SOLITON/EXCITON TRANSPORT IN PROTEINS

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Abstract.

The study of electron/proton transport in α -helix sections of proteins have illustrated the existence of soliton-like mechanisms. This paper investigates the existence possible like soliton-type mechanisms in other parts of the protein. We use classical Hamiltonian analysis in our investigations as opposed to Quantum Hamiltonian analysis which was used by Ciblis and Cosic in studying the same problem.

Key words. Soliton, transport in proteins, Classical Hamiltonian, Klein Gordon.

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1. Introduction. Many biological processes are associated with a space propagation of energy and electrons along protein molecules. For example, the energy released (under normal physiological conditions releases 0.42eV of energy) under hydrolysis of ATP molecule. The major question is *What happens to this energy?* How does it perform useful work? Is the energy used through non-equilibrium process or does it thermalize and then work through an equilibrium processes? One hypothesis is some cases is trasferred along α -helical protein molecules as the vibration oscillation of atoms $C = O$ of peptide groups contained in these molecules. This energy is about half(.21eV or $1665cm^{-1}$) of the energy released during ATP hydrolysis. Moreover, the amide-I vibration stays nearly constant from protein to protein, indicating that it is rather weakly coupled to other degrees of freedom. All these factors lead to the assumption that energy released by ATP might stay localised and stored in the amide-I vibration, for example see Davydov [13]. He suggested that the amide-I energy could stay localised through nonlinear interactions of the vibrational excitation and the deformation in the protein structure caused by the presence of the excitation. The excitation and the deformation balance each other and form a soliton. Therefore, a soliton is a *localized packet of energy*. Protein molecules also transport electrons from donors to acceptors very effectively.

There is also much evidence that shows that biological processes can be induced or modualted by the induction of light of particular frequencies, for example see the work Cosics[8]and [10]. This is caused directly by light-induced changes in the energitic states of molecules and in particular proteins. The function of some proteins (proton pumps) is directly connected with absorption of visible light of defined wavelengths as in the case of rhodopsins. The strong light absorption is due to the presence of a color

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prosthetic group bound to the protein, whilst the frequency selectivity of this absorption is defined by the amino acid sequences of the protein[8],[10].

On the other hand, there is evidence that light of defined frequency can induce or enhance some biological processes which are normally controlled only by proteins, see Cosic[8]. All these frequency selective effects of light on biological processes involving protein activation involves energies of the same order and nature as electromagnetic irradiation of light. These phenomena are discussed in terms of the Resonant recognition Model(RRM) which proposes that the protein interactions are based on resonant electromagnetic energy transfer within the range of infra-red and visible light, see Cosic[8].

2. A summarized discussion of RRM model. All protein molecules are made from a linear sequence of amino acids. The RRM model interprets this linear information using signal analysis methods [8]. Firstly, the amino acid sequences are transformed into numerical series using the electron-ion interaction potential for each amino acid (Veljkovic and Slavic[40]). Their values describe the average states of valence electrons in the amino acid. Numerical series obtained in this way can then be transformed into the frequency domain using Fast Fourier Transform in order to extract information pertinent to the biological function.

To determine the common frequency components for a group of protein sequences, the absolute values of multiples cross-spectral function coefficients are calculated. Peak frequencies in the multiple cross-spectral function denote common frequency components for the analysed sequences. Signal to noise ratio for each peak was considered as measure of similarity between analysed sequences. This ratio was calculated as the ratio between signal intensity at the particular peak frequency and the spectrum mean value (ratio of least 20 sequence is considered significant). The presence of a peak with significant ratio in a multiple cross spectral function of a group of sequences with the same biological function means that all of the analysed sequences within the group have this frequency component in common. This frequency is related to the biological function as it was found in previous investigations [8] that:

- (i) such a peak exists only for the group of proteins with the same biological function;
- (ii) no significant peak exists for biologically unrelated proteins; and
- (iii) peak frequencies are different for different biological functions.

