Discrete breathers in protein secondary structure

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Abstract

The role of the rigidity of a peptide chain in its equilibrium dynamics is investigated within a realistic model with stringent microscopically derived coupling interaction potential and effective on-site potential. The coupling interaction characterizing the chain rigidity and the effective on-site potentials are calculated for three main types of protein secondary structure. The coupling interaction is found to be surprisingly weak for all of them but different in character: repulsive for α-helix and anti-parallel β-sheet structures and attractive for parallel β-sheet structure. The effective on-site potential is found to be a hard one for α-helix and anti-parallel β-sheet and a soft one for parallel β-sheet. In all three types of protein secondary structures a stable zig-zag shape discrete breather (DB) associated with the oscillations of torsional (dihedral) angles can exist due to weakness of the coupling interaction. However, since the absorption of far infrared radiation (IR) by proteins is known to require the existence of rather long chains of hydrogen bonds that takes place only in α-helicies, then one can conclude that the excitation of a DB in such a way is possible in α-helix and seems to be hardly possible in β-sheet structures. The interpretation of the recent experiments of Xie et al. on far IR laser pulse spectroscopy of proteins is suggested. The frequency of a DB in the α-helix is obtained in the region of 115 cm$^{-1}$ in accordance with these experiments.

1 Introduction

Nonlinearity opens new perspectives for solving the problem of localization and storage of energy by biomolecules [1], [2], [3]. This problem is especially urgent within the context of enzymatic catalysis. How does an enzyme store and utilize the energy released at substrate binding? The answer to this question is very poorly understood not only at quantitative but even at qualitative level.

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By now it is clear that dynamical contributions from linear modes into the mechanism of enzyme action are negligible because of high friction in such a condensed matter as protein interior leading to fast dissipation of energy [4]. In contrast nonlinear systems provide us with examples of surprising behavior: the higher the friction is the slower the dissipation of energy proceeds [5]! Though the generosity of this striking result is under question one can hope that since proteins are very rich structures for exhibiting nonlinear phenomena then some of them may play a functional role in enzymatic reactions. Among nonlinear phenomena in biomolecules the so called discrete breather (DB) or else intrinsic localized mode was put in the forefront during the last decade and even overshadowed such a fashionable concept as soliton. However most results on DBs were obtained within unrealistic models with toy potentials. That is why the progress in application of this new paradigm to proteins requires taking into account detailed information on protein dynamics if one wish to pass from toy models to realistic ones.

Last years are marked by noticeable progress in revealing subtleties of protein dynamics gained by infra-red (IR) spectroscopy [6], [7], [8], [9], [10], [11], normal mode analysis [12], [13], [14] and molecular-dynamics simulations (see the recent reviews [15], [16] and refs. therein). On the one hand time-resolved 2D measurements data suggest that in α-helicies there are distributions of the torsional (dihedral) angles (φ and ψ) around their average values with a width of 20 degrees and that the conformation fluctuates on a time scale of picoseconds [7] confirming previous molecular-dynamics studies. On the other hand the experiments of Xie et al. [10], [11] demonstrate that very long-lived oscillations can exist in the α-helix proteins (myoglobin, bacteriorhodopsin) but not in the β-sheet one (photoactive yellow protein) when excited by a far IR laser pulse. The oscillations are observed in the Amide-I band (ω ∼ 1500 cm⁻¹) [10] and more vividly in the low-frequency band ω ∼ 100 cm⁻¹ [11]. The absorption of radiation by proteins in the latter case is commonly attributed to the excitation of longitudinal and transverse modes of one-dimensional hydrogen bonded chains in α-helicies [17]. The normal mode analysis of myoglobin [12], [13], [14] testifies that the anharmonic decay rate of higher frequency localized normal modes, calculated by perturbation theory, is typically nearly independent of temperature, consistent with results of pump-probe studies on myoglobin. In fact, the long-lived vibrations in the Amide-I region of myoglobin [10] are not all that long-lived, about 15 ps, so that this is really a predictable result. Indeed, Leitner [14] and Yu and Leitner [12] have presented calculations of anharmonic decay rates in the Amide-I region of myoglobin, revealing that vibrational lifetimes of order 1-10 ps are quite likely and unsurprising. On the other hand, the results of [11] remain a puzzle. In this study, long-lived excitations of over 500 ps are found near 115 cm⁻¹. Though there are no direct comparisons for bacteriorhodopsin, the anharmonic decay rates in myoglobin near 100 cm⁻¹ computed by Yu and Leitner are two orders of magnitude faster than this.
According to the conjecture of the authors of [10], [11] their result suggests that a breather can be created in an $\alpha$-helix. Another interpretation of these experiment within the framework of Davydov’s soliton concept is also suggested [18]. The latter utilizes the possibility of longitudinal mode excitation at the absorption of far IR radiation by proteins. However this interpretation encounters with difficulties at the point emphasized in [10] that $\alpha$-helices in myoglobin or bacteriorhodopsin are too short for such soliton could efficiently propagate in them. In this chapter the hypothesis is put forward that the long-lived oscillations in $\alpha$-helicis are the fluctuations of the torsional angles of peptide groups around their equilibrium values. The aim of this chapter is to derive the possibility of the existence of a DB in polypeptide chain from its microscopic model and to interpret the phenomena observed the papers [10], [11]. Our approach emphasizes another possibility as opposed to the paper [18]: the excitation of transverse mode of one-dimensional hydrogen bonded chains in $\alpha$-helices at the absorption of far IR radiation by proteins is actually that of oscillations of the peptide groups around their equilibrium positions in peptide chain (the oxygen and nitrogen atoms oscillate transverse to the chain of peptide groups). This type of motion is shown to enable the existence of DBs in $\alpha$-helices. Thus the DB in the peptide chain of $\alpha$-helices can provide sustaining the long-lived oscillations excited by the absorption in the low-frequency band $\omega \sim 100 \text{ cm}^{-1}$.

