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The catalytic role of proteins in the electron transport process of biological systems

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Abstract. It is shown that the protein molecule may play a catalytic role to facilitate electron transport between the donor and acceptor molecules attached to it. The proton is transported along the backbone hydrogen bonds of α-helices and involves keto–enol transitions. After the proton is transferred, leaving behind an enol chain instead of the original keto chain, the protein may return to the keto chain, making the injected electron transfer in the backward direction. With such a resetting mechanism, this is a viable possibility for repeated electron transport along the α-helical protein molecule.

1. Introduction

A great many biological phenomena, such as photosynthesis, cell respiration, enzyme activity and others, are related to electron transfer from donor to acceptor molecules through molecular structures. Such molecular structures are often called the *electron transport chain*. The process of transferring an electron is accompanied by oxidation of the donor and reduction of the acceptor. It is therefore an oxidation–reduction reaction. Sometimes the oxidation–reduction reaction is also accompanied by the transfer of a proton.

It is shown experimentally (see e.g. [1]) that transferred electron covers distances of order 30–70 Å. It is unlikely that electron transfer covering such large distances is realized via a simple mechanism of tunnelling. The question concerning the possibility of electron movement along protein molecules has been discussed in the literature [2, 3]. One of the possible explanations for electron transfer over such large distances is related to the idea that the transfer process is facilitated by the participation of protein molecules between the donor and electron acceptor molecules. Unfortunately, the electron transfer process has usually been studied in protein systems with the detailed molecular structure unknown.

It is extremely important to know the molecular structure when explaining the molecular mechanism of electron transfer. The α-helical proteins may serve as ideal molecular structures that transport an electron from one molecule to another. Overlapping of electron wavefunctions of the peptide groups, arranged in different chains, is of less importance. Hence the movement of an electron, supplied by a donor molecule, may be considered separately in each chain.

In 1941, Szent-Györgyi put forward the hypothesis that ideas on electrons moving along proteins are important for understanding the mechanisms of many biochemical processes. At physiological temperatures, the protein is a good insulator. Electron transport along the π-electron system of proteins is impossible. It is nevertheless possible to transport charge carriers through them. If a proton injection mechanism is used at the anode and a small

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electric field is applied across the hydrogen-bonded chain, protons are emitted at the cathode [4]. Actually, in the protonated protein, involving a proton impurity H^+, the band structures may be changed. Therefore, electrons may move along the electron system of protonated proteins.

In previous papers [5, 6], we studied hydrogen-bonded formamide chains using MOPAC, a molecular-dynamics package. Our main finding was that the temperature-induced keto–enol transition assists cooperative proton motion in a formamide chain. This is a possible mechanism for transferring a proton impurity H^+, leaving behind an enol chain instead of the original keto chain. The difficulty with it is that there appears to be no energetically feasible way to set the protein back to the keto chain except to transfer the proton impurity H^+ back again, leaving no net proton transfer. Without a resetting mechanism, this is not a viable possibility for repeated proton transfer along an α-helical protein.

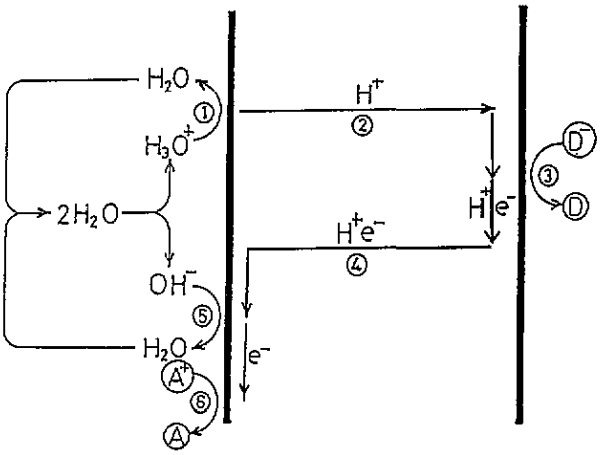
In this paper, however, by employing the simplest model, we study the effect of an α-helical protein molecule on electron transfer between donor and acceptor molecules. In particular, the protein molecule plays a catalytic role to facilitate electron transport between the donor and acceptor molecules attached to it. After the proton is transferred, leaving behind an enol chain instead of the original keto chain, the protein may return to the keto chain, making the injected electron transfer in the backward direction. With such a resetting mechanism, this is a viable possibility for repeated electron transport along the α-helical protein molecule.