Furthermore, it was shown that the proteins and their targets have the same characteristic frequency in common, see Cosic [8],[10]. Therefore, it can be concluded that these frequencies characterized not only general function but also recognition and interaction between particular protein and its target. This interaction can be considered as resonant energy transfer between interacting molecules. This energy can be transferred through oscillations of a physical field possibly electromagnetic in its nature. As

there is evidence that proteins have certain conducting or semiconducting properties(see Davydov[13])then charge moving through the protein backbone and passing different energy levels caused by different amino acid side groups can produce sufficient conditions for the specific electromagnetic radiation or absorbtion. The frequency range of this field depends on charge velocity estimated to be $7.87 \times 10^5 ms^{-1}$ and the distance between amino acids in protein which is $3.8 \text{ \AA}$, see Cosic[8],[10]. Having this in mind, the frequency range obtained for protein interactions was $10^{13} \text{ to } 10^{15} Hz$, see Cosic[8],[10]. All the results obtained in RRM model lead to the the conclusion that specificity of protein interactions are based on the resonant electromagnetic energy transfer on a frequency specific for each observed interaction. This has been tested on a number of examples including light absorbing proteins (Cosic[8]), growth factor activation(Cosic[6],[7]), enzyme activation(Cosic[9]) and red/far red and blue light receptors in plants(Cosic and Birch[11]). The physical basis of RRM postulates is the possibility of charge tranfer through protein backbone. The possibility and nature of charge or energy transfer along the protein backbone is discussed here.

3. The problem under investigation. This paper investigates the possiblity of a soliton-like mechanim being involved in the resonance recognition process. As the RRM derives a set of frequencies computed from data on the whole length of the protein, it has been assumed that the charge or excitations travelling along the back bone can produce vibrations(oscillations) of particular frequencies. The assumptions here is that solitons would travel along the backbone . Therefore, the quotient of soliton velocity/length of protein backbone could be of the order of RRM frequencies.

4. Preliminary work and known results on soliton-like mechanisms in proteins. There are instances of protein to protein reactions where an electron is transfered $30\text{-}70\text{\AA}$ from the reactive site unassisted by a chemical carrier. The energy required for an electron to escape its ground state in a protein is approximately $2.3\text{-}3.5 \text{ eV}$. The background thermal energy at 300° K is approximately 0.025 eV and optical excitation of the protein is unlikely,see Kharkyanen [23]. The electron transfer is difficult to explain with either standard chemical theory or by quantum mechanical tunneling,see, Davydov[13].

One explanation to the problem of electron transport involves the introduction of solitons. The general properties of solitons are solitons are solitary waves(waves localized in space) with the following properties:

1. they preserves their shape and velocities.
2. they are extremely stable to perturbations(In particular collisions with small amplitude linear waves),
3. they are even stable with respect to collusions with other solitons. In such collusion they pass through each other and recover their speed and shape after interaction. The outcome of the collusion of two solitons is a

simple phase shift of each excitation.

Davydov[13] investigated the conditions that would necessitate the formation of excitons and solitons within proteins. His simplest model considers only resonant interactions of vibrational excitations of peptide groups and this was extended to cover the three spine model for the α -protein. His model assumes that there is a dipole-dipole interaction between the blocks and that there is perturbation of the bond structure within the blocks. This model is equally applicable to electron transport. Careful inspection of the α -helix structure of proteins reveals three channels situated approximately in the longitudinal direction of the sequence

where the dotted lines represent hydrogen bonds. For detailed analysis it is necessary to consider the interaction of all three channels. He(Davydov) first considered a one-dimensional periodic array of block of atoms:

Here we will only consider one, since it suffices to convey the basic idea. The Hamiltonian Davydov used to describe the situation is:

$$H = \sum_n [E_0 B_n^\dagger B_n - J(B_{n+1}^\dagger B_n + B_n^\dagger B_{n+1})]$$

$$+ \sum_n \left[\frac{v_n^2}{2m} + \frac{1}{2} w (u_{n+1} - u_n)^2 \right] + \chi \sum_n (u_{n+1} - u_{n-1}) B_n^\dagger B_n$$

$$(4.1) \quad = \hat{H}_{CO} + \hat{H}_{ph} + \hat{H}_{int}.$$

Here, $B_n^\dagger$ and B_n are boson creation annihilation operators for quanta of intramolecular vibrations with energy $E_0 = 1665 \text{ cm}^{-1}$ at site n (the CO stretch mode or amide-I mode), u_n and v_n are the molecular displacement and momentum operators for the molecule at site n (the entire peptide group), m and w are the molecular mass and intermolecular force constant, and J is the intersite transfer energy produced by dipole-dipole interactions. The nonlinear coupling constant χ arises from the modulation of the on-site by the molecular displacements. It is the derivative of the amide-I energy with respect to the length between peptide groups(1) of the adjacent hydrogen bond:

$$\chi \equiv \frac{dE_0}{dl}.$$

The vibration part $\hat{H}_{CO}$, the phonon part $\hat{H}_{ph}$, and the interaction part $\hat{H}_{int}$ are defined to be individual terms in (4.1).

For later comparison we write here the equation of motion for the Heisenberg operator $B_n(t)$,

$$(4.2) \quad i\hbar\dot{B}_n = E_0 B_n - J(B_{n+1} + B_{n-1}) + \chi B_n(u_{n+1} - u_{n-1}).$$

The form of this equation is such that a phase transformation

$$(4.3) \quad B_n(t) = \tilde{B}_n(t) \exp\left(\frac{-iE_0 t}{\hbar}\right)$$

removes the energy of the amide-I quantum from the equation, that is, the equation for $\tilde{B}_n(t)$ is (4.2) but without the term proportional to E_0 .

Davydov minimizes the average value of H with respect to some wave function. This leads to the differential-difference equations. Extensive numerical and theoretical analysis of these differential-difference equations yields the following results: It is reasonable to expect soliton formation at the level of energy released by ATP hydrolysis

and such a soliton travels rather slowly with respect to the speed of longitudinal sound waves. Taking a continuum approximations of the differential-difference equations results in nonlinear Schrödinger equation(NLS), the solution to which is a soliton. Davydov's work was collaborated by a numerical study(Hyman[21]). They found out that for soliton to form threshold conditions were necessary;

- (i) nonlinear cross-coupling between the $C = O$ vibrations and $H..O$ comprehension wave must be sufficiently strong and
- (ii) the $C = O$ vibrations must be energetic enough to provide a self-focusing effect.

Takeno [35]-[38] proposed an alternative model for propagation of biological energy in the α -helix protein. He has argued that the dispersion term in the Davydov model(4.1), may not be appropriate for the migration of vibrational energy. This particular type of exchange interaction is more relevant for electrons or electronic excitons. His approach is basically classical and therefore does not have the constraint of the number of amide-I quanta. He first introduced his Hamiltonian in its simplest form, with acoustic phonons, in order to compare with the Davydov model. Takeno has also generalised his theory to deal with more complex systems where the amide-I energy is coupled to both acoustic and optic phonons.

The the simplified version of Takeno's Hamiltonian is

$$(4.4) \quad \begin{aligned} H_T = & \sum_n \left[\frac{p_n^2}{2\mu} + \frac{1}{2} \mu \omega_0^2 \rho_n^2 - 2L \rho_{n+1} \rho_n \right] \\ & + \sum_n \left[\frac{v_n^2}{2m} + \frac{1}{2} K_a (u_{n+1} - u_n)^2 \right] + \sum_n \left[\frac{1}{2} A_a \rho_n^2 (u_{n+1} - u_{n-1}) \right] \end{aligned}$$

Here ρ_n and p_n are the displacement and momentum coordinates for the high frequency intramolecular (amide-I) oscillator with mass μ and frequency ω_0 ; L is the coupling strength between neighboring oscillators, which we have restricted to the nearest neighbors. Also, u_n and v_n are the displacement and momentum coordinates for the molecule at site n ; m and K_a are the molecular mass and intramolecular force constant (K_a is the same as w in the Davydov model). The last term couples these two oscillating fields with coupling constant A_a .