DBs or else intrinsic localized modes (time periodic spatially localized oscillations with significant amplitudes of several units in a chain of weakly coupled non-linear oscillators while others are at rest or oscillate with negligible amplitudes) discovered by Sievers and Takeno in 1988 [23] and proved by MacKay and Aubry [24] to be structurally stable are well understood and commonly appreciated as generic phenomenon in nature at present (see [25] and refs. therein). The key ingredient for the existence of a DB is the requirement of weak coupling interaction between adjacent nonlinear oscillators [24], [25]. DBs have become a new and very fruitful paradigm in nonlinear physics. The concept of DB has been applying to DNA dynamics for a long time [19], [1], [2], [3], [20], [21]. Its application to protein dynamics is damped by a point of view (see e.g. [3]) that proteins are less capable than DNA to exhibiting DBs because they are much less regular structures. However there are fragments of secondary structures in proteins that are highly regular. In [26] a model for $\alpha$-helix protein is considered that exhibits DB existence in the chains of peptide groups connected by hydrogen bonds in the spirit of Davydov’s model for a soliton. In this chapter a model is constructed that pursues the same goal but for the peptide groups connected by C - C bonds in secondary structures of the backbone. Another distinction from [26] and from all other paper on DBs in biomolecules is that we deal with realistic effective on-site potentials and coupling interaction potentials rather than with model toy ones. These potentials are derived from a stringent microscopic model of the polypeptide chain and thus the present work seems to be a step to ab initio calculation of DBs in
biomolecules. There are few analytical models treating non-linear mechanics of peptide chain backbone [2], [27], [28], [29]. The reason for transparent lack of activity on analytical modeling of peptide chain backbone mechanics seems to stem from meager direct experimental evidence for nonlinear excitations in it. Nevertheless the experiment [11] can be considered as that and motivates the present attempt to construct a simple and tractable but at the same time microscopically stringent model of polypeptide backbone dynamics.

2 The Hamiltonian of the model

A schematic picture of a polypeptide chain with all designations used further is presented in Fig.1. The mutual orientation of two adjacent peptide groups is characterized by the torsional (dihedral) angles $\phi_i$ and $\psi_i$. The angle $\phi_i$ characterizes the rotation round the bond $C^\alpha_i - N_i$ and that $\psi_i$ characterizes the rotation round the bond $C^\alpha_i - C'_i$. Further we consider the equilibrium dynamics in protein secondary structures in which the equilibrium values of the torsional angles are the same for all peptide groups (they are listed at the end of the next Sec.). We consider small deviations $\phi_i(t)$ and $\psi_i(t)$ of the torsional angles from their equilibrium values ($\phi_i = \phi_i^0 + \phi_i(t)$ and $\psi_i = \psi_i^0 + \psi_i(t)$) with $|\phi_i(t)| \leq 20^\circ$ and $|\psi_i(t)| \leq 20^\circ$. At such amplitudes of the deviations the hydrogen bonds confining the peptide group in the secondary structure are not broken [4]. Finally we consider a peculiar type of motion $\psi_{i-1}(t) = \phi_i(t)$. The latter means that the peptide group rotates as a whole respective some effective axis $\sigma$ passing through the center of the C–N bond parallel to the bonds $C^\alpha_i - C'_i$ and $N_{i+1} - C^\alpha_{i+1}$ that are assumed to be approximately parallel ($\angle C^\alpha_i - C'_i - N_{i+1} = 113^\circ$ and $\angle C'_i - N_{i+1} - C^\alpha_{i+1} = 123^\circ$ [30]). This type of motion is stipulated by the fact that the peptide group is a planar rigid structure [4], [30]. For the sake of uniformity of designations we further denote $x_i = 2\phi_i(t) = 2\psi_{i-1}(t)$ (see Fig.2) and thus

