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Solitons on H bonds in proteins

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Abstract

A model for soliton dynamics on a hydrogen-bond network in helical proteins is proposed. It employs the formalism of fully integrable Toda lattices in three dimensions which admit 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.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

The present paper is addressing important new experimental protein results, 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-IR 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 lifetimes 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 lifetimes of the modes an alternative interpretation was given in terms of hydrogen-bond excitations running along the α-helix without causing major large scale deformations [2]. The response at $\sim$100 cm^{-1}, typically found in poly-amides, is generally accepted to be due to phonons extended over H-bond 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 α-helices, and connecting every third residue. Every residue is additionally connected to its neighbours along the spiral spine by a strong peptide bond. Bacteriorhodopsine consists of seven connected α-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 α-helix. We find that, apart from phonon modes, there are long-lived excitations which may serve as an 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, travelling along the hydrogen strands of an α-helix and coupled with the peptide bonds. Their long lifetime 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 paper we propose to model the dynamic modes by mapping quantitatively an α-helix onto a periodic frame that supports solitons, like a Toda lattice. Since a Toda lattice involves only local interactions 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 behaviour of the full helix, and we shall neglect explicitly considering the internal excitations in the (H–N–C=O) units.

The dynamical behaviour of an α-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 coupling between the C=O and O$\cdots$H excitations investigated the effects of the 3D coupling [6]. 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.

2. 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 is 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:

$$V(r) = \frac{a}{b}\mathrm{e}^{-bx} + ax, \tag{1}$$

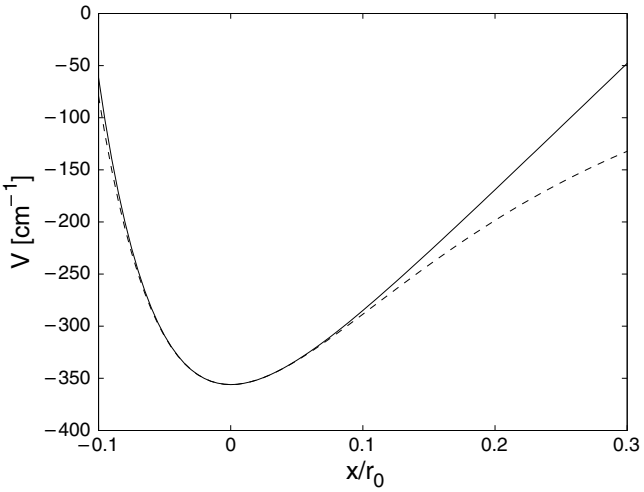

Figure 1. Comparison between the Lennard-Jones potential (broken curve) and a fit with Toda potential (full curve) for the hydrogen bond. The agreement is good for physically relevant excitation energies $\sim$100 cm^{-1}.

where $x = r - r_0$ is the displacement from the equilibrium and a and b are two parameters. As we can see from figure 1, a Toda potential is asymmetric in a way similar to a Lennard-Jones potential. 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. An expansion around the equilibrium $r = r_0$ gives

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

showing that the product ab corresponds to the force constant k in a harmonic approximation. By equating the coefficients of the Toda expansion equation (2) to the expansion of a Lennard-Jones potential for the hydrogen bond, a and b can be estimated yielding $a = kr_0/21$ and $b = 21/r_0$.

The harmonic frequency ν of a phonon (at maximum density of states) is given by

$$2\pi\nu = 2\sqrt{k/m}. \tag{3}$$

In a chain of amino acids connected by hydrogen bonds O $\cdots$ H, $k \approx 1.41 \times 10^4$ dyn cm^{-1} and $m = 1.7 \times 10^{-22}$ g is the average mass of the residues [7]. 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} [7].

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 that of the hydrogen bonds [2] (simulations with other choices of parameters for the peptide bonds have been done, up to a $\pm$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 show in the following sections, the two bonds have a very different role in 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.

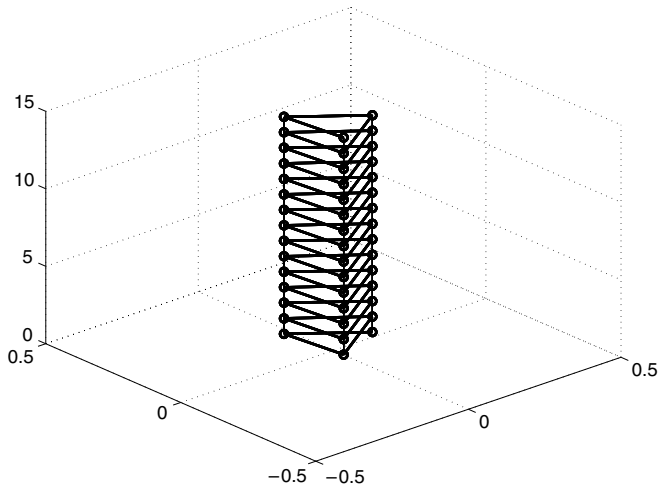

Figure 2. The system modelled. Each dot is an amino acid, i.e. the (H–N–C=O) unit including various side chains bound to the C atom. The heavy and thin lines represent, respectively, the peptide and hydrogen bonds. The space unit has been normalized to the equilibrium distance of the hydrogen bond. The 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.