In order to make a comparison with the Davydov model, we now for a moment view (4.4) as a quantum Hamiltonian, with the displacement and momentum coordinates replaced by operators. We introduce creation and annihilation operators for the high-frequency oscillator at site n by the equations

$$(4.5) \quad \rho_n = \sqrt{\frac{\hbar}{2\mu\omega_0}}(B_n^\dagger + B_n); \quad p_n = i\sqrt{\frac{\hbar\mu\omega_0}{2}}(B_n^\dagger - B_n)$$

then the ρ_n -dependent parts of (4.4) can be written as

$$(4.6) \quad H_v = \sum_n \hbar\omega_0(B_n^\dagger B_n + \frac{1}{2}) - \frac{\hbar L}{\mu\omega_0} \sum_n (B_{n+1}^\dagger B_n^\dagger + B_n^\dagger B_{n+1}^\dagger + B_{n+1}^\dagger B_n + B_{n+1} B_n),$$

$$(4.7) \quad H' = \frac{\hbar A_a}{4\mu\omega_a} \sum_n (B_n^\dagger B_n^\dagger + 2B_n^\dagger B_n + B_n B_n)(u_{n+1} - u_{n-1}).$$

Comparing (4.7) with the Davydov Hamiltonian it is clear that there are additional $B_n^\dagger B_n^\dagger$ and $B_n B_n$ terms both in the dispersive and interaction parts of the quantum version of the Takeno Hamiltonian. The equation operator B_n obtained from (4.4) is

$$(4.8) \quad i\hbar\dot{B}_n = \hbar\omega_n B_n - \frac{\hbar L}{\mu\omega_0}(B_{n+1}^\dagger + B_{n+1} + B_{n-1}^\dagger + B_{n-1}) + \frac{\hbar A_a}{2\mu\omega_0}(B_n^\dagger + B_n)(u_{n+1} - u_{n-1}).$$

This differs from equation (4.8), the corresponding equations using Hamiltonian (4.1), by the presence of the creation operators on the right-hand side. The presence of those terms means that a phase transformation of the form (4.3) cannot remove the energy of the amide-I quantum $\hbar\omega_0 = E_0$ from the equation. Carrying out that transformation on

TABLE 1
 α helix parameters.

Parameter	Value	unit	Reference
E_0	1665	cm^{-1}	[25]
J	7.8	cm^{-1}	[25]
w	13	Nm^{-1}	[22]
m	114	m_p	[30]
χ	0.62	$10^{-10}m$	[3]

equation(4.8) produces factors oscillating at $2\omega_0$ in the creation operator terms. In this formulation the magnitude of E_0 relative to other energies in the problem remains important.

We note that if we drop the creation operators from(4.7), then we can relate the parameters of the two theories by

$$(4.9) \quad L = (\frac{\mu\omega_0}{\hbar})J, \quad A_a = (\frac{2\mu\omega_0}{\hbar})\chi.$$

The equation of motion derived from classical Hamitonian(4.4) are

$$(4.10) \quad \mu\ddot{\rho}_n + \mu\omega_0^2\rho_n - 2L(\rho_{n+1} + \rho_{n-1}) + A_a\rho_n(u_{n+1} - u_{n-1}) = 0,$$

$$(4.11) \quad m\ddot{u}_n - K_a(u_{n+1} - 2u_n + u_{n-1}) - \frac{1}{2}A_a(\rho_{n+1}^2 - \rho_{n-1}^2) = 0.$$

Takeno now proceeds by making a continuum approximations to equations(4.10) and (4.11)and obtains this way coupled nonlinear Klein-Gordon equations for the coordinates $\rho(x, t)$ and $u(x, t)$. A rotating-wave approximation then finally leads to an NLS equation with a classical for the amplitude of the amide-I vibration $\rho(x, t)$ compared to Davydov's NLS equation for the probability amplitude:

$$(4.12) \quad i\rho^+_t + \frac{1}{2m_0}\rho^+_{xx} + g|\rho|^2\rho^+ = 0,$$

where $m_0 = \frac{\omega(k)\mu}{L\gamma l^2}$, the nonlinearity parameter is

$$g = \frac{12l^2 A_a}{4m\sqrt{\mu^2\omega_0^2 - L\mu + L\mu\gamma l^2(c_2^2 - c^2)}},$$

