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LONG DISTANCE ELECTRON TRANSFER IN POLYMERS AND PROTEINS

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INTRODUCTION

A key stumbling block in efficient artificial photosynthetic charge separation is preventing energy wasting diffusive recombination of the initial photochemical redox products. Clearly nature has found a solution to this problem by controlling the spatial arrangement of the various redox proteins in the chloroplast, so that charge separation occurs without diffusion. However, attempts to mimic this efficient biological solution are limited not only by our ignorance of the molecular structure of the chloroplast, but also by a more fundamental ignorance of the key parameters which control the rates of diffusion free (long distance) electron transfer reactions.

The studies described herein are the result of initial efforts in our laboratory to understand the parameters which control electron transfer rates in diffusion free systems. The systems investigated range from "simple" random donor-acceptor ensembles to studies of electron transfer in specific physiological protein protein complexes.

A SHORT PRIMER ON THEORY

Since we wish to "understand" long distance electron transfer, it is ultimately necessary to place our observations in the context of a quantitative theory. The present discussion is necessarily brief. For a full description, a number of excellent reviews are available.[1]

For better or worse, there is certainly no shortage of theories to describe long distance electron transfer reactions. Although such theories have a long history, the present brief discussion will focus on the classical theory of Marcus,[1b] and recent quantum mechanical modifications by Hopfield,[1c] Jortner[1d] and others.[1e-g]

First, following Marcus, we write a rate constant (transition probability) as $k = \nu_{electronic}(F.C.)$, where F.C. is the Franck Condon weighted density of states. The Born Oppenheimer approximation is invoked to separate out the electronic and nuclear terms, so that each might be considered separately. The Classical (Marcus) theory makes further assumptions. First, it assumes that Franck Condon restrictions apply, so that all nuclear coordinates rearrange before electron transfer occurs. Second, it assumes that all the critical

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reorganizations (all internal and solvent vibrational modes, $\hbar\omega$) which occur on electron transfer can be classically populated (ie: $\hbar\omega \ll kT$). In this case the Franck Condon factor is given by the familiar quadratic Marcus formula: $E_{act} = \frac{(\Delta E - Er)^2}{4Er}$ where ΔE is the driving force for reaction and Er the total reorganization energy for electron transfer. This second assumption is removed in the recent quantum formulations, but the quantum formulas reduce to the Marcus equation when $\hbar\omega \ll kT$. In the general case, with classical (medium) modes $\hbar\omega_s \ll kT$ and an average high frequency mode $\hbar\omega_v > kT$ we obtain

$$k(r) = (\pi/\hbar^2\lambda_s kT)^{1/2} |V(r)|^2 \sum_{W=0}^{\infty} (e^{-S}S^W/W!) \exp -[(\Delta G+\lambda_s+W\hbar\omega)^2/4\lambda_s kT]$$

$\lambda = \sum \Delta_i \hbar\omega_i$; $\Delta_i = (\mu_i\omega_i/2\hbar)^{1/2}\Delta R_i$ where ΔR_i = nuclear displacement

μ_i = reduced mass for Nth vibration, W = number of high frequency vibrational in product(s)

$V(r) = \exp(-\alpha R)$

Classical theory makes one assumption about the electronic term as well. It is assumed that electron transfer reactions involve relatively strong coupling between the reactant and product surfaces (fig. 1,2). An upper and lower surface are created by an avoided crossing, with a separation H_{AB}. When H_{AB} is large, any reaction which reaches the nuclear configuration at the classical turning point will proceed to products with unit probability. Thus, we say the reaction is adiabatic (Fig. 1).

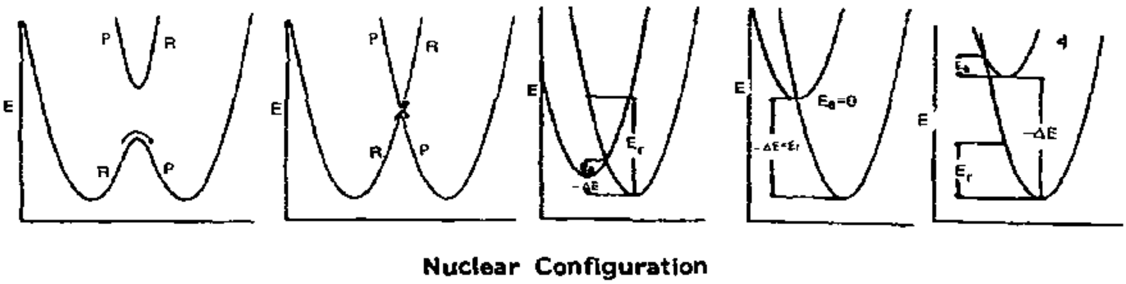


Fig. 1. Comparison of adiabatic (left) and non adiabatic (right) reaction surfaces

Fig. 2. Dependence of activation energy (Eact) on ΔE and reorganization energy (Er) left-right; "normal", activationless inverted kinetics.

