Solitons on H-bonds in proteins

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A model for soliton dynamics on a hydrogen-bond network in helical proteins is proposed. It employs in three dimensions the formalism of fully integrable Toda lattices which admits phonons as well as solitons along the hydrogen-bonds of the helices. A simulation of the three dimensional Toda lattice system shows that the solitons are spontaneously created and are stable and moving along the helix axis. A perturbation on one of the three H-bond lines forms solitons on the other H-bonds as well. The robust solitary wave may explain very long-lived modes in the frequency range of 100 cm$^{-1}$ which are found in recent X-ray laser experiments. The dynamics parameters of the Toda lattice are in accordance with the usual Lennard-Jones parameters used for realistic H-bond potentials in proteins.

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I. INTRODUCTION

The present paper is addressing important new experimental protein results that have come out, and in particular the recent InfraRed (IR) measurements of long-lived excitations at 118 cm$^{-1}$ using the pump probe technique on Bacteriorhodopsine [1]. These results are interesting because excitations at these energies do not correspond to any local vibrational mode. Since they are in the far infrared region they have been interpreted as collective modes, that is, modes that involve a large number of amino acids, possibly involving large scale deformations of the protein. If so, one would expect strong damping and short life times because of steric hindrance from the remaining protein and from the surrounding solvent. The relevance of these observations lies in the fact that such states, corresponding to large protein domains, provide information on the dynamics and stability of secondary and higher structures, and thus on the functions and the conformational changes of a protein. However, the phenomenon of collective modes is not fully understood from a theoretical point of view, since both models and numerical simulations face the difficulty of a large number of degrees of freedom with complex interactions. In order to shed some light on the paradoxical long life times of the modes an alternative interpretation was given in terms of hydrogen-bond excitations running along the $\alpha$-helix without causing major large scale deformations [2]. The response at $\sim 100$ cm$^{-1}$, typically found in poly-amides, are generally accepted to be due to phonons extended over H-bonds chains [3]. Poly-amides form molecular chains consisting of hydrogen bonded units of (H-N-C=O) which are similar to those found running almost parallel to the axis along the $\alpha$-helices, and connecting every third residue. Every residue is additionally connected to its neighbors along the spiral spine by a strong peptide bond. Bacteriorhodopsine consists of 7 connected $\alpha$-helices, with an average length of 25 residues. To test that the simple chain picture is relevant for Bacteriorhodopsine, we here perform numerical simulations using the special 3D-architecture of the $\alpha$-helix. We find that apart from phonon modes, there are long-lived excitations which may serve as energy reservoir for other excitations. They are not directly observable as a finite frequency response signal in the excitation spectrum. They are localized modes, or solitons, traveling along the hydrogen strands of an $\alpha$-helix and coupled with the peptide bonds. Their long life time is due to the fact that such waves, being non-oscillatory and localized, interact only weakly with the other modes of the protein and with the surrounding medium and thus are not strongly damped.

In this work we propose to model the dynamic modes by mapping quantitatively an $\alpha$-helix onto a periodic frame that supports solitons, like a Toda lattice. Since a Toda lattice involves only local interaction and allows one to describe solitons as explicit analytical solutions, such a model would provide a useful tool, both for quick numerical simulations and feasible mathematical approaches. Here we present a numerical study with special emphasis on the spatio-temporal behavior of the full helix, and we shall neglect explicitly considering the internal excitations in the (H-N-C=O) units.

The dynamical behavior of an $\alpha$-helix has been much studied in the past, particularly using simplified 1D models [4, 5]. The main emphasis has been on the, so-called Davydov soliton, which is related to the C=O excitation at $\nu \sim 1650$ cm$^{-1}$. A recent study using only non-linear

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coupling between the C=O and O⋯H excitations investigated the effects of the 3D coupling. The interaction model is rather different from ours, and in particular the helix was assumed to be confined in a narrow cylinder.