$$c_2 = l\sqrt{\frac{K_a}{m}}.$$

The self-trapped state of amide-I energy is described by the well-known one-soliton solution

$$(4.13) \quad \rho^+(x, t) = \alpha \operatorname{sech}[\alpha \sqrt{m_0 g}(x - ct)] \exp[i(k_1 x - \omega_1 t)]$$

with $k_1 = m_0 c$, $\omega_1 = \frac{m_0}{2} c^2 - \frac{\alpha^2}{2} g$, where α is a constant having the dimension of length. From equation(4.12) the energy E_c of solitons is given by $E_c = \omega(k) - [\frac{(k^2 - k_1^2)}{2m_0} - \frac{\alpha^2}{2} g]$. E_c becomes

$$\sqrt{\omega_0^2 - \frac{L}{\mu} + \frac{k_1^2}{2m_0} - \frac{\alpha^2}{2} g}, \text{ for } c_1 k_1 \ll 1.$$

For $c_1 k_1 \ll 1$ this is lower than the energy $\omega(k_1)$ of phonon-free vibrons by the factor $\frac{\alpha^2}{2} g$ is referred as the binding energy of vibron soliton. This ensures the stability of the vibron solitons as compared with vibrons themselves. The situation described by (4.12) has a finite interval where the amide-I oscillators are excited, accompanied by a lattice displacement which pulls the peptide groups closer together in that region. It is easy to show [it can be done similar the way it was shown by Davydov[14] in the quantum case] that this configuration has a lower energy than the spatially extended solution to (4.12) and thus self-trapped(self-focusing).

It can be shown that the soliton moving a velocity c carries an energy

$$(4.14) \quad E_c = E_0 + \frac{1}{2} m_{tsol} c^2,$$

where E_0 is the internal energy of the soliton and m_{tsol} is the effective mass of the soliton.

5. Applying the classical method. It should be noted that although Davydov, Takeno and others have primarily been concerned with the propagation of a soliton in the α -helix, the same equations can be used to model electrons travelling along the protein backbone. Cibilis and Cosic[5] took three approaches to examine the possibility of solitons being linked to the RRM;

- (i) Direct comparison with known results on soliton work,
- (ii) The derivation of the soliton velocity in terms of fundamental protein parameters based(on Davydov's previous work), and
- (iii) An investigation into the bounds of the soliton velocity within a protein, based on the fact that solitons cannot propagate faster than the speed of compression in a protein.

In this work, we follow the same three above approaches taken by Ciblis and Cosic[5] but here we apply Takeno's work which is a classical approach compared to Davydov work(which is mainly quantum mechanics approach):

(a) Direct comparison with known results on soliton work.

(b) The derivation of the soliton velocity in terms of fundamental protein parameters based(on Takeno's previous work), and

(c) An investigation into the bounds of the soliton velocity within a protein, based on the fact that solitons cannot propagate faster than the speed of compression in a protein.

In Ciblis and Cosic work[5], they used a number of equations presented by Davydov[14], that may be used to define the velocity of a soliton in terms of protein parameters. As mentioned before the equations are based on a one dimensional array of cells coupled via dipole-dipole interactions and a local perturbation of that chain. The equations are as follows;

$$(5.1) \quad E_c = E_0 + \frac{1}{2}m_{dsol}c^2$$

where E_0 is the internal energy of the soliton,
 m_{dsol} is the effective mass of the soliton,
 c is the velocity of the soliton,
 c_a is the speed of sound through the protein and

$$m_{dsol} = \frac{\hbar^2}{2Jl^2} + \frac{4\chi^4(1 + \frac{3}{2}s^2 - \frac{1}{2}s^4)}{3w^2Jc_a^2(1 - s^2)^3}$$

where
 $s = \frac{c}{c_a}$,
 $\hbar$ = Planck's constant divided by 2π
 J = dipole-dipole coupling constant between cells of the chain
 l = the distance between unit cells
 w = the stretching constant
 $\omega_0 = \frac{E_0}{\hbar}$ χ = soliton-phonon coupling constant

Using these equations it is possible to substitute m_{dsol} into (5.1) and solve the resulting equation for the velocity corresponding to a soliton with energy E_c and E_0 . Using Mathematica 3.0 and the result quartic equation provided four possible values of velocity. Ciblis and Cosic varied the values of E_0 and E_c calculated values of a soliton's velocity and thus examined if solitons were implicated in RRM interactions.