For long distance electron transfer, this assumption must be abandoned. As the distance between the reactants increases their interaction energy, H_{AB}, decreases. As H_{AB} becomes very small, many trajectories will not lead to product formation, but will simply pass the transition state, proceed up the R surface, and return to the reactant well. (Fig 1)

For such "nonadiabatic" reactions, the probability of proceeding from reactants to products can simply be formulated as a problem in electron tunneling. In this formation (following Gamow)[6] the probability of barrier penetration

depends on the barrier height, V, given as the difference in vertical ionization potential between the donor and the surrounding medium. The probability also depends on the barrier width, R, given as the distance (in A) between the donor and acceptor.

With this parameterization the frequency factor becomes

$$\nu_{elec} = kT/h \exp(-\alpha R) \qquad (2)$$

where $\alpha = (4m\bar{V})^{1/2})/h$: $\quad (\alpha = (\bar{V})^{1/2})$.

This basic treatment is common to the popular quantum mechanical models of electron transfer. However, the parameterization of eqn. 2 varies tremendously between theories, depending on the chemical intuition of each theorist. For example, Jortner sets $\alpha = 2$, While Hopfield suggests $\alpha = 1.4$. While the simplicity of this approach to understanding the dependence of rate on distance is attractive, it may not (always) be correct. A different approach to understanding long range electron transfer has been presented by Beitz and Miller[1], based on a general superexchange model. In this model, the electron exchange interaction depends on the product of "n" nearest neighbor interactions, as $H_{AB} = \beta(\beta/B)^n$ where β is the exchange energy (for example, the Huckel exchange parameter beween adjacent carbons in benzene) and B is the electron (or hole) binding energy. This model allows for ready charge propagation via either electron ("conduction band") or hole ("valence band") tunneling. An important difference between the Gamow type barrier tunneling models and the superexchange model lies in the dependence of H_{AB} on electron (hole) binding energy. Finally, Beratan and Hopfield[1f] have noted experimental electron transfer results on mixed valence ruthenium adducts of general structure:

can be best explained in terms of through bond coupling through the carbon framework, rather than via a through space model described above.

With these caveats in mind, the primary problem in understanding long distance electron transfer reduces to

1) Is equation 2 valid?

2) If so, what values of α are appropriate to describe electron transfer? Is one α value (or a small range) sufficient, or is each reaction "unique"?

EXPERIMENTS IN RANDOM ENSEMBLES

Static Quenching: The Perrin Model

Our first approach to these problems was to set up random ensembles contain-

ing ranges of known donor acceptor distances.[2-4] This is easily accomplished by codissolving the donor (a photoexcitable chromophore, e.g., $Ru(bpy)_3^{2+}$) and acceptor (in large excess) in a fluid. The solution is cooled until it becomes rigid, so that diffusion is negligible in the time scale of interest. Most of our early studies were carried out in glycerol. When rigorously dried, glycerol has a viscosity $\eta > 10^4$ at $T < 270°K$. Thus on the short timescale of an excited state lifetime ($\tau < 10^{-6}$ sec) diffusion is negligible. By monitoring (electron transfer) quenching of the excited state emission, information may be obtained on the dependence of rate on distance. The results of our first static emission quenching experiments are shown in figure 3. Clearly, diffusional (Stern Volmer) quenching cannot explain the results. A diffusional model

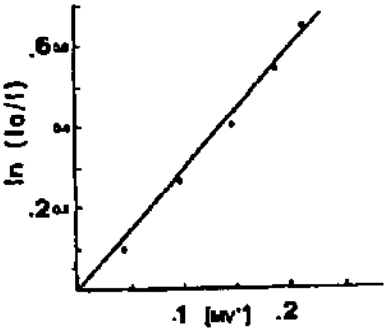
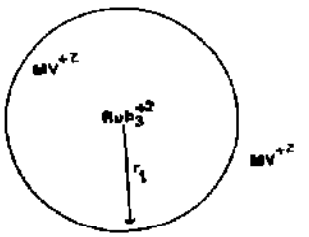


