Collective Excitations in α-helical Protein Structures Interacting with the Water Environment

Vasiliy N. Kadantsev[1], *Alexey Goltsov*[2*]

[1] *Moscow Technological University (MIREA), Moscow, Russia*

[2] *School of Applied Sciences, Abertay University, Dundee, UK*

[*]Corresponding authors: Alexey Goltsov, *alexey.goltsov@gmail.com*

ORCID ID: 0000-0001-6725-189X

Abstract

Low-frequency vibrational excitations of protein macromolecules in the terahertz frequency region are suggested to contribute to many biological processes such as enzymatic activity, energy/charge transport, protein folding, and others. To explain high effectiveness of energy storage and transport in proteins, two possible mechanisms of the long-lived excitation in proteins were proposed by H. Fröhlich and A.S. Davydov in the form of either vibrational modes or solitary waves, respectively. In this paper, we developed a quantum dynamic model of vibrational excitation in α-helical proteins interacting with their environment formed by water molecules. In the model, we distinguished three coupled subsystems, i.e. (i) a chain of hydrogen-bonded peptide groups (PGs), interacting with (ii) the subsystem of side residuals which in turn interacts with (iii) the environment, surrounding water responsible for dissipation and fluctuation processes in the system. It was shown that under reasonable approximations the equation of motion for phonon variables of the PG chain can be transformed to nonlinear Schrodinger equation for order parameter which admits bifurcation into the solution corresponding to weak damped vibrational modes (Fröhlich-type regime). A bifurcation parameter in the model is derived through the strength of interaction between alpha-helical protein and its environment. As shown, in the bifurcation region, a solution corresponding to Davydov soliton can exist. The suggested mechanism underlying emerging macroscopic dissipative structures in the form of collective vibrational modes is discussed in connection with the recent experimental data on the long-lived collective protein excitations in the terahertz frequency region.

Keywords: α-helical protein; collective excitation; phonons; solitons; Fröhlich condensation; biological effect; terahertz radiation

1. Introduction

A concept of protein molecules as dynamic systems is backed by the numerous experimental and theoretical investigations of the correlation between protein dynamics, structure and functions. Currently, intense efforts are undertaken to elucidate contribution of internal protein motion to protein functions such as enzyme activity, charge/energy transport, structural, sensor, signal transduction, and others (Niessen *et al.*, 2017a), (Lindorff-Larsen *et al.*, 2005), (Kamerlin and Warshel, 2010). Protein vibration excitations related to their functions include either localised oscillation of atom groups and bonds or the large-scale vibrations of subdomains of the proteins. High-frequency vibrations of atom groups and intrapeptide bonds (e.g. C=O stretching) lie within the IR optical spectrum, while low-frequency collective vibrational modes are ranged at the lowest end of the far IR spectrum and in the terahertz frequency range (Xie, Yao and Ying, 2014), (Balu *et al.*, 2008).

Different types of the collective modes are reported to be excited in protein molecules, i.e. normal vibration modes (Acbas *et al.*, 2014; Turton *et al.*, 2014), sound waves (phonons) (Liu *et al.*, 2008), and coherent vibrational states (Del Giudice *et al.*, 1986; Rolczynski *et al.*, 2018) which are observed on a timescale from picosecond to nanosecond. Vital cellular processes are suggested to link to the excitation of the long-lived collective degreases of freedom in macromolecules which are characterised by a weak coupling to the other ones and related to the substantially non-equilibrium processes in proteins (Mohseni *et al.*, 2014). The isolation and investigation of weakly relaxing excitations of types of phonons, exitons, plasmons and others have given an insight into a vast amount of experimental facts in solid and soft physics. Similarity of the non-linear mechanisms underlying formation of the collective excitations in different molecular systems suggestes that long-lived non-equilibrium states can be realised in the living systems and plays a crucial role in effectiveness of chemical energy transformation, transport and storage in cells (Lambert *et al.*, 2013), (Davydov, 1985). Investigation and elucidation of the physical mechanisms of the formation and physiological functions of these exitations in cellular molecular structures are one of the formidable challenges in molecular biophysics and the subject of intensive experimental and theoretical works over the past decades (Engel *et al.*, 2007; Acbas *et al.*, 2014; Turton *et al.*, 2014; Goncharuk *et al.*, 2017; Niessen *et al.*, 2017b), (Kuramochi *et al.*, 2019).