2. Basic reaction processes of electron–proton transfer in α-helical protein

Our mechanism involves a simple, cyclic alteration in the hydrogen-bond lengths of α-helical protein accessible to a migrating proton–electron. There are six reaction processes (1)–(6) through which both an electron and a proton may be transferred in the space between the donor zone and the acceptor one as sketched in figure 1.

The first process is protonation. Through this protonation, energy of about 200 kcal mol^{-1} is released. The second one is proton transfer. Using that energy, the proton carries itself to the end of the donor molecule. The third one is electron donation. The donor molecule D^- gives off an excess electron and the proton impurity H^+ traps it to make a bound state H^* (charged radical) like a hydrogen atom. The fourth one is the transfer of charged radical H^*. When the chain returns to its initial state, this charged radical H^* goes back to the acceptor site. The fifth one is deprotonation. The proton in the charged radical H^* combines with a hydroxyl ion OH^- to form a water molecule. The sixth one is electron acceptance. The electron taken off is captured by the acceptor molecule A^+.

Among these processes, the second and fourth are our main subjects (see figure 2). In the second process the proton can move in asymmetric double-well potentials created by the pairs of nearest-neighbour peptide groups [5, 6]. On the other hand, in the fourth process the transfer of the charged radical H^* is associated with the release of energy on moving along the potential gradient. The stabilization of electron movement is very appreciable in the protein, because an electron is strongly bound to the proton motion as a charged radical H^* in a chain (see figures 2(*b*) and (*c*)). Therefore, the device presented here can function as a *unidirectional electron pump* or as a *motor*. If the electron–proton transfer finds experimental support in proteins, our model very likely plays a certain role in a number of biochemical reactions.



①PROTONATION
$H_3O^+ \longrightarrow H_2O + H^+$ (200 Kcal/mol)

②PROTON TRANSFER

③ELECTRON DONATION
$D^- \longrightarrow D + e^-$

④ELECTRON-PROTON TRANSFER

⑤DEPROTONATION
$OH^- + H^+ \longrightarrow H_2O$

⑥ELECTRON ACCEPTING
$A^+ + e^- \longrightarrow A$

Figure 1. Basic reaction processes of electron–proton transport.

3. Cooperative proton motion in a formamide chain

Following the due order of discussion, we will touch upon the proton transfer process (2) first. We need to examine the proton transfer reactions in the protonated formamide chain. Quite recently, we studied hydrogen-bonded formamide chains using MOPAC, a molecular-dynamics package [6]. Our finding there was that the temperature-induced keto–enol transition assists cooperative proton motion in a formamide chain. In order to make this paper self-contained, we give a brief description of our model system, which is the same as that treated in [6]. Therefore, concerning details of the description of the model system, we refer to [6] and here we only give the most essential points needed in the present study.

Two non-equivalent backbone geometries can be envisioned for formamide: the keto form (which is thermodynamically the more stable form) and the enol form. The keto form is converted into the enol form upon heating. Such conversion may promote transfer processes of protons in the hydrogen bridges. The structures of protonated formamide dimers under consideration are shown in figure 3. It can be seen how a hydrogen-bonded