Fig. 3. "Perrin plot" for $Ru(Bpy)_3^{2*}$ + MV in rigid glycerol (-20°C)



Perrin Formulation

$I_0/I = e^{N_0 V a}$

N_0=Avogadro's number

V=volume of quenching sphere

a=concentration of MV^{+2}

Fig. 4. Schematic illustration of long distance quenching. When the donor acceptor distance is Rq, $k(et) = 1/\tau_o$.

predicts I_0/I should depend linearly on acceptor, where in fact a logarithmic dependence is observed.[2]

This result is easily understood in terms of a simple model suggested by Perrin (fig. 4). We assume that the quenching mechanism depends strongly on distance (for electron transfer, $k^\circ(\exp^{-\alpha R}$, vide supra). There exists a "critical" distance, R_c, such that $k_R = kem = (\tau_0)^{-1}$. If the donor acceptor separation, $R < R_c + \alpha$ then the quenching rate $kq >> kem$ and essentially all emission will be quenched. With this assumption, the Perrin relation follows. With this analysis, the slope of the plot in fig. 3 gives the critical distance for electron transfer, and so defines an "accessible distance" for electron transfer within the time τ_0.

As shown in fig. 5, these accessible distances depend markedly on ΔE, as predicted by classical theories of nuclear reorganization. At optimal ΔE values, a rate of 10^6 s^{-1} is obtained at separations of ca. 10A between the nearest π carbons of the donor and acceptor.

Simultaneous and independent work by John Miller and Gerhard Closs and their coworkers at Argonne National Labs using organic donor acceptor pairs in MTHF have resulted in essentially equivalent conclusions.[5]

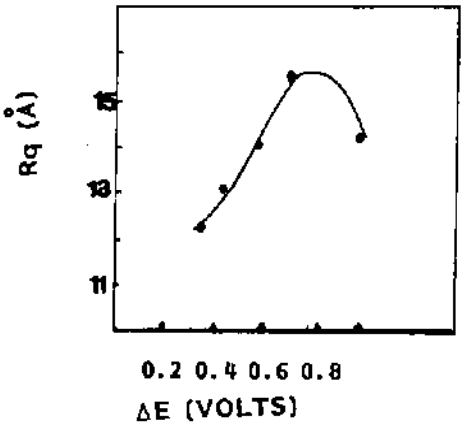


Fig. 5 Dependence of critical distance for electron transfer or ΔG for the $Ru(LL)_3^{2+*}$ + MV^{2+} reaction in rigid glycerol (-20°C).

Time Resolved Emission Quenching: Estimates of α

While such data are useful in defining estimates of reasonable rates at long distances, static measurements alone cannot provide any estimate of the parameter α. Such information may in principle be obtained by time resolving the emission quenching. Many donor acceptor distances, each with a characteristic transfer rate, exist in a random ensemble. Thus a complex, nonexponential rate expression is required to describe electron transfer luminescence quenching in random ensembles. Conversely, given such an expression, if the donor acceptor distribution function is known, then "α" may be obtained by a one parameter fit of the complex decay curve.

Fortunately, the required expression was derived some time ago by Inokuti and Hirayama (and independently, in a different context, by Hopfield). In essence, the emission intensity at time t, $I_{em}(t)$ is given by [28]

$$I_{em}(t) = \exp[(t-/\tau_0) - \gamma^{-3}\, C/c_0\sigma(e\gamma t/\tau_0)] \qquad (3)$$

C is the acceptor concentration, $g(\tau) = (\ln z)^3$ and $\gamma = 2R_0/l$. A fit of the experimental lifetime decay for the system $Ru(3,4,7,8\ me_4phen)^{2+}$ and *methyl viologen by eqn.3 is shown in fig.6. The data, over four decades in time, are surprisingly well described by eqn. 3, using $\ell = 0.5$ ($\alpha = 1.2$) as the only adjustable parameter.[3]

*It is important to study essentially activationless reactions to minimize any effect of time dependent solvent relaxation on the lineshape, as discussed in detail elsewhere [7-11].