The physical mechanism of the collective coherent excitations far from thermal equilibrium and their possible role in biosystems functions have been proposed and

investigated early by H. Fröhlich (Fröhlich, 1968a). He has developed a phenomenological kinetic model of collective longitudinal vibrational-polar modes (phonons) excited in the 0.1 GHz - 1 THz frequency range and suggested their role in biological processes such as enzymatic catalysis, biomembrane function, protein-protein interaction, and the interaction of biosystems with microwave radiation (Fröhlich, 1970, 1980).

The general idea underlying the suggested mechanism of long-lived coherent vibrations in biological systems is in an assumption that vibrational modes can condense into the lowest-frequency vibrational mode like the phenomenon of Bose-Einstein condensation. In contrast to Bose-Einstein condensation occurring in thermal equilibrium, Fröhlich condensation takes place in non-equilibrium condition at the energy supply and dissipation in non-linear molecular structures (Mesquita, Vasconcellos and Luzzi, 2004). Thus, excitation of the Fröhlich mode, in the form of the coherent dynamic structure, can be considered as the emergence of a space-temporal dissipative structure in according to Prigogine's theory (Prigogine and Lefever, 1973) which is governed by the self-organization principals of Haken's synergetics in non-linear systems (Haken, 1983). At present, further investigation of the Fröhlich condensation in quantum dynamics and quasi-classical approaches were undertaken in order to determine the physical conditions of phonon condensation in proteins functioning far from thermal equilibrium (Vasconcellos *et al.*, 2012), (Salari *et al.*, 2011), (Preto, 2017), (Reimers *et al.*, 2009), (Nardecchia *et al.*, 2018).

Another type of coherent excitations in the form of solitary waves was proposed theoretically by A.S. Davydov in order to unravel one of the central problems in bioenergetics, i.e. a highly effective long-distance transport of energy/charge within macromolecules (Davydov, 1985). As a result of a series of his works, the theory of soliton transport of energy/charge in the α-helical proteins has been developed (Davydov, 1977, 1985). Additionally, it was concluded that the α-helical peptide structure plays a significant role in the formation of the soliton, travelling a long distance with weak decay.

The soliton model was applied to describe the transport of energy, released in the hydrolysis of ATP and localised in the amide-I vibration (C=O bond), along the chain of peptide groups at room temperature (Davydov, 1985). Mechanisms of localisation, storage, and transport of energy are defined in the model as non-linear interactions of the high-frequency amide-I excitation (1667 cm^{-1}) and low-frequency acoustic modes in the 1D protein structure.

An alternative to the quantum Davydov model (Davydov, 1977), a classical vibrational model of the interpeptide excitation dynamics was suggested by Takeno, who studied soliton

stability at room temperature (Takeno, 1984). Various theoretical aspects of soliton dynamics in protein macromolecules, including soliton stability, thermalisation, solitons' interaction and others were investigated in various approximations (Lawrence *et al.*, 1987), (Lupichev, Savin and Kadantsev, 2015). The unified approaches to the description of both Davydov soliton mode and Fröhlich condensation mode excitations in proteins at the conditions far away from thermal equilibrium were developed (Del Giudice *et al.*, 1986; Bolterauer and Tuszyński, 1989; Bolterauer, Tuszyński and Satarić, 1991; Mesquita, Vasconcellos and Luzzi, 2004).

Searching for the experimental observation both of these types of coherent excitations in proteins remains an area of intense experimental research and source of lively debate (Reimers *et al.*, 2009; Salari *et al.*, 2011; Preto, 2017), (Nardecchia *et al.*, 2018), (Weightman, 2014). Experimental evidence of the coherent vibrational states in protein macromolecules was obtained by the IR, Raman, terahertz spectroscopy and their combinations (Nardecchia *et al.*, 2018), (Lundholm *et al.*, 2015). The main efforts on the detection of long-lived vibrational excitations in living systems include investigation of resonance effects of microwave irradiation on cellular functions in the THz frequency band predicted by Fröhlich (Pokorný, 1999), (Foletti *et al.*, 2013), (Markov, 2015), (Fröhlich, 1980). Theoretical investigation in this field of electromagnetic biology mainly aim at the identification of biological structures enabling to maintain collective vibration states (α-helical protein structure, cytoskeleton microtubules, biomembranes and others) and calculation of the vibration spectrum of collective excitations containing specific frequency domains to inform an experimental search for resonance effects of terahertz irradiation on cells (Fröhlich, 1988), (Pokorný, 2004), (Kadantsev and Savin, 1997), (Nardecchia *et al.*, 2018). The resonance interaction of cells with terahertz irradiation is considered as the possible mechanism which can be explored in the development of various medical applications for the non-invasive diagnostics and therapy (Foletti *et al.*, 2013), (Markov, 2015), (Siegel, 2004), (Foletti *et al.*, 2013).

