Electron Transfer between Globular Proteins: The Dependence of the Transfer Rate on the Distance

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Abstract - Under the assumption that electron transfer between globular proteins takes place via a polaron-type collective excitation, the dependence of the transfer rate on the distance between the donor and acceptor centers was calculated with regard for their fine electron structures. The electron structure of the heme was computed using the quantum-chemical method MNDO-PM3. The results obtained were compared with experimental data on interprotein and intraglobular electron transfer. It was shown that, within the framework of the model proposed, electron transfer is not described by an exponential dependence and requires no definite route, since the entire protein macromolecule participates in the formation of the excited state.

Key words: globular proteins, electron transfer, polaron model, heme, quantum-chemical calculation, overlap integrals

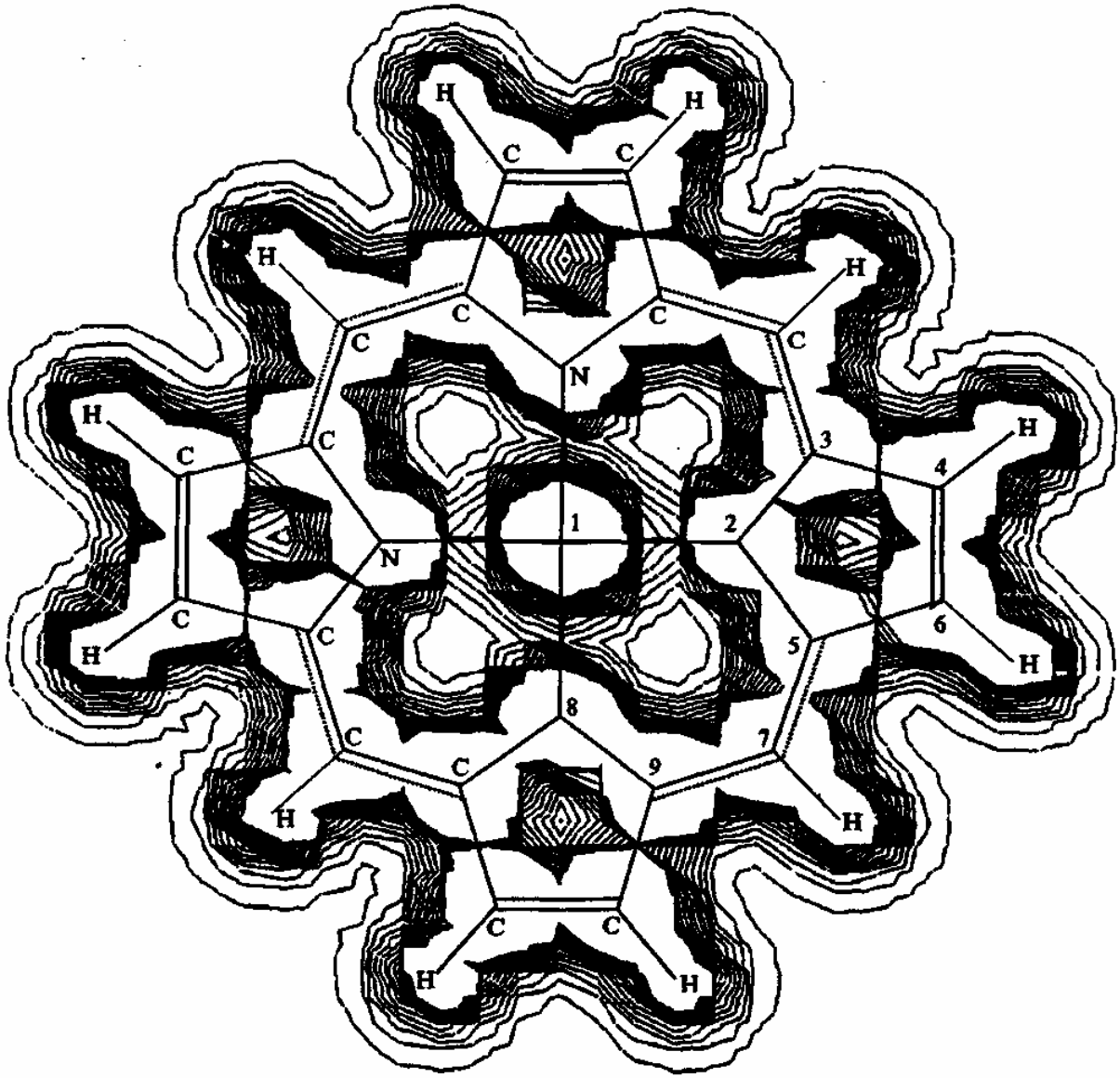
INTRODUCTION

In this work, we continue our calculations of electron transfer between globular proteins in solution. The basic concept of the mechanism of such a transfer has been presented in [1]. In [2], the model has been described, and preliminary computations of the matrix element for probability of electron transfer have been performed for the case when the electron wave function of heme is approximated by a uniform distribution within an 11.35 × 11.35 × 5.35 A potential box, and when the excited electron state is located symmetrically with respect to the donor and acceptor centers. In this work, we carried out further calculations with allowance made for the fine electron density distribution on the heme, and considered the effect of the asymmetry of the excited electron state position on the transfer rate. We also compared the results thus obtained with the experimental data, and discuss the uniqueness of the electron transfer route.

ELECTRON STRUCTURE OF HEME

The electron density at heme was computed for metalloporphyrin containing ***Zn*** as the metal atom. The calculations were made by the MNDO-PM3 method (modified neglect of differential overlap, parametrization model 3) [3] as it is applied in the AMPAC software package. This procedure stands out among the previous semiempirical techniques by the virtue that it allows one to compute the whole complex of the structural physicochemical properties of a given molecular system within the framework of a single approach in a unified manner. The accuracy of representation of the observed geometric, spectral (microwave, ***IR***, optical), mass spectrometric, thermodynamic, and many other characteristics is high enough, and the error does not, as a rule, exceed several percent.