$$\phi_i = \phi_i^0 + x_i/2; \quad \psi_{i-1} = \psi_{i-1}^0 + x_i/2 \quad (1)$$

The moment of inertia of the peptide group relative to the axis $\sigma$ can be easily calculated and is $I \approx 7.34 \times 10^{-39} \text{g cm}^2$. The Hamiltonian of the polypeptide chain in our model with nearest neighbor interactions is

$$H = \sum_i \left\{ \frac{I}{2} \left( \frac{dx_i}{dt} \right)^2 + U_{loc}(x_i) + U(x_i; x_{i+1}) \right\} \quad (2)$$

Here $U_{loc}(x_i)$ includes interactions defining the local potential of the peptide group (namely hydrogen bonds, the so-called torsional potentials and the van
der Waals interaction of covalently non-bonded atoms of the peptide group with the atoms of adjacent side chains) defining its separate motion while \( U(x_i; x_{i+1}) \) includes the coupling interactions (namely the van der Waals interaction of covalently non-bonded atoms of adjacent peptide groups \( i \) and \( i+1 \) and their electrostatic interaction) intermixing the motions of these groups and leading to the rigidity of the peptide chain. It should be stressed that the latter potential also contributes into the separate motion of the peptide groups. We can define the effective on-site potential for such motion as

\[
V_{\text{eff}}(x_i) = U_{\text{loc}}(x_i) + U(x_i; 0) + U(0; x_i)
\]  

(3)

and the coupling interaction potential as

\[
U(x_i; x_{i+1}) = U_{\text{vdw}}(x_i; x_{i+1}) + U_{\text{el}}(x_i; x_{i+1})
\]  

(4)

Thus the equation of motion is

\[
\frac{d^2 x_i}{dt^2} = -\frac{dU_{\text{loc}}(x_i)}{dx_i} - \frac{dU(x_{i-1}; x_i)}{dx_i} - \frac{dU(x_i; x_{i+1})}{dx_i}
\]  

(5)

In the following two sections we consider in details the functions \( U_{\text{loc}}(x_i) \) and \( U(x_i; x_{i+1}) \). At doing it we will freely pass back and forth between the variables according to the rule (1) which can be rewritten as

\[
\Delta \varphi_i = x_i/2; \quad \Delta \psi_i = x_{i+1}/2
\]  

(6)

3 Coupling interaction defining the rigidity of a polypeptide chain

Both interactions in (4) intermixing the motions of the adjacent peptide groups and contributing to the coupling interaction are described by the central potentials \( W_{mn}^{\text{vdw}}(R_{mn}(\varphi_i; \psi_i)) \) and \( W_{mn}^{\text{el}}(R_{mn}(\varphi_i; \psi_i)) \) between the atom \( A_n \) of the \( i \)-th peptide group and the atom \( A_m \) of the \( i+1 \)-th one with \( R_{mn} \) being the distance between the atoms \( A_n \) and \( A_m \). The electrostatic potential is

\[
W_{mn}^{\text{el}}(R_{mn}) = \frac{q_m q_n}{\varepsilon R_{mn}}
\]  

(7)

where \( q_m \) and \( q_n \) are partial charges on the atoms \( A_m \) and \( A_n \) respectively (\( q(N) = -0.28e; q(H) = 0.28e; q(O) = -0.39e; q(C) = 0.39e \) where \( e = 4.8 \times 10^{-10} \) CGS [30]) and \( \varepsilon \) is the dielectric constant which for protein interior should be better conceived as some adjustable parameter (\( \approx 2 \div 10 \) with 3.5 being commonly accepted value close to high frequency permeability of
peptides) [30], [4]. In some studies $\varepsilon$ is supposed to be solvent dependent and chosen, e.g., 4 for $CCl_4$, 6 $\div$ 7 for $CHCl_3$ and 10 for $H_2O$ [31], [32]. For the van der Waals potential one can choose any of the numerous forms suggested in the literature, e.g., the Lennard-Jones one (6-12) or the Buckingham one (6-exp). In this chapter we use for numerical estimates the former one

$$W_{vdw}(R_{mn}) = -\frac{A_{mn}}{R_{mn}^6} + \frac{B_{mn}}{R_{mn}^{12}}$$

with the set of the well known parameters of Scott and Scheraga (other sets were also verified and found to give similar results).