"Hole" Transfer Studies in Polymers (Lexan):: Dependence of α on binding energy

For comparison, studies of "hole" transfer should be mentioned. We have com-

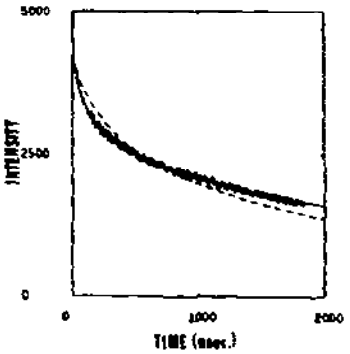


Fig. 6. Quenching of Emission of $Ru(bpy^{2+})_3$ by methyl viologen in rigid glycerol (-20°C) solid line shows fit to eqns 2 + 3 assuming α =1.3 as only adjustable parameter.

pleted detailed studies of the electron reaction $Ru(LL)_3^{2+}$ + aniline -X⟶X-aniline$^+$ + $Ru(LL^-)_3$. (LL = phenanthroline homolog). The results of time resolved experiments analyzed as outlined in the preceding section, give α = 1.1 (fig. 7) for LL = 4,4,(COOEt)bipyridine and X = $N(CH_3)_2$ (TMPD). We then measured how critical quenching radii (R_c) depend on ruthenium ligand, LL. As the ligand substituents change, the reaction driving force, and binding energy both change. These parameters could be separated by changing the aniline derivative. By changing only the acceptor, ΔE changes, but the (Ru) donor binding energy remains constant. The results of these experiments, shown in fig. 8, are surprising. Within experimental error, equivalent R_c values are obtained at constant ΔE, regardless of whether donor or acceptor is changed. In other words, although effective tunneling distances are sensitive to Franck Condon factors as theory suggests, they are only weakly sensitive to donor (hole) binding energy.

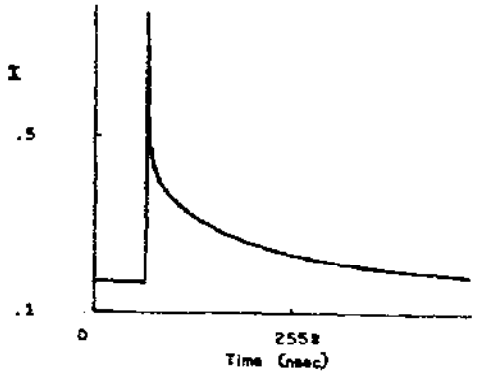


Fig. 7. Fit of emission quenching to eqns 2 + 3 assuming =1.1 for $Ru(4,4'-CO_2t)bpy)_3^{2+}$ TMPD in a lexan film.

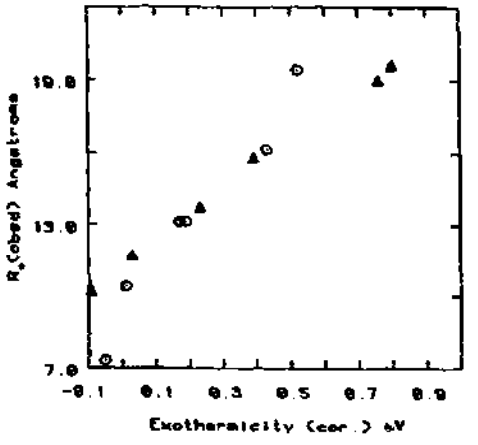


Fig. 8. Critical quenching distances for $RuLL_3$ + aniline derivatives. Ru ester + different anilines different Ru adducts + TMPD.

These results are not consistent with Gamow type models: if α depended on $(B)^{1/2}$ then the $Ru(me_2\ bipyridine)_3^{2+*}$/TMPD reaction should proceed 10^3 times -slower than the isoenergetic $Ru((COOEt)_2bpy)_3^{2+*}$/Cl-aniline reaction, contrary to experiment. We therefore believe that a superexchange type model[19] is likely to provide a better basis for understanding long distance electron transfer. Such a model would go far toward explaining the insensitivity of measured α values to the nature of donors and media.