By MNDO-PM3, we optimized the geometry of both a neutral ***Zn***-porphyrin molecule and its cation radical, and also calculated the spectra of their lower electron excited states. The conformation was opti-mized throughout degrees of freedom with the PRECISE program option, which substantially raises the



me.e.

Fig. 1. Optimized structure of and electron density distribution on the heme: (1) the metal atom, (2, 8) nitrogen atoms, and (3-7, 9) carbon atoms.

optimization accuracy. Figure 1 displays the initial structure of molecules with the D4h symmetry, the optimized structure, as well as the electron density distribution on the heme. The table lists some basic characteristics of the optimized geometry of the ground electron state of metalloporphyrin, along with the averaged experimental data [4].

The table shows a good enough agreement between calculated and experimental bond lengths and angles [4]. The found ionization potential I = 7.68 eV also correlates quite satisfactorily with the experimental value I = 7.0 eV estimated approximately from electrochemical data [5]. We also calculated the optical spectrum of the molecule under investigation with consideration for the 36 lower electron configurations corresponding to all different spin occupations of these orbitals. Two lower singlet-singlet transitions S_0-S_1 and S_0 - S_2 proved to be degenerate, and their energies were ΔE = 2.43 eV, which agrees with the Results of optimization of ***Zn***-porphyrin structure by MNDO-PM3 experimental data (ΔE = 2.2-2.34 eV) [5]. Thus, the MNDO parameterization model 3 gave quite an adequate description of the electron structure of metallo-porphyrin.

Bond	Value	Angle	Value	Atom	Effective charge
1-2	2.028 (2.028)	1-2-3	126.5 (126.5)	1	-0.095
2-3	1.401 (1.373)	2-1-8	90.0 (90.0)	2	0.205
3-4	1.458 (1.445)	2-3-4	108.8 (109.9)	3	-0.150
4-6	1.363 (1.363)	3-4-6	107.7 (106.8)	4	-0.121
5-7	1.389 (1.389)	2-5-7	126.2 (125.9)	7	0.002
		3-2-5	106.9 (106.5)	26	0.125
		6-5-7	124.9 (124.7)	28	0.110
		5-7-9	124.4 (125.7)		

Note: Parenthesized are the experimental values [4]. The notation is the same as in Fig. 1.