In this work, we develop further the molecular models of the collective excitations in α-helical peptide macromolecules (Kadantsev, Lupichov and Savin, 1987; Kadantsev, Lupichcv and Savin, 1994; Lupichev, Savin and Kadantsev, 2015), (Kadantsev and Goltsov, 2018) and extend quantum dynamics approach to take into account proteins interacting within the environment. The proteins interaction with surrounding water possessing specific properties in the hydration shell has been shown to contribute significantly to various structural, dynamic and functional properties of biological molecules (Bellissent-Funel *et al.*, 2016). In the model development we followed the Fröhlich approach (Fröhlich, 1968a) and distinguished three subsystems in the protein molecule interacting with its environment: (i) a chain of hydrogen-

bonded peptide groups (PGs) interacting with (ii) the subsystem of side residuals of the protein which in turn interact with (iii) surrounding water. We show that consideration of the interaction between macromolecules and their water environment significantly effects on the dynamic behaviours of the α-helical structures and contributes to the formation of coherent vibrational states of the PG chain. We used the quantum mechanics approach which have been developed earlier to model autolocalized states (polaron) of quantum quasiparticle (valence electron) of intramolecular excitations in the PG chain (Kadantsev, Lupichov and Savin, 1987; Kadantsev, Lupichcv and Savin, 1994; Lupichev, Savin and Kadantsev, 2015). The developed model is used to investigate conditions when the molecular interaction between the PGs, side residual chain and water environment leads to the excitations of vibrational and soliton types in α-helical protein structures.

2. Phonons in a one-dimensional chain of hydrogen-bonded peptide groups interacting with side radicals

The secondary protein structure, α-helix, is formed as a result of folding up of polypeptide chain in a helix due to the interaction of amino acid residues (Fig. 1a). This interaction determines space periodicity of the secondary structure in proteins, and in turn, its stability is ensured by hydrogen bonds between NH- and CO-groups of the backbone (Fig. 1b).

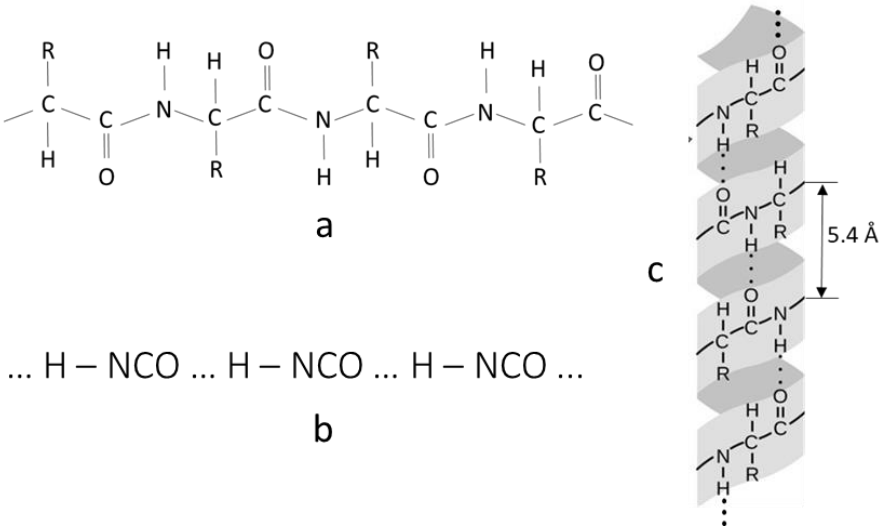

Fig. 1. (a) A polypeptide chain with amino acid residues (R). (b) The chain of hydrogen-bonded peptide groups. (c) Structure of α-helical protein, where one of the three hydrogen-bonded PG chains with the side-chains of amino acid residues are shown. Hydrogen-bonds are depicted by dots.

The α-helix has a form of a coil, and its inner part consists of a tightly twisted backbone with amino acid radicals directed outwards (Fig. 1c). Electrical charge distribution in the peptide group forms its electrical dipole moment equal to 3.5 D and directed along H-bond (Davydov, 1977).