The distance $R_{mn}$ as a function of the angles $\varphi_i$ and $\psi_i$ is

$$R_{mn}(\varphi_i, \psi_i) = \left\{p_m^{\varphi} + r_n^{\varphi} + 2pr_{mn}[\sin \theta (\cos \gamma_m \sin \alpha_n \cos \varphi_i - \sin \gamma_m \cos \alpha_n \cos \psi_i) - \sin \gamma_m \sin \alpha_n (\cos \psi_i \cos \varphi_i \cos \theta - \sin \psi_i \sin \varphi_i) - \cos \gamma_m \cos \alpha_n \cos \theta]\right\}^{1/2}$$

The interaction potential for both van der Waals and electrostatic interactions has the form

$$U^{el, vdw}(x_i; x_{i+1}) = \sum_{mn} W^{el, vdw}(R_{mn}(x_i; x_{i+1}))$$

where the summation in $n$ is over atoms in the $i$-th peptide group and that in $m$ is over atoms in the $i$+1-th one.

In what follows we work with full realistic coupling interaction potential described above. However for making use of suggestive analogies with the known literature results obtained on toy models we calculate the so called coupling constant which is a key characteristic of the truncated coupling interaction potential. Expanding the potential we obtain that to the leading order in the terms $x_i \ll 1$ and $x_{i+1} \ll 1$ the rigidity of the peptide chain is determined by the term of the potential which intermixes the motion of the adjacent peptide groups

$$U^{mix}(x_i; x_{i+1}) \approx (-K)x_i x_{i+1}$$

where the coupling constant is

$$-K = -(K^{vdw} + K^{el}) = \ldots$$
\[
\frac{\partial^2 U^{vdw}(x_i; x_{i+1})}{\partial x_i \partial x_{i+1}} \bigg|_{x_i=0; x_{i+1}=0} + \frac{\partial^2 U^{el}(x_i; x_{i+1})}{\partial x_i \partial x_{i+1}} \bigg|_{x_i=0; x_{i+1}=0} = 0
\]

(12)

The results of calculations of the contributions into the coupling constant for different types of protein secondary structures are as follows:

a). $\alpha$-helix (right) $\varphi_i^0 = -57^\circ$; $\psi_i^0 = -47^\circ$ [30]: $-K^{vdw} \approx 4.24 \cdot 10^{-15}$ erg; $-K^{el} \approx 2.4 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$; $-K \approx 6.24 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$.

b). anti-parallel $\beta$-sheet $\varphi_i^0 = -139^\circ$; $\psi_i^0 = 135^\circ$ [30]: $-K^{vdw} \approx -5.0 \cdot 10^{-16}$ erg; $-K^{el} \approx 2.64 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$; $-K \approx 2.14 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$.

c). parallel $\beta$-sheet $\varphi_i^0 = -119^\circ$; $\psi_i^0 = 113^\circ$ [30]: $-K^{vdw} \approx -8.3 \cdot 10^{-15}$ erg; $-K^{el} \approx 2.96 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$; $-K \approx -5.34 \cdot 10^{-15}$ erg at $\varepsilon = 3.5$.

4 Local potential of the peptide group

The local potential $U_{loc}(x_i)$ is composed as follows

\[
U_{loc}(x_i) = U_{sc}(x_i) + U_{hb}(x_i) + U_{tors}(x_i)
\]

(13)

Here $U_{sc}(x_i)$ is the energy of van der Waals interactions of the atoms of the i-th peptide group with those of the side chains $R_i$ and $R_{i-1}$ and also with the atoms $H^i$ and $H^{i-1}$, $U_{hb}(x_i) = U_{hb}^{(1)}(x_i) + U_{hb}^{(2)}(x_i)$ is the energy of two hydrogen bonds of the i-th peptide group and $U_{tors}(x_i) = U_{tors}^\varphi(\varphi_i) + U_{tors}^\psi(\psi_{i-1})$ is the energy of the torsional potentials for the rotation of the angles $\varphi_i$ and $\psi_{i-1}$. For the latter we take the usual form

\[
U_{tors}^\varphi(\varphi_i) = E_\varphi(1 + \cos 3\varphi_i)
\]