3. Model description

In this work we thus modelled 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 has been carried out. A picture of the system modelled is shown in figure 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 jth amino acid and numbering the amino acids as they appear along the spiral, the Hamiltonian is given by

$$H = E_{\text{kin}} + V_{\text{H}} + V_{\text{peptide}} = \tfrac{1}{2}\sum_{j=1}^{N} p_j^2 + \sum_{j=1}^{N} V_{a,b}(x_j, x_{j+1}, x_{j-1}) + \sum_{j=1}^{N} V_{c,d}(x_j, x_{j+3}, x_{j-3}), \tag{4}$$

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 is obtained straightforwardly.

4. Solitons along the H bonds

Let us consider an α-helix with a perturbation along one of the H-bond chains. The energy flow along the helix is shown in figures 3 and 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 (figure 5). We see that some energy is soon

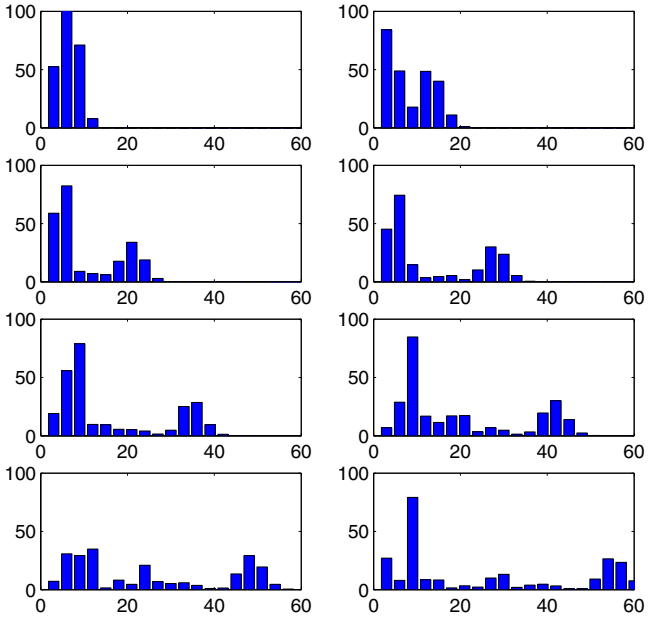

Figure 3. Propagation of a perturbation along the hydrogen bonds, in the presence of the peptide bonds. Although a large amount of energy remains localized close to the perturbed amino acid, a soliton is formed spontaneously. The perturbation has an energy of 618 cm^{-1}. The snapshots are taken every 0.1 ps. The other two hydrogen chains not shown have an analogous behaviour. The vertical axis gives the energy in cm^{-1} and the horizontal axis indicates the residue number.

transferred along the peptide bond to other chains. 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 travelling together. If the energy flow of the entire helix is plotted (figure 4), one finds that the solitons of the three hydrogen chains compose a united triple soliton, travelling 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-dimensional lattices that can support solitary waves. On the other hand, the peptide bond acts as a coupling among the H-bond chains: it induces solitons from one chain to another and entrains them, but otherwise does not qualitatively affect their dynamics. This observation can be verified noticing that, after the triple wave is formed, each soliton behaves as if it was on an independent, one-dimensional lattice with the constant of the hydrogen bonds. In fact, the dynamics of a soliton on a one-dimensional Toda lattice is characterized by the following relations [8]. The energy is

$$E = \frac{2a}{b}(\sinh\kappa\cosh\kappa - \kappa); \tag{5}$$

the profile, in terms of the displacements $|x_j|$ from the equilibrium distance, is given by

$$e^{-bx_j} - 1 = \frac{m}{ab}\beta^2\,\mathrm{sech}^2(\kappa j \pm \beta t); \tag{6}$$