Finally, these polymeric hosts provide a valuable medium for studies of temperature dependence. The dependence of R_c on ΔE shown in fig. 8 suggests a total reorganization energy of -0.7V. It seems likely that this total largely reflects a large internal reorganization energy for the aniline derivatives. For the TMPD/$TMPD^{\cdot+}$ couple, we calculate an energy of -0.4 V. Assuming a solvent contribution of ca. 0.2 V, only a very weak temperature dependence of rate is expected, $kT \sim 200\ cm^{-1}$ but a dramatic dependence of rate on temperature occurs by 77°K.(Fig. 9). These predictions are borne out by experiment, providing a unique experimental separation of λ_s and λ_v in a molecularly doped polymer.

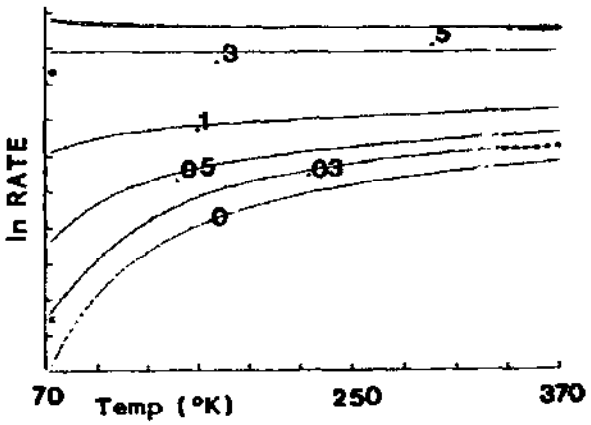


Fig. 9. Temperature dependence of e.t. in Lexan measured by static quenching. Fits shown for λ_s = 0.3v, λv = 0.4v, $h\omega = 1200\ cm^{-1}$.

PHOTOINDUCED ELECTRON TRANSFER IN PROTEINS

The photochemical experiments with random ensembles, when combined with the pioneering pulse radiolysis studies by Miller and others,[12-14] definitively establish that electron transfers can occur at rapid rates over long distances. As a next step to understand and ultimately mimic biological electron transfer, we have begun studies of "intramolecular" long distance electron transfer in proteins.

There are several requirements for an "ideal" protein system for study. First, in order to ultimately facilitate structure function comparisons, proteins studied should be of known (high resolution X ray) structure. Second, physiological redox protein couples are preferred, since such systems are more likely to provide information on biological design than studies of nonphysiol-

ogical redox couples.

Finally, as a practical matter, it is necessary to be able to externally initiate "intramolecular" electron transfer within the preformed protein protein complex. This final requirement is most easily met by photoinduced electron transfer, although pulse radiolysis offers a valid alternative in some cases. In order to utilize photochemical electron transfer, we have replaced the Fe containing porphyrin active sites in several redox proteins with equivalent photoactive porphyrins (e.g., Zn protoporphyrin). In this way we have obtained photoredox active derivatives of cytochrome c, cytochrome c peroxidase, cytochrome b5, and hemoglobin. Using these systems, preliminary data have been obtained for photoinduced or radiolysis induced intramolecular electron transfer within the following physiological protein complexes: Zn hemoglobin*/Fe(III) cyt b5, Fe(III) cyt b5/Zn cyt c,* Fe(III) cyt b5/H_2 porph cyt c*, Fe(III) cyt b5 (H_2 porph)cyt c, Fe(II) cyt b5/Fe(III) cyt c, Fe(III) cyt c, Fe(II) cyt c peroxidase, and H_2 porph cyt c/ cyt c peroxidase.

Hemoglobin ZnP Fe^{III}Hb was found by Hoffman et al[15] to undergo surprisingly efficient (ϕ = 0.15) NET photoreduction of $Fe^{III} \rightarrow Fe^{II}$. This is surprising, since the absence of a sacrificial electron donor, NO net photochemistry should occur. This result was interpreted in terms of the following scheme:

I $\quad \alpha ZnP/\beta\ Fe(III)P \xrightarrow{h\nu}{}_{isc} {}^3(\alpha ZnP)^*/\beta\ Fe(III)P$

II $\quad {}^3(\alpha ZnP)^*/\beta\ Fe(III)P \xrightarrow{k_{et}} \alpha ZnP^{\dot{+}}/\beta\ Fe(II)P$

III $\quad {}^3(\alpha ZnP)^*/\beta\ Fe(III) \xrightarrow{k_t} \alpha ZnP/\ Fe(III)P$ (+ heat)