Consider a one-dimensional chain of hydrogen-bonded peptide groups with hydrogen bonds between (NH)- and CO-groups (Fig. 1b). Assume intrinsic motion of proton and the rest of the PGs (NCO) and define equilibrium positions of the PGs in the *l*-site z=*la* (*l*=0, 1, 2, …) along the α-helix (the z-axis), where a= 5.4 Å is chain spacing. Denote displacement of the atoms from equilibrium positions of the PG in the *l*-site by $\xi_{l,1}$ for hydrogen and $\xi_{l,2}$ for the rest of the PG atoms. In harmonic approximation, potential energy of interaction between atoms of the nearest PGs and nearest residues R is expressed by a quadratic form:

$$U = \frac{1}{2}\sum_{l}\left[\chi_{1,2}\left(\zeta_{l+1,1}-\zeta_{l,1}\right)^2+\chi_{2,1}\left(\zeta_{l,1}-\zeta_{l,2}\right)^2+\chi_{0,1}\xi_{l,1}^2+\chi_{0,2}\xi_{l,2}^2\right], \qquad (1)$$

where $\chi_{1,2}$ and $\chi_{2,1}$ are elastic coefficients of hydrogen and valence bonds respectively; $\chi_{0,1}$ and $\chi_{0,2}$ are elastic coefficients of the interaction of protons and NCO group with the side chain of residues, respectively. Choose the following cyclic boundary condition for the PG chain

$$\zeta_{l,\alpha} = \zeta_{l+N,\alpha} \text{ for } \alpha\text{=1 and 2}, \qquad (2)$$

where N is a number of GPs in the chain.

To write the Hamiltonian of the PG chain, express the operators of atom displacement from equilibrium positions through the operators of the creation $b_{-k,s}^{+}$ and annihilation $b_{k,s}$ of phonons as

$$\xi_{l,1}^{(s)} = \sum_{k}\left[\frac{\hbar}{2m_{\alpha}N\Omega_s(k)}\right]^{1/2} e^{ikx}\left(b_{k,s}+b_{-k,s}^{+}\right), \qquad (3)$$

where the operators of the creation and annihilation satisfy the commutative relationships

$$[b_{k,s}, b_{k',s'}^{+}] = \delta_{kk'}\delta_{ss'} \text{ and } [b_{k,s}, b_{k',s'}] = 0. \qquad (4)$$

Here δ is the Kronecker symbol, k is the wave number taking N values in the first Brillouin zone

$$k = \frac{2\pi\eta}{Na}, \text{where } \eta = 0, \pm1, \cdots, \pm\frac{N}{2}, \qquad (5)$$

and index s points to either acoustic (s=1) or optic (s=2) phonons.

The Hamiltonian of phonons in the PG chain can be written in the harmonic approximation as

$$H_p = \sum_{k,s} \hbar\, \Omega_s(k) \left(b_{k,s}^{+} b_{k,s} + \frac{1}{2} \right), \tag{6}$$

where two functions $\Omega_s(k)$ define dispersion relationship for frequencies of acoustic and optic branches of the vibration in the PG chain with s = 1 and 2 respectively.

The dispersion relationship $\Omega_s(k)$ for the PG chain with interaction defined by eq. (1) can be obtained in the form

$$\Omega_s^2(k) = A + (-1)^s \sqrt{A^2 - B(k)}, \tag{8}$$

where

$$A = \frac{1}{m_1 m_2} \left[m_1 \chi_{0,2} + m_2 \chi_{0,1} + (m_1 + m_2)(\chi_{1,2} + \chi_{2,1}) \right]$$

and

$$B = \frac{1}{m_1 m_2} \left[(\chi_{0,1} + \chi_{0,2})(\chi_{1,2} + \chi_{2,1}) + \chi_{0,1}\chi_{0,2} + 4\chi_{1,2}\chi_{2,1} sin^2 \left(\frac{ka}{2} \right) \right].$$

Here $m_1 = m_p$ and $m_2 = 41.7 m_p$ are mass of proton and the PG group respectively. Dispersion curves calculated at the values of elastic constants of the PG chain (Lupichev, Savin and Kadantsev, 2015) are shown in Fig. 2. As seen, according to dispersion equation (8), the PG chain with interaction (1) obeys a narrow band of the normal modes of the vibrations $\Omega_s(k)$ in the terahertz frequency range.

