transfers an electron to the Trp-191 indolyl radical cation in the oxidized form of cytochrome *c* peroxidase. The rate constant of 2×10^6 s^{-1} is consistent with theoretical predictions for the electron transfer pathway proposed by Pelletier and Kraut. Electron transfer to the oxyferryl heme in cytochrome *c* peroxidase is much slower, and appears to be controlled by proton transfer to the oxygen atom on Fe(IV)=O to form Fe(III)–OH, or release of the oxygen atom as H_2O. This type of linkage between electron transfer and proton transfer occurs in a number of energy coupling mechanisms, including proton pumping by cytochrome *c* oxidase.