Electron tunneling pathways in proteins: influences on the transfer rate

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Abstract

A strategy for calculating the tunneling matrix element dependence on the medium intervening between donor and acceptor in specific proteins is described. The scheme is based on prior studies of small molecules and is general enough to allow inclusion of through bond and through space contributions to the electronic tunneling interaction. This strategy should allow the prediction of relative electron transfer rates in a number of proteins. It will therefore serve as a design tool and will be explicitly testable, in contrast with calculations on single molecules. As an example, the method is applied to ruthenated myoglobin and the tunneling matrix elements are estimated. Quantitative improvements of the model are described and effects due to motion of the bridging protein are discussed. The method should be of use for designing target proteins having tailored electron transfer rates for production with site directed mutagenesis. The relevance of the technique to understanding certain photosynthetic reaction center electron transfer rates is discussed.

1. Introduction

The DeVault–Chance experiment first demonstrated tunneling in a biological system and continues to motivate fundamental studies of reaction rate theory (DeVault and Chance 1966, DeVault 1984). While the origin of the activationless behavior at low temperature has been assigned to nuclear tunneling, electron tunneling occurs in these reactions over the full temperature range (Hopfield 1974, Chance et al. 1979). Considerable effort has been spent calculating the expected temperature dependence of the rate in these and other biological systems. The fact that the electron tunnels means that an understanding of the overall rate, and its distance dependence, should follow from a detailed description of the protein's role as a 'tunneling barrier'.

Tunneling rates are exquisitely sensitive to the energetics of the intervening medium and the donor-acceptor separation (Hopfield 1974). The medium is responsible for the donor–acceptor interaction, which decays roughly exponentially with separation distance. The electron transfer rate is proportional to the square of this interaction energy. The interaction is weak and it is difficult to calculate its absolute size with much confidence. Our approach to this problem has been to estimate the dependence of the matrix element on the length and chemical composition of the intervening medium, rather than to attempt detailed numerical estimates of the matrix element (Beratan and Hopfield 1984, Onuchic and Beratan 1987, Onuchic et al. 1986). As such, we have asked questions about how the topology and orbital energetics of the intervening medium modify the donor–acceptor interaction in weakly coupled photosynthetic model systems. From these model systems we are attempting to develop a set of self-consistent parameters to calculate the electronic tunneling interaction in proteins. In this paper we will summarize the model as it applies to proteins, give examples of modified...
proteins for which the model is beginning to make predictions, and use it to speculate on mediation of the tunneling interaction in bacterial photosynthetic reaction centers.

2. Electron transfer and bridge protein tunneling

The energy required to oxidize or reduce the intervening protein residues from the localized electron transfer active states is much larger than \( k_B T \) at room temperature (this energy is actually larger than that of visible light as well). Since the electron transfer distances are so large, the transfer rate is controlled by the electron tunneling matrix element over the full temperature range of the experiments. When this was realized (Hopfield 1974, Jortner 1976, Grigorov and Chernavskii 1972) it became clear that the temperature independence of the DeVault–Chance experiment at low temperature arose from the onset of nuclear tunneling. (Bixon and Jortner recently proposed an alternative explanation of the temperature dependence of this reaction (Bixon and Jortner 1986) based on electron transfer involving different cytochromes as possible donors instead of nuclear tunneling. Such an alternative seems implausible because of the results showing nuclear tunneling in analogous synthetically modified systems. The possibility of having multiple donors in modified hemoglobins (Peterson-Kennedy et al. 1986) which indeed show 'nuclear tunneling' does not exist.) These nuclear modes undergo reorganizations which are coupled to removal/introduction of charge at the two localization sites in the protein. This important distinction between electronic and nuclear coupling allowed progress on two fronts: the challenge of understanding the transition between nuclear tunneling and thermally activated regimes, and the problem of describing the protein mediation of the electronic tunneling. It was clear very early that the protein mediated the tunneling, i.e., tunneling is not controlled by the (very weak) direct coupling between donor and acceptor sites. The rates of electron transfer between donor and acceptor could not be explained by ignoring the mediating effects of the protein.

In parallel with the protein experiments, chemists were studying bridge mediated tunneling transport reactions (Halpern and Orgel 1960, McConnell 1961) and the crucial influence of the bridge was becoming apparent. Rough estimates were made of the donor–acceptor interaction energy (the tunneling matrix element) dependence on the separation distance in the reaction center (Hopfield 1974, Jortner 1976, Grigorov and Chernavskii 1972). Proteins were pictured, for example, as square tunneling barriers a few electron volts high (Hopfield 1974). Meanwhile, synthetic model building bloomed and began to probe the nature of the bridge mediation of electron tunneling. It was not until the 1980's that truly molecular descriptions of long distance tunneling through proteins and hydrocarbon spacers were presented (Larsson 1981, Beratan and Hopfield 1984, Onuchic and Beratan 1987). These studies predicted a sensitive dependence of the interaction energy on the topology of the bridging groups (because of interference and orientation effects), the orbital energies of these groups relative to the tunneling electron (because of weak coupling mixing arguments), and the dominance of through bond vs. through space coupling. Beginning with testable models for electron transport in model compounds, we have begun to investigate the molecular origins of the electronic coupling in proteins (Beratan et al. 1987, Cowan et al. 1988), and this is the subject of the paper. The prior work and the work we will describe here is based on a one-electron tight-binding model for the electronic structure of the protein. The fact that the 'one-electron' is actually an effective electron has been discussed (Onuchic and Beratan 1987, Onuchic et al. 1986) and, therefore, justifies this approximation. This strategy is supported by more elaborate quantum chemical calculations (Newton 1988). In the future we intend to use quantum chemical approaches as one technique to obtain estimates for the parameters in our Hamiltonian.

How the protein environment controls the rate of electron transfer in photosynthetic bacteria has been of interest for the last two decades. The ability to separate charge with a yield close to 100%, and maintain long lived charge separation (order of 1 s), makes the photosynthetic system very efficient for converting light into chemical energy (Govindjee 1982). The striking question is what makes the system work so efficiently. Since we know that the electron transport processes involved in the primary events of photosynthesis are electron tunnel-