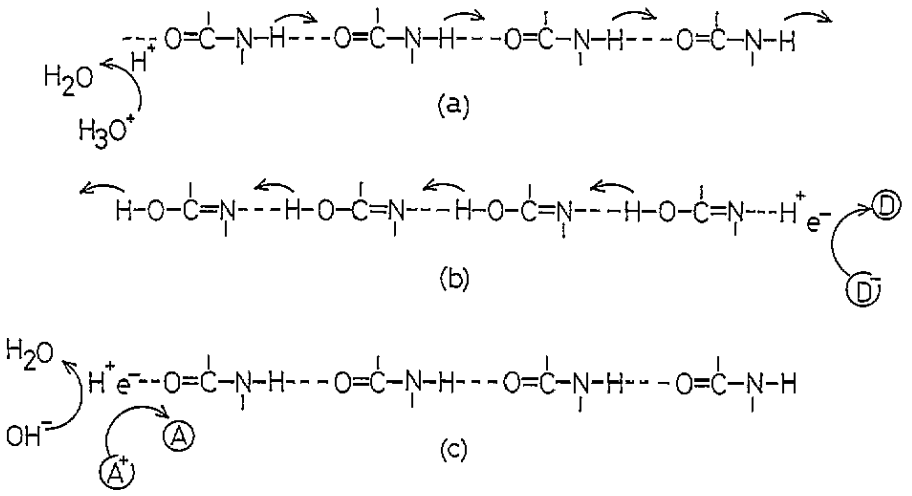


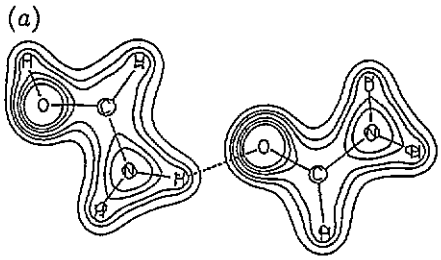
Figure 2. Electron–proton transport between donor and acceptor molecules in hydrogen-bonded chains: (*a*) transfer of proton impurity H^+ along the chain; (*b*) formation of charged radical H^* and its transport; (*c*) acceptance of electron from donor molecule.

dimer can transport a proton from the left to the right side of figure 3. The transition state in figure 3(*b*) is in between the keto and enol forms. The hydrogen-bond length in the dimer system $H^+(CH_3NO)_2$ is variable, i.e. the activation energy of the proton transfer is pooled into the hydrogen-bond stretching vibration, which shortens the hydrogen-bond length. As a consequence, the barrier for proton transfer is reduced. Note that proton transfer is always accompanied by spontaneous charge fluctuation. In fact, when the proton is pushed to midway, the excess charges accumulate around the relevant proton.

The energies of the proton transfer reaction for model systems $H^+(CH_3NO)_n$ with $n = 3$ and 4 are shown in figures 4 and 5. The flexible intermolecular proton transfer systems studied are subject to a stepwise reaction mechanism. In each step only one proton jumps along the hydrogen bridge in the model chain systems $H^+(CH_3NO)_n$. It is understandable that it costs too much energy to transfer a number of protons along the hydrogen bridges at the same time. The reaction profiles are then asymmetric, as indicated schematically in figure 6, where the protons move in a stepwise fashion along the asymmetric potentials. The most interesting feature here is that the proton transfer may couple with the keto–enol transition of the formamide molecules. In this case the low-frequency hydrogen-bond stretching vibration modulates the hydrogen-bond length and induces the keto–enol transition of the formamide molecules. In effect, the keto–enol transition of the molecule may favour the transfer process of the proton along the hydrogen bridges. Such coupling, in fact, plays a crucial role in making the proton transfer on different hydrogen bridges couple strongly with each other to produce a cooperative excitation. So these are the essential points of our results obtained in the proton transfer process (2).

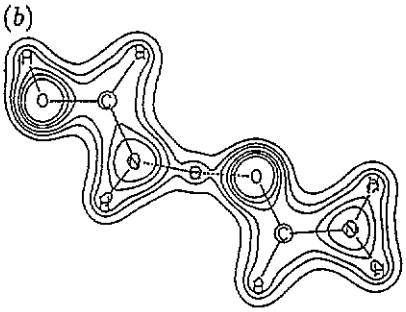
4. Electron transport by proton shuttle in α-helical protein

In this section, we consider the following interesting case: the proton impurity H^+ can play the role of *shuttle* for the electron, which can therefore propagate through the insulating



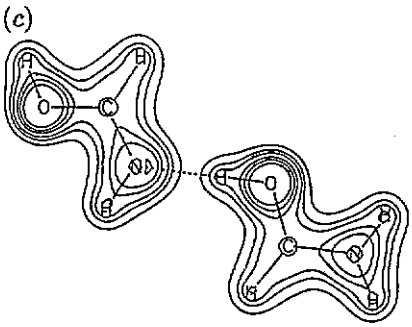
HOCHNH–H ---------- OCHNH$_2$

18·056 e (+19) +0·944 | 17·944 e (+18) +0·056



HOCHNH--------H--------OCHNH$_2$

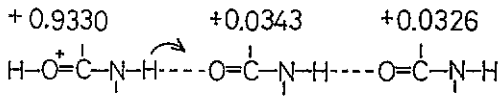
17·606 e (+18) +0·394 | 0·707 e (+1) +0·293 | 17·687 e (+18) +0·313