(14)

\[
U_{tors}^\psi(\psi_i) = E_\psi(1 + \cos 3\psi_i)
\]

(15)

with $E_\varphi \approx 1$ kkal/mol and $E_\psi \approx 1$ kkal/mol. In all further simulations we choose the side chain to be Alanine ($R_i$ is $C_3^H(H)_3$) and initially find the value of the angle $\chi_1$ (see Fig.1) to minimize the energy. For the $U_{hb}^{(j)}(x_i)$ ($j=1,2$) we take the potential [31], [32]

\[
U_{hb}^{(j)}(x_i) = D(1 - \exp[-n(r(x_i) - r_0)])^2 - D
\]

(16)

where $n=3$ Å$^{-1}$, $r_0=1.8$ Å, $D \approx 4 \div 6$ kkal/mol at $\varepsilon = 3.5$ is an adjustable parameter of the hydrogen bond energy with $D=5$ kkal/mol being a conventional
value [4] (in [32] D is assumed to be a decreasing value at increasing \( \varepsilon \) with \( D=0.5 \) kcal/mol at \( \varepsilon = 10 \) and \( r(x_i) \) is the current length of the hydrogen bond. The dependence of the latter on \( x_i \) requires some simple and straightforward but very cumbersome trigonometry which we omit here to save room. It should be only mentioned that this dependence can be expressed via the sets of the adjustable parameters \( P, L, \eta \) and \( R, L, \kappa \) (see Fig.1). Here \( L \) is the length of the hydrogen bond at equilibrium \( (x_i=0) \) (in the literature the values from 1.8 Å till 2.5 Å are figured), \( \eta \) and \( \kappa \) are the angles characterizing the extent of linearity of the hydrogen bonds and finally \( R \) and \( P \) are the distances from crossing of the perpendiculars of the \( O_{i-1} \) and \( H_i \) atoms on the axis \( \sigma \) to their hydrogen bond partners respectively at equilibrium \( (x_i=0) \). In the present model we assume the partners to have fixed positions. Since in the \( \alpha \)-helix the partners come from third peptide groups along the chain from a given one this assumption imposes a restriction on the size of a DB which can be considered, namely the assumption can be justified for DBs comprising no more than 5 sites (peptide groups). The elimination of the restriction for the \( \alpha \)-helix would actually mean taking into account the long range interaction \( U_{\text{hb}}(x_i; x_{i\pm 3}) \) along the peptide chain. Such complication is left for future work and in this chapter we exemplify the existence of a DB in the \( \alpha \)-helix by a 3-site one. For \( \beta \)-sheets the restriction can be discarded because the partners usually belong to very distant peptide groups from a given one.

The adjustable parameters are chosen to satisfy the following set of requirements: 1. For all three types of protein secondary structure the effective on-site potential \( V_{\text{eff}}(x_i) \) must have a minimum at equilibrium \( (x_i = 0) \) because the structures are steady stable ones. 2. For the anti-parallel \( \beta \)-sheet the angles \( \eta \) and \( \kappa \) are known to be very close to 180° [30]. 3. For the \( \alpha \)-helix the spectroscopic frequency

\[
(1/\lambda)_{sp} = \frac{\sqrt{V''_{\text{eff}}(x_i=0)/I}}{2\pi c}
\]

must be 115 \( cm^{-1} \) for the model to give interpretation of the experiment of [11]. Here \( \lambda \) is a wavelength, \( c \) is the light speed and the dash denotes a derivative in \( x_i \). These requirements are satisfied, e.g., at the following values of the common adjustable parameters: \( \varepsilon = 3.5, D=5.7 \) kcal/mol, \( E_{\varphi} = 1 \) kcal/mol and \( E_{\psi} = 1 \) kcal/mol and the following values of the particular adjustable parameters:

a). \( \alpha \)-helix (right) \( \varphi^0_i = -57^\circ; \psi^0_i = -47^\circ \) [30]: \( L=2.026 \) Å, \( R=3.68 \) Å, \( P=3.34 \) Å, \( \eta = 170^\circ, \kappa = 170^\circ \).

b). anti-parallel \( \beta \)-sheet \( \varphi^0_i = -139^\circ; \psi^0_i = 135^\circ \) [30]: \( L=2 \) Å, \( R=3.61 \) Å, \( P=2.82 \) Å, \( \eta = 180^\circ, \kappa = 180^\circ \).
c). parallel $\beta$-sheet $\varphi_0 = -119^\circ$; $\psi_0 = 113^\circ$ [30]: $L=1.887$ Å, $R=3.55$ Å, $P=3.03$ Å, $\eta = 170^\circ$, $\kappa = 170^\circ$.