and finally the speed v is

$$v = \sqrt{\frac{ab}{m}}\frac{\sinh\kappa}{\kappa}. \tag{7}$$

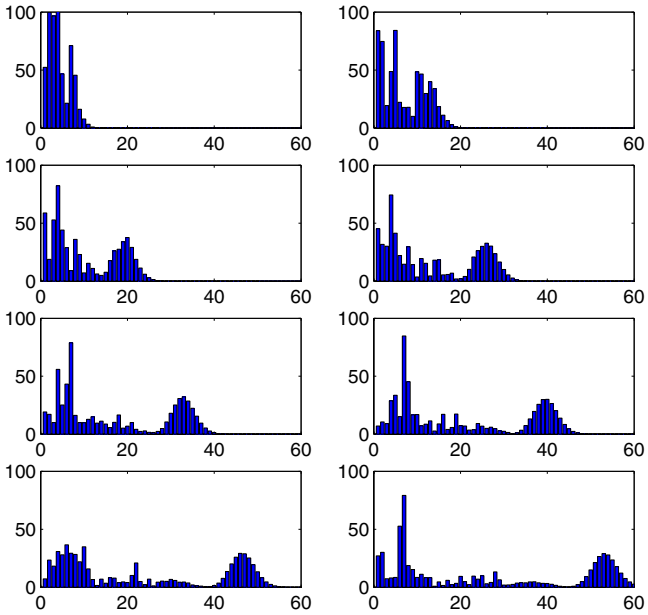

Figure 4. Energy flow along the whole helix. The three solitons along the hydrogen bonds compose a united soliton, travelling along the whole system.

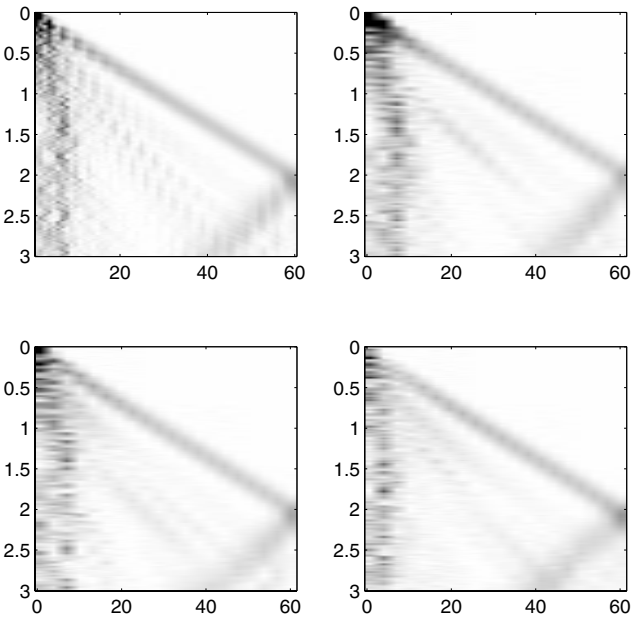

Figure 5. Space–time plot of the energy flow. The top-left picture gives all the amino acids, while the others show the amino acids belonging to the same chain of hydrogen bonds. Time is in picoseconds. The vertical axis gives the time in picoseconds and the horizontal axis indicates the residue number.

In such relations, $\beta = \sqrt{ab/m}\sinh\kappa$ and κ is a parameter that completely characterizes the soliton dynamics and shape (I/κ being proportional to the width of the soliton). If κ

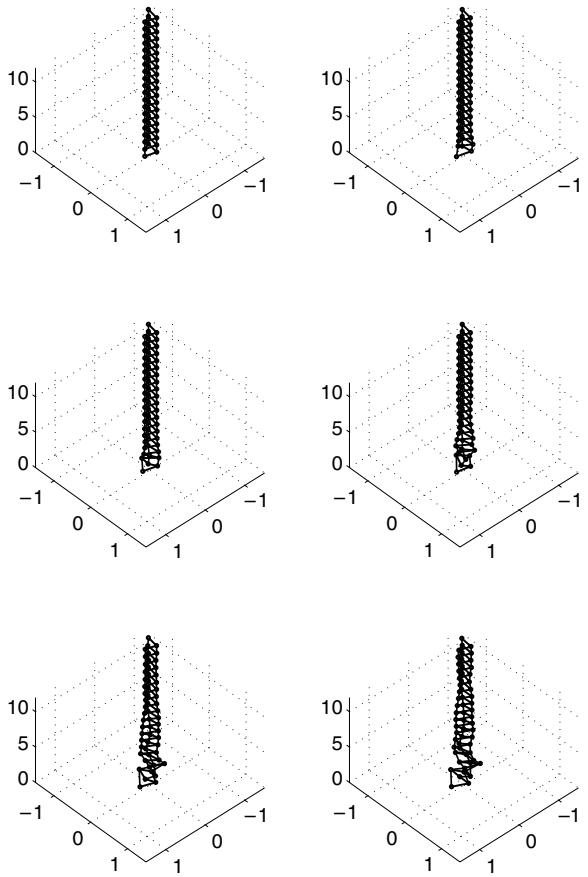

Figure 6. Conformational change of the α-helix after a perturbation that gives an impulse to the first amino acid (along the axial direction and toward the helix). There are two responses: a large and slow distortion mode, and a localized and quickly (supersonically) moving pulse, due to the soliton (for the latter see the enlargement in figure 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 ps. See figure 5 for an overview of the energy flow along the helix.