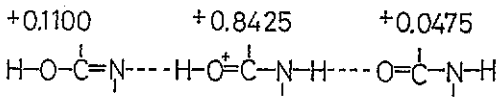
HOCHNH ---------- H–OCHNH$_2$

17·869 e (+18) +0·131 | 18·131 e (+19) +0·869

Figure 3. Electric charge accumulation around the protonated formamide dimer $H^+(CH_3NO)_2$ at 300 K: (*a*) charge accumulation of the dimer with keto form; (*b*) charge accumulation of the dimer in the transition state; (*c*) charge accumulation of the dimer with enol form.



(a) PT(0)



(b) PT(1)

Figure 4. Intermolecular proton transfer accompanied by charge accumulation in the protonated formamide trimer $H^+(CH_3NO)$: (*a*) trimer with keto (PT(0)) form; (*b*) trimer with enol (PT(1)) form.

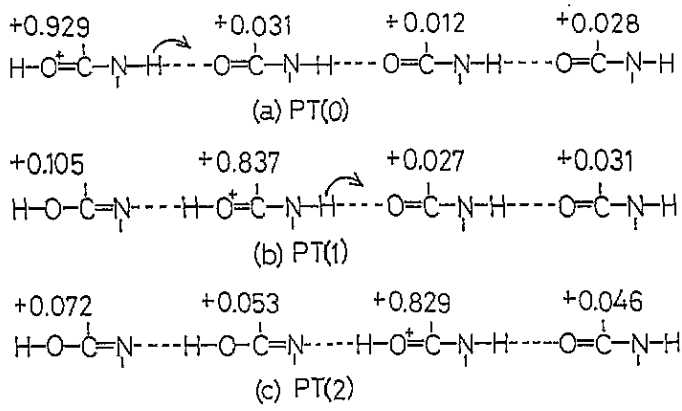


Figure 5. Stepwise intermolecular proton transfer accompanied by charge accumulation in the protonated formamide tetramer $H^+(CH_3NO)_4$: (*a*) tetramer with keto (PT(0)) form; (*b*) tetramer with one proton transferred (PT(1)); (*c*) tetramer with two protons transferred (PT(2)).

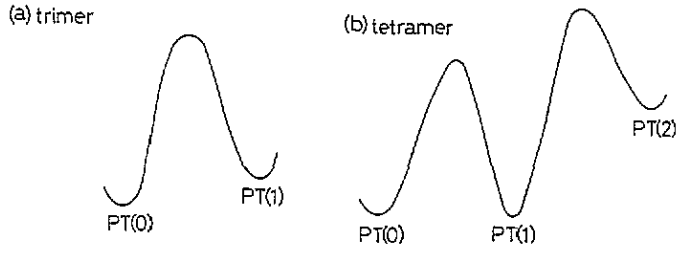


Figure 6. Potential energy surfaces of the protonated formamide chain molecules $H^+(CH_3NO)_n$ for (*a*) $n = 3$ and (*b*) $n = 4$.

protein (proton shuttle). Figure 7 represents schematically the mechanism of charge transport.

When even a weak external electric field is applied, the proton impurity H^+ created by the protonation starts moving to the donor molecule D^-. If the proton impurity H^+ arrives at the donor site D^-, it may fulfil the appropriate condition allowing it to exchange an electron with the donor molecule D^-. Thus, the proton impurity H^+ will trap one electron from the donor molecule D^- and, because of its fractional positive charge, it does not become neutral but acquires a negative fractional charge and becomes charged radical H^*.

If the binding energy is sufficient to keep the electron tightly bound on the proton impurity H^+, then the charged radical H^* starts moving in the opposite direction. When the charged radical H^* arrives at the acceptor molecule A^+, it gives back its electron and again becomes proton impurity H^+. Thus the electron can close the circuit from the donor molecule D^-, while the proton impurity H^+, becoming free of the electron, starts the cycle again from the stage as a *motor*. In this case, the proton impurity H^+ can play the role of the *shuttle* for the electron, which can therefore propagate through the insulating protein.

In particular, the transport of the electron from donor to acceptor molecules may be realized through the three basic processes as shown in figure 8.