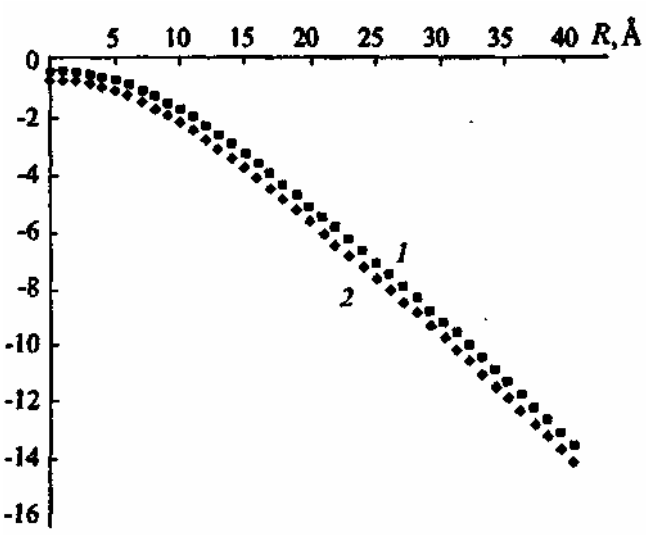


Fig. 2. Comparison of the calculated logarithms of the overlap integrals (1) $ln[I_y^*(R)]$ for uniform electron density distribution on the heme and (2) $ln[I_y(R)]$ with regard for the fine electron structure of heme.

CALCULATION OF THE MATRIX ELEMENT

To estimate how the electron density distribution on the heme can influence the interprotein electron transfer rate, we computed the integral $I_y(R)$ of overlap between the wave function of the excited intermediate state (of polaron type) and the wave function of the ground state of the heme. In calculations for heme, we used the wave function of electrons from only the outer shells; namely, **1*s*** for hydrogen, **2*s*** for nitrogen and carbon, and **4*s*** for the metal atom. The antisymmetrization was ignored. Owing to the symmetry of the wave function of the excited state, the contributions of the ρ states are small; therefore, they were also disregarded. Thus, the wave function of the heme was approximated as a sum of atomic s functions localized according to the calculated geometry of metalloporphyrin:

$$\varphi_{heme}(r) = C_n \sum_i \psi_i^s(r) \ . \quad (1)$$

Figure 2 presents the results of calculations and also the comparison with the computations in the crude model of uniform electron density distribution on the heme. It is evident that the fine electron structure has only a slight influence on the overlap integral. Therefore, the main results from [2] remain valid for the electron density distribution on the heme obtained here as well.

We also computed the effect of the asymmetry of the excited electron state position with respect to the donor and the acceptor. We considered two hemes at a distance of 18 Å from each other (this distance is typical of self-exchange reactions [6, 7]). The excited state was taken to be at distance R from the donor. Then the dependence of the matrix element on distance is

$$H_{et} \propto I(R)\, I(!^* - R) = P(R) \ . \quad (2)$$

Figure 3 demonstrates the dependence of the transfer probability for various orientations of the donor and acceptor hemes. One can see that the asymmetry of the excited electron state position with respect to the donor and the acceptor substantially (by an order of magnitude) changes the transfer probability.

RESULTS AND DISCUSSION

Figure 4 presents the comparison of the results of our calculations with the experimental data on self-exchange reactions between globular proteins ***cyt c /cyt c*** and ***cyt b_5 /cyt b_5*** [6-8], as well as with information on intraprotein transfer in cyt c [9]. Figure 4 displays the dependence $k_{ef}(R) = SH^2_{et}$ (the notation is the same as in [1, 2]). In processing the experimental data in [6-8], electron transfer in the above reactions has been assumed to take place with formation of a protein-protein complex, and the steric factor $S \neq 1$ related to the probability of formation of this, complex has been estimated. In our computations, $k_{ef}(R) = k_0 P(R)$, and the steric factor 5 was included into the parameter $k_0 = 10^{10}$ s^{-1}, since transfer can be realized in a certain range of distances between the hemes, rather than when the arrangement of the hemes is fixed. The calculated curve 1 corresponds to the most favorable arrangement when the excited electron state is equidistant from the donor and the acceptor, and the hemes are parallel to each other and lie in the same plane. Curve 2 describes an unfavorable arrangement when the hemes are parallel to each other but lie in different planes, and the excited electron state is localized at one of the hemes. It is seen that the computation results agree satisfactorily with the experimental data on interglobular transport and disagree with those on intraprotein transfer. This can be due to two reasons: (***i***) the effective distance of intraprotein transfer can substantially differ from the true spacing between the donor and the acceptor, since the excited electron state in the systems under investigation can form at the protein periphery far from the acceptor; and (***ii***) the parameter k_0, related to the energy characteristics of the donor, the acceptor, and the excited state, can differ considerably for the two transfer modes.