In this paper we follow a similar approach used by Ciblis and Cosic, but now we use Takeno's work, and present equations that may define the velocity of a soliton in terms of protein parameters.

$$(5.2) \quad E_c = E_0 + \frac{1}{2}m_{tsol}c^2$$

Using these equations it is possible to substitute m_{tsol} into (5.2) and solve the resulting equation for the velocity corresponding to a soliton with energy E_c and E_0 . By varying the values of E_0 and E_c it is possible to calculate values of a soliton's velocity and thus examined if solitons were implicated in RRM interactions.

5.1. Direct comparison with known results. A numerical finding (Hyman and others[21]) of solitons in the α -helix shows that both solitons and excitons could exist in the α -helix of a protein. Their analysis was based on initially approximating a set of difference-differential equations and the initial equations were then decomposed into a coupled system of first order real equations and then solved. They computed the minimum soliton speed near the threshold as $1.26 \times 10^3 ms^{-1}$, which is approximately 0.11 time the speed of a compression wave. The maximum theoretical speed for a soliton was found by Hyman and others to be $1.1 \times 10^4 ms^{-1}$.

The charge velocity approximately computed by RRM estimates is $8 \times 10^5 ms^{-1}$ (see Cosic[11]). Soliton modelled by Hyman and others is slower by several orders of magnitude. It is also greater than the speed of compression for these peripheral amide-I strands.

Cibilis and Cosic[5] suggested that assumptions regarding parameters values may need revision. To investigate this further, a model for calculating the stretching constant, K_a , for a section of α -helix was used to see if the values used in Hyman[21] could be varied. Chou[4] in his modelling work used a value for the stretching constant for a hydrogen bond equal to $13 Nm^{-1}$. The stretching constant used by Hyman and others was $76 Nm^{-1}$. Chou[4] provides a method for calculating the stretching constant for a section of α -helix. Values for the stretching constant using this method for differing sections of α -helix was found to be dependent on the number of constituent of amino acids (see figure 1, Cibilis and Cosic[5]). Therefore, K_a the stretching constant varies by an order of magnitude or more. This variation in the H-bond constant was also noted by Scott[31]. Thus, a change in the assumed value may have on the soliton velocity predicted, and numerous cases with differing values of (of an order or more) for K_a need be considered.

5.2. How does a classical model compare previous results. If our model is applied to predict the velocity of a soliton in the backbone (In particular N-C-C chain). Our model will give better results than the results obtained by Cibilis and Cosic[5] for the following reasons.

Although vibron solitons in the present theory in our model and those in Davydov theory used by Cibilis and Cosic[5] are both described by NLS equation, their natures are fairly different from each other. This stems from

the difference of model Hamiltonian for amide-I vibrons in helical proteins to which the discussion given better is applicable, provided inter-spine interactions are neglected. Namely, vibrons in the present are described by a set of coupled molecular vibration oscillators as given by the first term of the Takeno's Hamiltonian(4.4), where as the corresponding ones in the Davydov's theory are regarded as being of quantal nature having the form of excitons with transfer by exchange interactions. The NLS equation here arises from modulations of vibrons by nonlinear coupling with acoustic phonon propating along the helics of the α -proteins, while that in the Davydov theory directly follows from the quantal Schrodinger equation for exciton probability. The present classical picture of vibron solitons appears to be more appropriate to describe vibrational energy transfer in α -helical proteins as a mobile entity of conformational change. The same explanation holds for application to backbone chain. Additional studies should be taken in the application of Takeno's Hamiltonian to see if they would cause an electron to propagate through a protein backbone.

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