The first process is the acceptance of the electron ejected by donor molecule D^- with energy level $\varepsilon_D < E_F$ (Fermi energy). Then the protein forms a so-called virtual state with

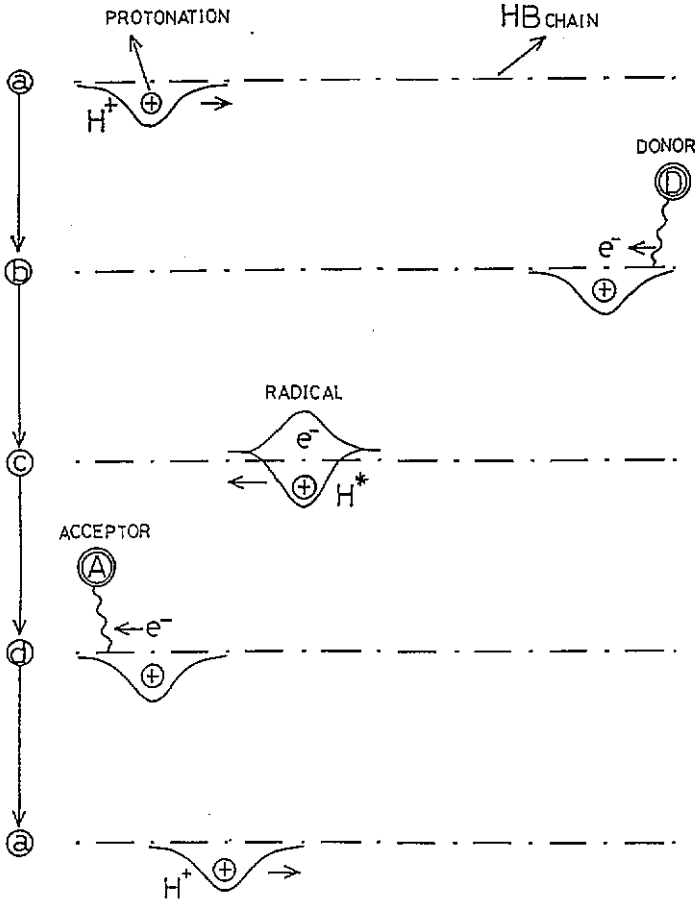


Figure 7. Schematic representation of electron transport assisted by the proton impurity H^+ in a hydrogen-bonded chain: (*a*) transfer of proton impurity H^+; (*b*) acceptance of electron ejected by donor molecule D; (*c*) formation of charged radical H^* and transport of the radical H^*; (*d*) ejection of electron from the protein molecule with the charged radical H^*.

an electron in energy level $\varepsilon > E_F$. Finally, the proton impurity H^+ traps the electron so that the charged radical H^* with $E_D^* < \varepsilon_D$ is formed below E_F. The second process is the transport of the charged radical H^* from donor to acceptor molecule along the hydrogen-bonded chain of the α-helical protein. The third process is the ejection of the electron from the protein with the charged radical H^*. Then, the electron is captured by the acceptor molecule A^+, which forms a virtual state with an electron in energy level $\varepsilon_A > E_F$. On the other hand, after the release of an electron, the protein may return to its original state (keto form). In addition, the acceptor molecule A^+ returns to its initial form A.

To gain further understanding of the electron transfer in a protein molecule, we need to introduce the physical model. It supports an electron transfer process accompanied by proton motion in the hydrogen bridge of the model protein system. We consider a regular hydrogen-bonded chain with the electron donor molecule D^- and acceptor molecule A^+ attached to the n_1th and n_2th sites of the chain, respectively (see figure 9). Let us denote by L the hopping integral for neighbouring sites of the chain, which are separated by the