It seems plausible that the found values of the parameters are not unique and some variation of them compatible with the requirements mentioned above is possible but we could find no reasonable ways to it. However full exploration of the parameter space of the present model is a daunting task and we can not exclude the possibility that the found values of the parameters differ from reality. Nevertheless considering them as most reasonable and coinciding with the conventional figures we further restrict ourselves by dealing with them only.

5 Results

In what follows we use dimensionless variables. We define the frequency

$$\omega = \sqrt{\frac{V''_{\text{eff}}(x_i = 0)}{I}}$$

(18)

and measure time in the units of $\omega^{-1}$ so that the dimensionless time is

$$\tau = t\omega$$

(19)

Also we measure energy in the units of $I\omega^2$ and denote the dimensionless coupling constant $\rho$

$$\rho = \frac{K}{I\omega^2}$$

(20)

The results of the investigation of the effective on-site potential and the coupling interaction potential can be summarized as follows:

a). $\alpha$-helix ($(1/\lambda)_{sp}=114.75$ cm$^{-1}$) : $\rho = -0.00193; V''_{\text{eff}}(x_i = 0) > 0$ (for $x \leq 0.3$ the expansion is $\frac{V''_{\text{eff}}(x)}{I\omega^2} \approx 0.5x^2 + 0.017x^3 - 0.235x^4 + 0.6x^5 - 1.936x^6 - 3.8x^7 + 8.437x^8 + 14.555x^9 + 0.094x^{10} - 42.98x^{11} + 47.6x^{12} + ...$). The effective on-site potential is presented in Fig.3.

b). anti-parallel $\beta$-sheet ($(1/\lambda)_{sp}=84.34$ cm$^{-1}$) : $\rho = -0.00115; V''_{\text{eff}}(x_i = 0) > 0$ (for $x \leq 0.3$ the expansion is $\frac{V''_{\text{eff}}(x)}{I\omega^2} \approx 0.5x^2 + 0.004x^3 - 0.035x^4 - 4.22x^6 - 0.0001x^7 + 19.08x^8 + 0.21x^{10} + 148.844x^{12} + ...$).
c). parallel $\beta$-sheet ($\lambda_{sp}=85.49 \text{ cm}^{-1}$) : $\rho = 0.0028; V''_{eff}(x_i = 0) < 0$ (for $x \leq 0.3$ the expansion is $V''_{eff}(x) \approx 0.5x^2 - 0.3x^3 + 2.3x^4 + 3.3x^5 - 15.9x^6 - 14.6x^7 + 57.65x^8 + 52.4x^9 + 0.64x^{10} - 158.2x^{11} + 403.3x^{12} + ...$).

These results mean the following. For all three structures the coupling interaction is surprisingly weak providing good conditions for the existence of a DB. For the $\alpha$-helix and the anti-parallel $\beta$-sheet the effective on-site potential is hard (goes more steep than a harmonic one) and the coupling interaction is repulsive (a non-zero value of a peptide group displacement tends to increase the values of the neighboring peptide groups displacements with the opposite sign). In accordance with the theorems of the paper [26] a stable DB must be of zig-zag shape (peptide groups undergo out of phase oscillations). For the parallel $\beta$-sheet the effective on-site potential is soft (goes less steep than a harmonic one) and the coupling interaction is attractive (a non-zero value of a peptide group displacement tends to increase the values of the neighboring peptide groups displacements with the same sign). In accordance with the theorems of the paper [26] a stable DB must also be of zig-zag shape. Thus for no type of protein secondary structure a bell shape DB (peptide groups undergo in phase oscillations) can be stable.