In conclusion, let us dwell on two questions that have actively been discussed lately.

On the exponential dependence of the transfer rate on the distance. In the general case, the dependence of the electron tunneling probability on the distance is exponential only at distances much longer than the size of characteristic changes of the tunneling barrier ($R \geq 20$ Å [2], in our model). Usually, the typical transfer distances are somewhat shorter than this distance. In addition, as noted above, the effective transport distance can differ from the minimal spacing between the donor and the acceptor, since in this region there may prove to be no polar groups necessary for formation of the excited state. Thus, steric, energy, and other factors can cause a substantial deviation from the exponential asymptotic dependence, which has been observed in experiments and numerical computations [9, 10].

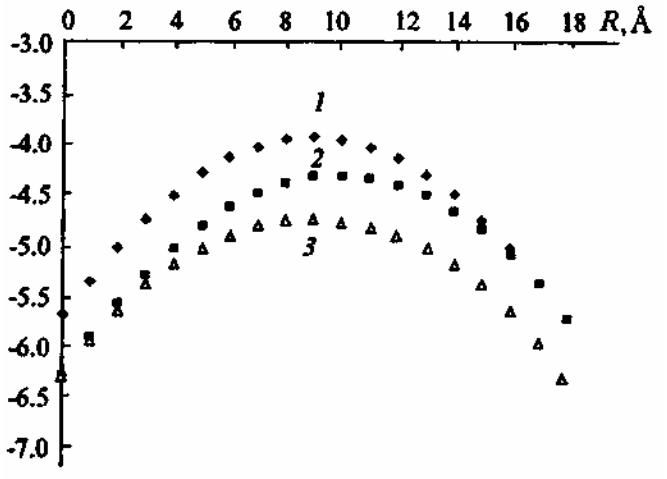


Fig. 3. Electron transfer probability versus electron state position with respect to the donor and the acceptor and versus heme orientation: (1) P_{yy}, the hemes lie in the same plane and are parallel to each other; (2) P_{yz}, the planes of the hemes are perpendicular; (3) P_{zz}, the hemes are parallel to each other but lie in different planes. The transfer distance is 18 Å.

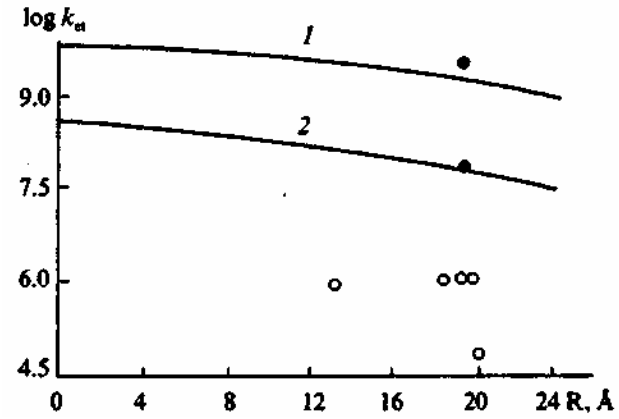


Fig. 4. Comparison of calculated and experimental rates $log[k_{cf}(R)/k^*]$ ($k^* = 1\ s^{-1}$) of (filled circles) interglobular transfer in self-exchange reactions [8] and (open circles) intraglobular transfer [9]. (1) Excited electron state position with respect to the donor and the acceptor is symmetrical, and the hemes are parallel to each other and lie in the same plane. (2) The hemes are parallel to each other but lie in different planes, and the excited state is localized at one of them.

On the electron transfer route. Currently, most of the numerical calculations of electron transfer in proteins have been made under the assumption that there exists a certain specific route along which the transfer proceeds [11, 12]. Our computations have revealed that there need not be such a route, and the transfer is likely to take place via an excited electron state that is formed with participation of the entire protein macromolecule. There is still no experimental data that could have argued in favor of one or the other hypothesis. Apparently, experiments on electron transfer in proteins with point mutations that disturb the putative presumed specific routes can resolve this problem.

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