Here we concentrate mainly on the excitations along the hydrogen bonds - and we have found, among other things, the soliton excitations to be phase locked, and hence the excited helix is spontaneously confined in a narrow cylinder.

II. PHYSICAL CONSIDERATIONS

An essential feature of the helices in a protein is the hydrogen bond structure that keeps the helix stable. Of course the basic structure of the helix is the poly-peptide backbone that is wound up in a homogeneous spiral whose pitch or residues per turn determine what type of helix being present, be it α-helix (the most common type) or a π-helix.

These bonds, especially in the case of the α-helix type where the hydrogen bonds run almost parallel to the helix axis, can be regarded as a lattice where the interaction between the constituents is a typical Lennard-Jones potential describing the Van der Walls forces. The interaction can when expanded up to the next lowest order including the cubic term be mapped onto the studied Toda lattice.

In one dimension and around an equilibrium position at \( r_0 \), a Toda potential has the following form:

\[
V(r) = \frac{a}{b} e^{-br} + ax,
\]

where \( x = r - r_0 \) is the displacement from the equilibrium and \( a \) and \( b \) are two parameters. As we can see from Fig. 1 a Toda potential is asymmetric in a way similar to a Lennard-Jones. It does not become flat at large distances but at short ranges it may be used to model the hard core repulsion on one side of the equilibrium and the weaker interaction on the other one. An expansion around the equilibrium \( r = r_0 \) gives:

\[
V(r) = \frac{a}{b} + \frac{1}{2} abx^2 - \frac{1}{6} ab^2 x^3 + o(x^4),
\]

showing that the product \( ab \) corresponds to the force constant \( k \) in a harmonic approximation. By equating the coefficients of the Toda expansion Eq. 2 to the expansion of a Lennard-Jones potential for the hydrogen bond, \( a \) and \( b \) can be estimated yielding \( a = k r_0/21 \) and \( b = 21/r_0 \).

The harmonic frequency \( \nu \) of a phonon (at maximum density of states) is given by:

\[
2\pi \nu = 2\sqrt{k/m},
\]

In a chain of amino acids connected by hydrogen bonds O⋯H, \( k \approx 1.41 \times 10^4 \) dynes/cm and \( m = 1.7 \times 10^{-22} \) g is the average mass of the residues. This estimation gives \( \nu = 97 \) cm\(^{-1} \). A complete normal mode calculation for an infinite poly(L-alanine) α-helix gives a peak exactly at 118 cm\(^{-1} \).

A similar fit may be given for the peptide bond and provides two Toda constants \( c \) and \( d \) with a corresponding force constant roughly 40 times the one of the hydrogen bonds (simulations with other choices of the parameters for the peptide bonds have been done, up to a ±20% parameter change, yielding qualitatively similar results). It is in this range that the Toda lattice can sustain stable solitons and hence give an argument for considering soliton dynamics on the hydrogen bond network. As we shall in the following sections, the two bonds have a very different role on the energy propagation. The hydrogen bonds provide three one dimensional, nonlinear lattices, where solitons appear, while the peptide bonds act as a strong coupling among the three lattices.

III. MODEL DESCRIPTION

In this work we thus modeled an α-helix with the aim of investigating the propagation of phonons and solitons along the hydrogen bond and the effect of the coupling with the peptide bond. Direct integration of the equation of motion have been made. A picture of the system modeled is shown in Fig. 2. The Hamiltonian of the system is given by adding together the kinetic energy, the potential energy of the three chains with the hydrogen bonds and the potential energy of the peptide bonds. Calling \( x_j \) and \( p_j \) the space coordinate and the momentum of the \( j \)-th amino acid and numbering the amino acids as they appear along the spiral, the Hamiltonian is given by:
FIG. 2: The system modeled. Each dot is an amino acid, i.e. the (H-N-C=O) unit including various side chains bound to the C-atom. The heavy and thin lines represent respectively the peptide and hydrogen bonds. The space unit has been normalized to the equilibrium distance of the hydrogen bond. The scale has been enlarged on the $x-y$ plane. The peptide bonds connect all the amino acids in a spiral. The hydrogen bonds connect the amino acids in three parallel chains.