In what follows we restrict ourselves by considering the case of a DB in the $\alpha$-helix because only for it the experimental data suggest such a phenomenon [11] (see the beginning of the Discussion). The set of difference equations (5) can not be solved analytically and is analyzed by direct numerical integration for 25 coupled equations (motivated by the fact that 25 is the average number of peptide groups in $\alpha$-helices of bacteriorhodopsin used in the experiment [11]). We use fixed-end boundary conditions $x_1(t) = x_{25}(t) = 0$ that seem to be more appropriate for the situation in proteins than commonly used periodic ones. We find as an example a 3-site DB. To prove that a localized and stable object can be obtained in the $\alpha$-helix we resort to the usual procedure [25]. We define the discrete per site energy in 3 lattice sites around the 13-th central one

$$E(3) = \frac{1}{3} \sum_{l=12}^{14} e_l$$

(21)

where $e_l$ is the individual symmetrized local site energy density

$$e_l = \frac{1}{2} \left( \frac{d x_i}{d \tau} \right)^2 + \frac{U_{loc}(x_i)}{I \omega^2} + \frac{1}{2I \omega^2} \left( U(x_{l-1}; x_l) + U(x_l; x_{l+1}) \right)$$

(22)

The existence of a localized and stable zig-zag shape DB is exemplified in Fig.4 by the fact that the energy $E(3)$ remains essentially constant with time and in Fig.5 by an explicit picture. It should be stressed that for our realistic
potentials it is rather difficult to switch out the coupling interaction without modifying the effective on-site potential. Thus the commonly accepted way to construct a DB starting from an uncoupled (or else anticontinuous) limit is inapplicable in our case. That is why, instead, we find the initial configuration to fall into a DB from the very beginning at a given coupling interaction for the $\alpha$-helix calculated in Sec.3. In Fig.4 and Fig.5 this configuration is chosen to be $x_{13}(0) = 0.3; \ x_{12}(0) = x_{14}(0) = -0.025$ while $x_i(0) = 0$ for all other $i$ and zero velocity at each site. The chosen amplitude $x_{13} = 0.3$ corresponds to the deviations of the torsional angles $\Delta \varphi_{13} = \Delta \psi_{12} = x_{13}/2 \approx 10^\circ$ from their equilibrium values.

6 Discussion

The results obtained testify that a localized and stable zig-zag shape DB can exist in all three types of protein secondary structure. However experimental data which can be interpreted with the help of the DB concept are available only for $\alpha$-helix proteins but not $\beta$-sheet ones [10], [11]. In our opinion the reason for this is in the way of excitation of long-lived oscillations in this experiments rather than in the propensities of different types of protein secondary structure to sustaining DBs. The absorption of far IR laser pulse used in [11] by proteins requires long one-dimensional hydrogen bonded chains [17] that take place in $\alpha$-helicies but are absent in $\beta$-sheets.

The revealed hardness of the effective on-site potential for the $\alpha$-helix and the anti-parallel $\beta$-sheet is in contrast with a widely spread point of view that such potential in biomolecules is mainly determined by hydrogen bonds and that is why should be a soft-type one [3], [26]. In our case detailed account of all interactions leads to a contrary result.