IV $\quad \alpha ZnP^{\dot{+}}/\beta\ Fe(II)P \xrightarrow{k_{decomp}} \alpha ZnP/\beta\ Fe(II)P$ + oxidized protein residue (unidentified)

V $\quad \alpha Zn^{\dot{+}}/\beta\ Fe(II)P \xrightarrow{k_{back}} \alpha ZnP/\beta\ Fe(III)P$

Hoffman has found that triplet decay is enhanced (by step II) only when the subunit contains $Fe(III)H_2O$. When the β subunit contains Fe^{II}, triplet decay (step III) is unaffected. The value of ket = 60 s^{-1} ($\approx k_T$), combined with the value ϕ = 0.15 suggests that 1) k decomp competes quite efficiently with k back, and 2) k back $\gg$ ket.

Zn Hemoglobin Fe^{III} cyt b5 complex, has been studied in our labs in collaboration with Grant Mauk. Cyt b5 functions in the erythrocyte to reduce met hemoglobin back to a functional deoxy form. This reaction is mediated via the formation of a tight (Km 10^{-4}M) and specific complex.[16] Utilizing the known structures of each individual protein in conjunction with computer graphics routines, Mauk and Poulos have postulated a reasonable structure for the physiological Hb/cyt b5 couple. In this structure, the hemes are held parallel to one another with a 10 A (edge-edge) separation (Fig. 10)[17]. The complex is stabilized by

specific "salt bridges". This proposed structure is now supported by a wide range of biological and chemical evidence.[18]

However, no rate date were previously available for HbIII/b5(II) → HbII/b5 (III) electron transfer within the complex. We have now measured this rate: $k = 0.05\ sec^{-1}$![18] Why is this rate so slow? We believe the answer comes from study of the ZnHb| Fe(III)cyt b5 reaction. When Zn substituted hemoglobin ($\alpha_2Zb\beta_2Zn$ or $\alpha_2Zn\beta_2FeCN$) is bound to Fe^{III}cyt b5 and the complex is irradiated, net photoreduction of cyt b5 occurs.[18] (ϕ=0.01). In light of Hoffman's work, this is not unexpected: cyt b5 simply plays an equivalent role to Fe^{III} in the $\alpha Zn/\beta Fe^{III}$ system. The lower quantum yield in the Hb/b5 system is consistent with $k_{back}^{Hb/b5} >> k_{back}^{Hb}$ (assuming that k decomp is constant in both cases). The rate of the forward electron transfer reaction ^{3}(ZnP*)/cyt b5 Fe^{III} $\xrightarrow{ket}$ ^{3}(ZnP*)cyt b5(Fe^{II}) can be obtained either from the rate of triplet decay or, although less accurately, from the rate of growth of the Fe(II)cyt b5. The rate constant so obtained is $ket = 6x10^3\ s^{-1}$. We see, then, that by increasing from 0.05V to ca. 0.8V, ket increases by five orders of magnitude, consistent with a reorganization energy ≥ 2V! It is quite interesting that Hoffman recently reported just such a large Er for the Zn*/Fe(III) Hb system. Two sources of Er are possible. A large internal reorganization occurs in the transition from six coordinate high spin H_2O Fe(III) Hb to five coordinate high spin (deoxy) Fe(II) Hb. What about medium reorganization energies for the protein "medium"? Several theorists have suggested that E_S will be small for proteins, but little experimental data is available on this point.[19]

A key question thus becomes: are hemoglobin reactions "anomalous", or does intra-protein e.t. generally depend strongly on ΔE (i.e.: are protein reorganization energies non negligible?) Some insight into this question is provided by studies of the cyt c/cyt b5 couple.

Zn(II) c/cyt b5 Fe^{III}

The physiological cyt c/cyt complex bears a striking structural resemblance to the Hb/cyt b5 complex (Fig. 10). Like Hb/b5, cyt c/b5 forms a strong non-covalent complex ($K_M < 10^{-6}$M). Spatially equivalent lysines are used on both cyt c and the Hb to form the b5 complex[17]. The topological similarity is supported by computer models which suggest that the hemes lie parallel in the cyt b5/cyt c complex with a distance of ca. 10 A edge edge. Indeed, it is possible to superimpose the Hb/b5 structure on the cyt c/cyt b5 structure and roughly retain the heme-heme alignments.