$$H = E_{\text{kin}} + V_H + V_{\text{peptide}} =$$

$$= \frac{1}{2} \sum_{j=1}^{N} p_j^2 + \sum_{j=1}^{N} V_{a,b}(x_j, x_{j+1}, x_{j-1}) + \sum_{j=1}^{N} V_{c,d}(x_j, x_{j+3}, x_{j-3}),$$

(4)

where $V$ are Toda potentials of parameters $a, b$ and $c, d$ and have obviously to include only the amino acids with $j - 1 > 0$, $j - 3 > 0$, $j + 1 < N$, $j + 3 < N$. The equation of motion are obtained straightforwardly.

IV. SOLITONS ALONG AN THE H-BONDS

Let us consider an $\alpha$-helix with a perturbation along one of H-bond chain. The energy flow along the helix is shown in Figs. 3, 4. Due to the presence of the peptide bonds, the perturbed chain is coupled with the other two chains present in the helix. As a consequence, not all the energy travels along the chain in a localized way, but part of it remains close to the perturbation point and spreads into the system at a slower speed. Another interesting phenomenon resulting from the fact that the three chains are bounded can be seen looking at the energy flow along the other two chains (Fig. 3). We see that some energy is soon transferred along the peptide bond to other chain. As in the case of the perturbed chain, we can identify two waves: one fast and localized and the other slow. The three solitons along the hydrogen bonds are traveling together. If the energy flow of the entire helix is plotted (Fig. 4), one finds that the solitons of the three hydrogen chains compose a united triple-soliton, traveling along the axis of the whole helix.

The basic mechanism of the triple soliton solution is given by the two different roles of the hydrogen and peptide bonds. The hydrogen bond provides three one-
The energy is:

\[ E = \frac{2a}{b} (\sinh \kappa \cosh \kappa - \kappa); \]  

the profile, in terms of the displacements \( |x_j| \) from the equilibrium distance is given by:

\[ e^{-bx_j} - 1 = \frac{m}{ab} \beta^2 \text{sech}^2(\kappa j \pm \beta t); \]  

finally the speed \( v \) is:

\[ v = \sqrt{\frac{ab \sinh \kappa}{m - \kappa}}. \]  

In such relations, \( \beta = \sqrt{ab/m \sinh \kappa} \) and \( \kappa \) is a parameter that completely characterize the soliton dynamics and shape (\( \kappa \) being proportional to the width of the soliton). If \( \kappa \) is computed by fitting the energy, the profile, and velocity of one of the soliton using the parameter of the \( H \)-bond chain only, approximately the same value is obtained in all the three fitting: respectively, 0.74, 0.85, and 0.78. Using the latter, this correspond to an energy of \( E = 41 \text{ cm}^{-1} \) distributed over about 8 sites (see fig. 4) and a velocity of \( v = 1.10 v_s \), where the sound velocity \( v_s = 1.73 \times 10^5 \text{ cm/sec} \).

In a perfect (infinite, 1D) Toda lattice, solitons and periodic waves (sinusoidal in the limit of small energies) can exist simultaneously, with infinite life time \[ \mathbb{S} \]. Small deviations from the ideal picture will lead to a small coupling and hence exchange of energy between the two modes. Moreover, the periodic wave can be obtained as a superposition of solitons \[ \mathbb{S} \]. The dispersion relation between the wavelength \( \lambda \) and the frequency \( \nu \) of the periodic wave is given by:

\[ 2F \nu = \sqrt{\frac{ab}{m}} \sqrt{\frac{1}{\sin^2(2F \lambda)} - \frac{G}{F}}, \]  

where \( \sinh \) is a Jacobian elliptic function and \( F \) and \( G \) are two parameters that depend on the profile. At the found relevant energies and deviations the Toda and the Van der Walls potential are almost identical, see Fig. 1. Hence we expect the obtained results to be essentially valid also for the latter more realistic potential.