is computed by fitting the energy, the profile and velocity of one of the solitons *using the parameter of the H-bond chain only*, approximately the same value is obtained in all the three fits: respectively, 0.74, 0.85 and 0.78. Using the latter, this correspond to an energy of $E = 41$ cm^{-1} distributed over about eight sites (see figure 4) and a (supersonic) velocity of $v = 1.10\ v_s$, where the sound velocity $v_s = 1.73 \times 10^5$ cm s^{-1}.

In a perfect (infinite, 1D) Toda lattice solitons and periodic waves (sinusoidal in the limit of small energies) can exist simultaneously, with infinite lifetime [8]. 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 [8] and vice versa. The dispersion relation between the wavelength λ and the frequency ν of the periodic wave is given by

$$2F\nu = \sqrt{\frac{ab}{m}} \Big/ \sqrt{\frac{1}{\mathrm{sn}^2(2F\lambda) - 1} + \frac{G}{F}}, \tag{8}$$

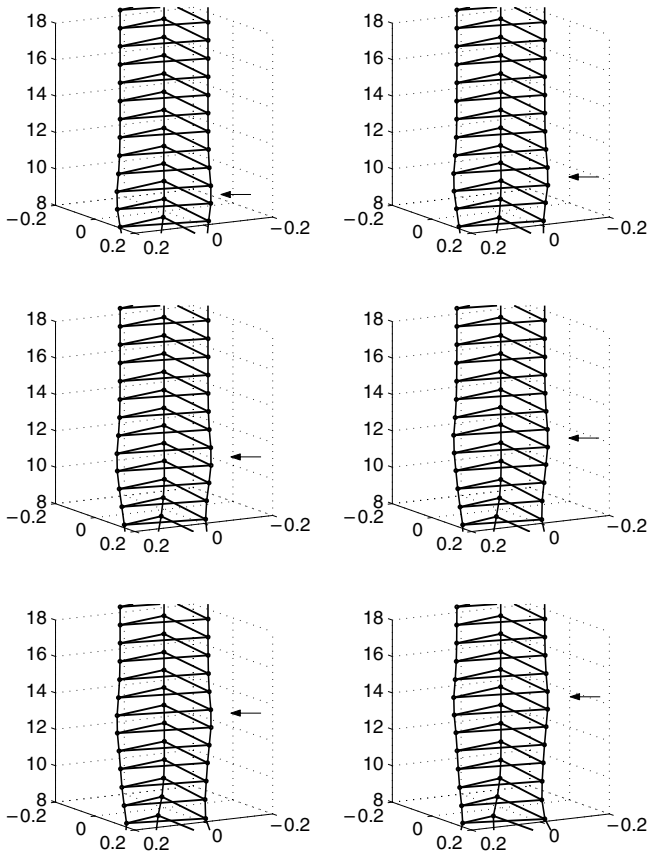

Figure 7. Enlargement of figure 6. The localized wave corresponding to the triple soliton travelling on the hydrogen chains along the helix. Snapshots every 0.6 ps starting from $t = 0.8$ ps. The arrows show the position of the soliton.

where sn 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 figure 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 affects 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 behaviour of the coupled solitons agree, to a good approximation with respect to the dynamics and shape, with 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 [6] 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 α-helix confined in space. For some perturbations we have also observed a train of solitons, emitted periodically by the distortion mode.

5. Discussion

An α-helix can be modelled 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 also be related to their folding/unfolding behaviour. 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 cm^{-1}, has been related to extended, collective modes. An unexplained feature of 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 by proposing that the behaviour 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 have a small interaction with the surroundings. 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 it is coupled through the peptide bond. The three solitons propagate together in a single, localized, fast wave along the helix. A second type of wave also appears 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 (figures 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 surroundings, the solitary wave allows us to keep an amount of energy over the helix with a minimal conformational change. The solitons in the actual α-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 appear 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 of importance for stabilizing the C=O excitation at $\nu \sim 1650\,\mathrm{cm}^{-1}$; the soliton mechanism here described may also provide a means for having an unexpected long lifetime of that mode. This fact has been observed and is reported by Austin *et al* [10] and [9]. More work is in progress to elaborate on the model presented.

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