Given this structural similarity, similar rates might be expected for electron transfer in the Hb/b5 complex and the cyt c/b5 complex. This is difficult to directly demonstrate. Unlike ZnHb, Zn cyt c does not have a "convenient" decomposition pathway with which to trap the redox products. Thus, if k back> ket, no net redox products will be observed. However, having demonstrated that

the Zn Hb triplet is quenched by electron transfer (with ket = $6x10^3$ s^{-1}) it is likely that such a mechanism might dominate Zn cyt c triplet quenching as well. The surprising result is that the Zn cyt c triplet is quenched by Fe(III) cyt b5 (but not by apo cyt b5, nor Zn(II)b5, nor Fe(II)b5) with a rate constant $k = 4 \times 10^5$ s^{-1}.[20] As shown in detail elsewhere, this rate constant cannot be explained by any energy transfer mechanism.[20] Thus, two physiological protein couples, which appear to be structurally quite similar, with equivalent chromophore separations and driving forces, differ in rate by almost 10^2. It is not clear why cyt c is a "better conductor" than Hb. A strong possibility, however, is that $(\Delta E\text{-}Er)_{Zn\,cyt\ c/b5} > (\Delta E\text{-}Er)_{ZnHb/b5}$. Preliminary ΔE measurements of ZnHb*($\Delta E \sim 0.7V$) and cyt c/b5 Zn cytc*($\Delta E \sim 0.85V$) support this notion. The key question is: how does the rate of electron transfer in the c/b5 couple depend on ΔE? The surprising answer is shown in Fig. 11. For a cyt/cyt couple, where previous theories suggested $Er \sim 0.1V$, we find $Er \sim 0.7V$!

Fig. 10. Idealised stereochemistry of cytc/cytb5 complex (courtesy T. Poulos) the Hb/b5 structure has a very similar heme/heme stereochemistry.

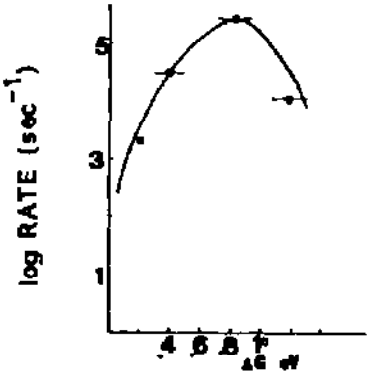


Fig. 11. Dependence of rate on G for N cytc/Ecytb5 reactions n=Fe(III), Znporph ,H_2porph, *(H_2porph).

Finally, we note that similar pattern seems to be emerging for the cyt c peroxidase/cyt c couple.[21-23] For the reaction (Fe(II)ccp + Fe(III)cytc E= 0.45V and h=0.2s^{-1}, while for Fe(III)ccp + (porph cytc)- E=1V and k=200s^{-1} Once again, we find Er>1V. It is perhaps unwise to draw sweeping conclusions from four case studies. Nonetheless, for all the cases which have been studied, protein reorganization energies are large. To R. J. P. Williams' query, "Is cyt c the perfect redox reactant?"[24] the surprising answer seems to be, "No. (unless you mean (Zn cyt c)*!"

Although only limited data exist so far, it is clear that conventional theories of biological e.t. require serious reexamination by bioinorganic and biomimetic chemists. Fortunately, it is also clear that the field of protein e. t. is poised for major advances in both theory and experiment, and that inorg-

anic photochemists will make significant contributions to the final understanding of biological electron transport.

SUMMARY

Initial work in our labs and many others has shown that some aspects of long distance electron transfer in simple glasses are reasonably described by current theories.[2-4,12-14] For example, electron transfer rates do decrease exponentially with increasing donor acceptor separation. Also, when diffusion is precluded, the full dependence of rate on exothermicity emerges, which is otherwise obscured. Some aspects of theory based on nuclear tunneling may require serious reexamination: for example, it appears that the dependence of long distance rate on electron (hole) binding energy is weaker than suggested by many popular theories. Work with proteins shows that while nature is a subtle designer, the general reactivity trends observed in proteins are quite similar to those found in polar glasses. Such studies of protein electron transfer have provided some surprises and challenges for experimentalists and theorists alike. As a clearer understanding of the governing principles of long distance biological electron transfer emerge, we hope it will become easier to design meaningful "biomimetic" strategies for solar energy conversion.

ACKNOWLEDGEMENTS

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