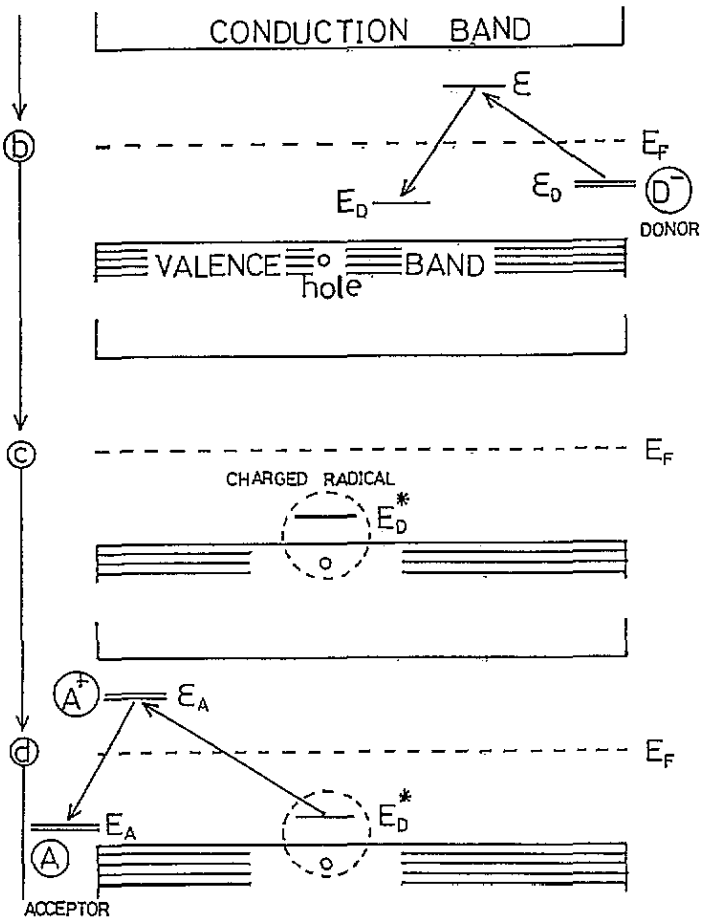


Figure 8. Transport of electron from donor to acceptor molecules.

distance a, T_1 is the electron resonance between the donor molecule D^- and the n_1th site of the chain, and T_2 is the same integral for acceptor molecule A^+ and the n_2th site of the chain.

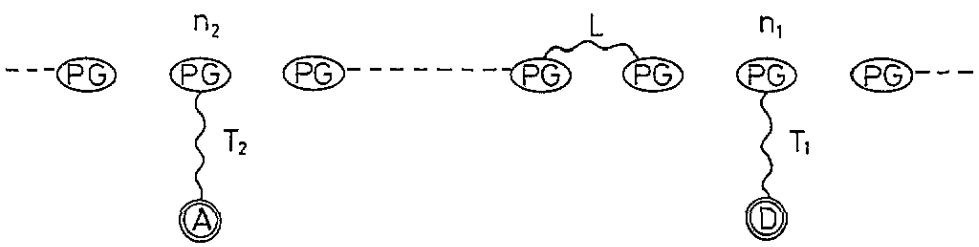


Figure 9. The hydrogen-bonded chain with donor and acceptor molecules.

4.1. Electron donation process

Using Davydov's notation [3], the energy states of an α-helical protein molecule consisting of N ($\gg 1$) peptide groups spaced a distance a apart are described by the Hamiltonian

$$H_P = \sum_n [\varepsilon P_n^+ P_n - \tfrac{1}{2} L(P_n^+ P_{n+1} + P_{n+1}^+ P_n)] \tag{1}$$

where ε is the energy of the least-bound electron in a peptide group, n the number of a peptide group in the molecule, and $\frac{1}{2}L$ the energy of the resonance exchange of electrons between peptide groups. The energy of a donor molecule attached to the groups n_1 has the form

$$H_D = \varepsilon_D D_{n_1}^+ D_{n_1} \qquad \varepsilon_D < \varepsilon. \tag{2}$$

The interaction between a donor molecule and a peptide group may be written in the form

$$H_{int} = T_1(P_{n_1}^+ D_{n_1} + P_{n_1} D_{n_1}^+). \tag{3}$$

The operators $P_n^+ P_n$ characterize the state in which the electron is at the level ε of a peptide group of number n; $D_{n_1}^+ D_{n_1}$ is the state in which the electron occupies the level of a donor molecule. The operators $P_n^+ P_{n'}$ define the electron transitions from the group n' to the group n. $D_{n_1} P_{n_1}^+$ is the electron transition from a donor to a peptide group.