The energy of the 3-site DB obtained for the $\alpha$-helix is $3E(3)I\omega^2 \approx 2 \cdot 10^{-12}$ erg $\approx 40k_BT$ at $T=300 \ K^\circ$. This value means that at room temperatures large amplitude DBs ($\Delta \varphi = \Delta \psi \approx 10^\circ$) can hardly be spontaneously excited by thermal fluctuations. However the latter may not be true for DBs with smaller amplitudes and here it seems timely to touch upon the question of influence of temperature on the existence of DBs in protein secondary structures. DBs are known to remain essentially stationary and localized and to be very long-lived at zero temperature. At non-zero temperatures thermal fluctuations tend to lead to DB motion and more rapid decay [2], [3], [33]. Within the framework of our interpretation of the the experiment of [11] with the help of a DB concept it should be recalled that the observed there long-lived oscillations in $\alpha$-helicies of bacteriorhodopsin excited by far IR laser pulse have a life-time of order of 500 ps accommodating approximately 1500 vibrations. The decay of a DB can be formally modeled by introducing a dissipative term.
\(-\gamma \frac{dx_i(t)}{dt}\) in the left hand side of the equation of motion (5) and corresponding white noise \(\zeta_i(t)\) in the right hand one. Here the friction coefficient \(\gamma\) must be related with the white noise correlation function via the fluctuation-dissipation theorem \(<\zeta_i(t)\zeta_i(0)> = 2k_B T \gamma \delta(t) \delta_{ij}\) where \(k_B\) is the Boltzman constant, \(T\) is the temperature, \(\delta(t)\) is Dirac \(\delta\)-function and \(\delta_{ij}\) is the Kronecker symbol. However such formal way of introducing dissipation does not reveal the microscopic origin of the friction coefficient \(\gamma\). To do it for the case of peptide chain dynamics is a difficult task which is out of the scope of this chapter. Here we can afford ourselves only some preliminary speculations on this subject. There are different contributions into the mechanism of friction that can be conceivable for the peptide chain rotational dynamics in protein interior. The most obvious hydrodynamic damping by interaction with solvent seems to be of minor importance because at considered deviations of the torsional angles \(\leq 10^\circ\) the linear displacements are much less than the diameter of a water molecule (see also [11] and refs. therein). In our opinion the dominant contribution into dissipation originates from the fact that the rotation of the peptide group at angle \(x\) round the axis \(\sigma\) requires some translational displacement of axis points where the atoms \(N_i\) and \(C'_{i-1}\) are initially situated (see Fig.2) that leads to transvers distortions of the backbone (actually this is the excitation of transvers linear phonon modes). Such process consumes energy leading to an acoustic damping mechanism. At a macroscopic level this dissipation mechanism can be described by the so called ”Landau damping” \(\gamma_{ac} \propto \omega^2\) [34]. However such phenomenological description requires support from microscopic consideration that is beyond our knowledge at present. Moreover the situation with dissipation is not so unambiguous as one can conceive from above. There are testimonies that in some cases of nonlinear lattices the energy relaxation from a DB first accelerates with the increase of the friction coefficient from zero value but then becomes slower and slower [5]! It is not clear at present whether this surprising result is generic or it is model dependent (e.g., dependent on the type of the thermostat used). In any case it opens interesting perspectives for application of the DB concept to the problem of localized vibrational energy storage in enzymes. In this connection the coincidence of the obtained value for the DB energy \((\approx 40k_BT\) at room temperature) with usual activation energies of enzymatic reactions is rather intriguing. One can imagine oneself that in secondary structures of enzymes there DBs can be excited at substrate binding and be long-lived enough to play some functional role as the sources of energy localization and storage utilizing in such a way the binding energy. For instance a DB may serve as the so called ”rate promoting vibration” (RPV) for enzymatic reactions involving environmentally assisted hydrogen tunneling. The RPV acquires more and more experimental testimonies [35], [36], [37], [38], [39] but its physical origin still remains mysterious. However the estimated dominant peaks in the spectral densities of the RPV indicate motions on the 150 \(cm^{-1}\) frequency scale [38] that is rather close to the obtained frequency 115 \(cm^{-1}\) of the DB in the \(\alpha\)-helix. Here we
refrain from further discussing this speculation.

7 Conclusion

The conclusions of this chapter are summarized as follows. The dynamics of a peptide chain is considered within a realistic model with stringent microscopically derived coupling interaction potential and effective on-site potential. The coupling interaction is found to be surprisingly weak for all three main types of protein secondary structure but different in character: repulsive for \(\alpha\)-helix and anti-parallel \(\beta\)-sheet structures and attractive for parallel \(\beta\)-sheet structure. The effective on-site potential is found to be a hard one for \(\alpha\)-helix and anti-parallel \(\beta\)-sheet and a soft one for parallel \(\beta\)-sheet. In all three types of protein secondary structure a stable zig-zag shape discrete breather associated with the oscillations of torsional (dihedral) angles can exist due to the weakness of the coupling interaction.

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Fig. 1. A schematic representation of the peptide chain with all designations necessary for the text. The covalent bonds are shown as bold lines. Dotted lines denote hydrogen bonds. Dashed lines denote auxiliary axes.
Fig. 2. A look on the chain from the axis of rotation $\sigma$ explaining the definition of the angle $x_i$ (defined in (1)).
Fig. 3. The normalized effective on-site potential $V_{\text{eff}}(x)$ (see (3)) for the $\alpha$-helix. Here $I$ is the moment of inertia of the peptide group relative the axis $\sigma$ and $\omega$ is the frequency. The range for the angular displacement $x$ (defined in (1)) is $4\pi$ because it is twice of the torsional angles $\varphi$ and $\psi$ (see (1)). The part of the potential over the upper cut off has a maximum with the value $\approx 1.3$. 
Fig. 4. The dependence of the energy in the 3-site discrete breather determined by (21) and (22) on dimensionless time $\tau$ (19) in the log-time scale for the $\alpha$-helix.
Fig. 5. The explicit picture of the long time (in dimensionless units (19)) behavior of the discrete breather in the α-helix of 25 peptide groups named here as sites. The displacement $x$ (defined in (1)) is the angular deviation of the peptide group from its equilibrium position.