Other simulations, performed by initializing the system with different energies, show solitons of different width, but again in agreement with the 1D Toda model. We have also studied the effect of changing the parameters of the hydrogen and peptide bonds and found that only the hydrogen bond parameters effects the dynamics and shape of the solitons.

We conclude that the peptide bond is important only for creating and entraining the three solitons, while the behavior of the coupled solitons agree to a good approximation with respect to the dynamics and shape to that one would have on the uncoupled, 1D lattice of the \( H \)-bonds. In particular, we do not see a concentration of energy on one strand, as reported by Hennig \[ \mathbb{X} \] for strong non-linear coupling. In fact the opposite: An excitation applied to one strand results in phase-locked solitons moving in parallel on all three strands. That is important for keeping the \( \alpha \)-helix confined in space. For some perturbation we have also observed a train of solitons, emitted periodically by the distortion mode.

V. DISCUSSION

An \( \alpha \)-helix can be modeled by three coupled Toda lattices. The specific topology of this system gives rise to peculiar collective oscillations that are of great relevance for proteins, since they control their structure formation and may be also related to their folding/unfolding behavior. In this work we have focused on a mode that has been observed in the pump-probe experiments and, given its relatively low energy \( \sim 100 \text{ cm}^{-1} \), has been related to extended, collective modes. An unexplained feature of
FIG. 6: Conformational change of the $\alpha$-helix after a perturbation that gives an impulse to the first amino acid (along the axial direction and toward the helix). There are two responses: a large and slow distortion mode, and a localized and quickly (supersonically) moving pulse, due to the soliton (for the latter see the enlargement in Fig. 7). A perturbation given in the opposite direction also gives rise to a qualitatively similar phenomenon. Snapshots at $t=0$, 0.3, 0.6, 1.2, 2.4 and 3 picoseconds. See Fig. 5 for an overview of the energy flow along the helix.

this mode is its long life. This is surprising, since a collective mode, involving the motion of a lot of amino acids should have a strong interaction with the rest of the protein and the solvent, and thus decay quickly. Following the suggestion in [2], this problem has been approached proposing that the behavior of such a mode involves considering also soliton solutions, i.e., localized waves that travel along the hydrogen bond chains of the helix and hence has a small interaction with the surrounding. We observed two types of waves. The soliton on one hydrogen chain induces a soliton on each of the other two hydrogen chains to which is coupled through the peptide bond. The three solitons propagate together in a single, localized, and fast wave along the helix. A second type of wave also appear in the system, as a comparatively slower distortion mode. Let us now discuss the two mechanisms in connection with the suggestion of [2]. It is useful to look at the conformational change corresponding to the two waves (Figs. 6 and 7). The solitary wave is then especially interesting. In fact, while the distortion mode results in a large conformational change and for this reason may be quickly damped by the interaction with the surrounding, the solitary wave allows to keep an amount of energy over the helix with a minimal conformational change. The solitons in the actual $\alpha$-helix are not perfect and will slowly disperse energy into excitations involving motion of the same atoms. That is in particular to the phonons exciting the very same units in an oscillatory motion along the H-strands with energies up to $\sim 100$ cm$^{-1}$. This fact, with the observation that the three locked solitons appears spontaneously, gives support to the idea proposed in [2].

Although we have not explicitly considered the internal excitations in the (H-N-C=O) units, it is clear that the energy may also be fed into the C=O excitation at $\nu \sim 1650$ cm$^{-1}$; the soliton mechanism here described hence may also provide a means for having unexpected long life time of that mode. This fact has been observed and is reported in this volume by Austin et al. and in Ref. [9]. More work is in progress to elaborate on the presented model.

FIG. 7: Enlargement of Fig. 6. The localized wave corresponding to the triple soliton traveling on the hydrogen chains along the helix. Snapshots every 0.6 picoseconds starting from $t=0.8$ picoseconds. The arrows show the position of the soliton.
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