Since we investigate the state of a single electron in a system, the system (donor + protein molecule) is defined by the Hamiltonian

$$H = \varepsilon_D D_{n_1}^+ D_{n_1} + \sum_k [\varepsilon_k C_k^+ C_k + V_{n_1}(k) D_{n_1}^+(k) C_k + V_{n_1}^*(k) D_{n_1} C_k^+] \tag{4}$$

where

$$P_n = \frac{1}{\sqrt{N}} \sum_k \exp(-ikna) C_k \qquad C_k = \frac{1}{\sqrt{N}} \sum_n \exp(inak) P_n$$

$$V_{n_1}(k) = T_1 N^{-1/2} \exp(-in_1 ka) \tag{5}$$

$$\varepsilon_k = \varepsilon - L\cos(ka) \tag{6}$$

are the energies of the conduction-band sublevels with k ranging over N equidistant values on the interval $-\pi/2a < k \leqslant \pi/2a$. The wavefunction of the system is written as

$$|\psi_{n_1}\rangle = \left(u_D D_{n_1}^+ + \sum_k u_k C_k^+\right)|0\rangle. \tag{7}$$

From the normalization condition of the function (7) we obtain the equality

$$|u_D|^2 + \sum_k |u_k|^2 = 1. \tag{8}$$

Minimizing the function

$$J \equiv \langle \Psi | H - E | \Psi \rangle \tag{9}$$

we obtain the equations defining $N + 1$ energy levels of the system,

$$\varepsilon_D - E = \frac{T_1^2}{N} \sum_k \frac{1}{\varepsilon_k - E}. \tag{10}$$

The electron level energy of the donor interacting with the protein molecule thus takes the value

$$E_D = \varepsilon_D - \frac{T_1^2}{[(\varepsilon - \varepsilon_D)^2 - L^2]^{1/2}}. \tag{11}$$

4.2. Electron transport by proton shuttle

In some cases, the proton impurity H^+ moving along the hydrogen-bonded chain may bind an electron that has fallen into the chain from an external donor molecule D^-. The state of such an excess electron in a strongly periodic chain, in the effective-electron mass approximation, is described by the following Schrödinger equation

$$\left(i\hbar\frac{\partial}{\partial t} - E_D + \frac{\hbar^2}{2m^*}\frac{\partial^2}{\partial x^2}\right)\Psi(x,t) = 0 \tag{12}$$

where m^* is the effective-electron mass and E_d is the energy of the excess electron in the undistorted chain. In the previous study [5], it was shown that the proton impurity H^+ may act as a soliton (proton soliton) under the appropriate condition. Then the local deformation of the chain corresponding to the proton soliton is manifested as an additional potential energy of the electron. Such an additional potential energy is called the deformation potential. Without taking account of the reverse effect of an electron on the soliton, the operator for the deformation potential provided by the soliton may be written as [5,7]

$$w(x,t) = w_0\,\mathrm{sech}^2[f(x - Vt)] \tag{13}$$

$$f = \frac{1}{2}\left(\frac{2AB + \gamma^2}{2m_p B(c_0^2 - V^2)}\right)^{1/2} \tag{14}$$

where m_p is the proton mass and c_0 is the characteristic velocity in the proton sublattice.

Under favourable conditions an electron may be captured by a potential well (13) and stay there. If a proton soliton exists in a chain, then the electron motion is determined by the following Schrödinger equation

$$\left(i\hbar\frac{\partial}{\partial t} - E_D + \frac{\hbar^2}{2m^*}\frac{\partial^2}{\partial x^2} + w(x,t)\right)\Psi(x,t) = 0. \tag{15}$$

Let us define the real amplitude function $\Phi(\xi)$ through the relation

$$\Psi(x,t) = \Phi(\xi)\exp\{(i/\hbar)[m^*xV - (E_D^* + \tfrac{1}{2}m^*V^2)t]\} \tag{16}$$

where $\xi = x - Vt$, and $E_D^* + \frac{1}{2}m^*V^2$ is the electron energy relative to the laboratory coordinate system. Substituting equation (16) into equation (15), we obtain the equation

$$\left(\frac{d^2}{d\xi^2} + \frac{2m^*}{\hbar^2}[E_D^* - E_D - w(\xi)]\right)\Phi(\xi) = 0. \tag{17}$$

The function $\Phi(\xi)$ satisfying such an equation characterizes the electron motion relative to a coordinate system moving with the proton soliton with a velocity V. In equation (17), $E = E_D^* - E_D < 0$ is the electron energy in the potential well $w(\xi)$. The lowest energy level is as follows

$$E_0 = -\hbar^2 f^2/(2m^*) \tag{18}$$

and is chracterized by the wavefunction

$$\Phi_0(\xi) = \tfrac{1}{2}f\,\mathrm{sech}(f\xi). \tag{19}$$

Of course, it should be borne in mind that electron transfer, carried out by the proton soliton, requires an expenditure of energy in their formation. Moving always with the velocity V, which is less than c_0, the charged radical H^* does not emit phonons. The problem of the realization of the possibilities considered above, of electron transfer by the proton soliton in real systems, demands a special study. In particular, it is necessary to take into account the reverse effect of an electron on the proton soliton. Apparently such an effect may not be negligible.

4.3. Electron acceptance process

Suppose now that there is an acceptor molecule attached to a peptide group at the point n_2. It has the level of excitation with energy ε_A. The Hamiltonian of the system (charged radical, acceptor) may then be written as

$$H = H_R + H_A + H_{int} \tag{20}$$

where

$$H_R = E_D^* \sum_n R_n^+ R_n - \tfrac{1}{2} L \sum_n (R_{n+1}^+ R_n + R_{n-1}^+ R_n) \tag{21}$$

$$H_A = \varepsilon_A A_{n_2}^+ A_{n_2} \tag{22}$$

$$H_{int} = T_2 (R_{n_2}^+ A_{n_2} + R_{n_2} A_{n_2}^+) \tag{23}$$

and we write

$$\tilde{V}_{n_2}(k) = T_2 N^{-1/2} \exp(-ikn_2 a). \tag{24}$$

The wavefunction of the stationary states is chosen as

$$|\tilde{\Psi}_{n_2}\rangle = \left(u_A A_{n_2}^+ + \sum_k \tilde{u}_k \tilde{C}_k^+ \right) |0\rangle$$

with the normalization condition

$$|u_A|^2 + \sum_k |\tilde{u}_k|^2 = 1. \tag{25}$$

The unknown functions u_A, $\tilde{u}_k$ and E are determined by the set of homogeneous equations

$$(E_k - E)\tilde{u}_k + \tilde{V}_{n_2}^+(k) u_A = 0 \qquad \sum_k \tilde{V}_{n_2}(k)\tilde{u}_k + (\varepsilon_A - E) u_A = 0 \tag{26}$$

where $E_k = E_D^* - L\cos(ka)$. From the condition that the set of equations (26) is solved non-trivially, we obtain the equation defining $N + 1$ energy levels of the system,

$$\varepsilon_A - E = \frac{T_2^2}{N} \sum_k \frac{1}{E_k - E}. \tag{27}$$

Then the electron energy of the acceptor interacting with the charged radical H* in the protein molecule is given by

$$E_A = \varepsilon_A - \frac{T_2^2}{[(E_D^* - \varepsilon_A)^2 - L^2]^{1/2}}. \tag{28}$$

Thus, the protein molecules can facilitate the electron transfer from the donor to the acceptor molecule. It is important here that the charged radical H* of the protein molecule appears in the theory as the shuttle. The electron is not excited thermally to the conduction band in order to pass the acceptor molecule. The effect of the protein molecule results in forming the shuttle by which electrons may be transported from the donor to the acceptor molecules.

5. Discussion

The model of electron transfer through proteins presented in this paper shows that, despite the insulator properties of proteins, the electron can be transferred through the hydrogen-bonded chain of an α-helical protein molecule. A functional protein might well be a *little universe* in which energy and information can be stored and transported. The storage and transport mechanisms would involve keto–enol transition of the hydrogen-bonding backbone structure. The essential point here is that the protein molecule can play a catalytic role to facilitate electron transfer from the donor to acceptor molecules. In fact, the proton impurity H^+ can play the role of the *shuttle* for the electron, which can therefore propagate through insulating proteins.

We conclude that both the free proton impurity H^+ and the charged radical H^* are expected to play a fundamental role in the transport properties of hydrogen-bonded materials such as proteins. However, more experimental studies are required to clarify the relation of the proposed simplified mechanism with the more complex dynamics of the real systems. Research in this domain is still in its infancy, and no theoretical system has been established. One further step in research is needed in order to make it possible for the present study to be applied in actual situations.

Acknowledgments

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