Similarly, introduce the phonon Hamiltonian for the residue system of the PG chain which can be represented as a system of *N* oscillators of mass *M* having own frequencies of oscillation $\Omega_t(q)$

$$H_C = \sum_{q,t} \hbar\, \Omega_t(q) \left(c_{q,t}^{+} c_{q,t} + \frac{1}{2} \right), \tag{9}$$

where $c_{q,t}^{+}$ and $c_{q,t}$ are the operators of the creation and annihilation of phonons in the residue side-chain which correspond to the displacement of the residues from their equilibrium positions ς_l. $\Omega_t(q)$ are the phonon frequency of type *t* in the residue side-chain and q is the wave number. The representation of the residue side-chain as a set of oscillators in the model is based on the experimental data on the protein side-chain dynamics obtained by the X-ray diffraction, NMR methods and spin labelling EPR spectroscopy which provides detailed information on the side-chain order parameter and mobility on the picosecond to microsecond timescale (Columbus and Hubbell, 2002), (Go, Noguti and Nishikawa, 1983), (Sivaramakrishnan *et al.*, 2008). Moreover, molecular dynamic and normal mode calculations of protein internal dynamics showed that harmonic approximation for the modelling of the

residue side-chain dynamics is the satisfactory approximation that gives the consistent description of the normal low-frequency modes in the range of 120-200 cm^{-1} (Go, Noguti and Nishikawa, 1983).

Consider interaction of the phonons in the PG and residue chains in the α-helical protein structure by adding the following anharmonic operator of interaction to the Hamiltonian of non-interacted chains

$$W = \sum_{l} V(l)\varsigma_l^{(t)}\xi_{l,1}\xi_{l,2}\,, \tag{10}$$

where

$$\varsigma_l^{(t)} = \sum_{q}\left[\frac{\hbar}{2MN\Omega_t(q)}\right]^{1/2} e^{ikx}\left(c_{q,t} + c_{-q,t}^{+}\right). \tag{11}$$

Substitution of eqs. (3) and (10) into eq. (9) gives the operator of anharmonic perturbation in the form

$$W = \sum_{k,k'}\left(V_{k,k'}c_{k-k'}^{+}b_k^{+}b_{k'} + H.c.\right), \tag{12}$$

where

$$V_{k,k'} = \left(\frac{\hbar^3}{8N^3m_1m_2M\Omega_s(k)\Omega_{s'}(k')\Omega_t(k-k')}\right)^{1/2}. \tag{13}$$

The matrix elements (13), which are different from zero on the functions of occupation numbers, corresponds to the processes occurring with energy and momentum conservation without consideration of umklapp process:

$$\Omega_t(k-k') + \Omega_s(k) = \Omega_{s'}(k').$$

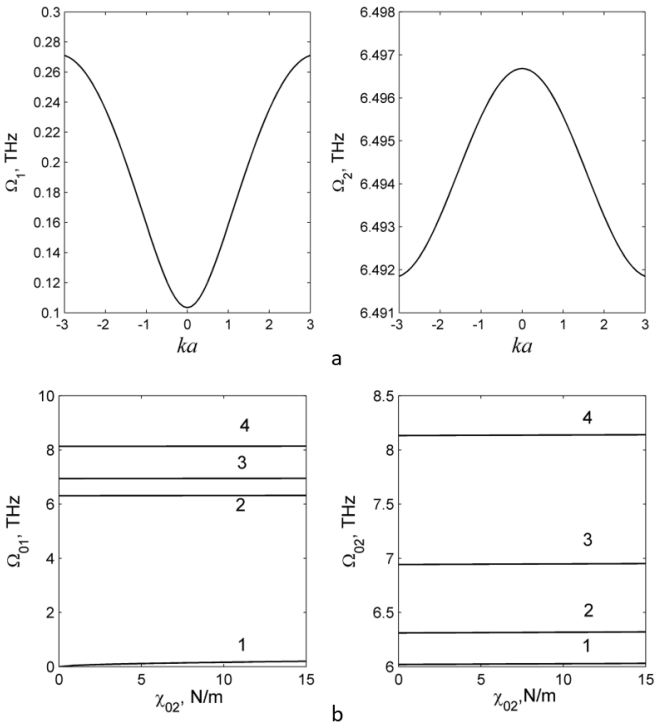

Fig. 2. Dispersion curves for the chain of hydrogen-bounded PGs calculated at the following elastic constants (Lupichev, Savin and Kadantsev, 2015). (a) s=1, $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$, $\chi_{0,1} = 5.0\ \mathrm{N}m^{-1}$, $\chi_{0,2} = 0\ \mathrm{N}m^{-1}$. (B) s=2, $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$, $\chi_{0,1} = 5.0\ \mathrm{N}m^{-1}$, $\chi_{0,2} = 0\ \mathrm{N}m^{-1}$. (b) Dependence of the frequency Ω_{01} (C) and Ω_{02} (D) (k=0) on constant χ_{02} at the fixed values of elastic constants $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$ and different constant $\chi_{0,1}$: line 1 - $\chi_{0,1} = 0.0\ \mathrm{N}m^{-1}$, line 2 - $\chi_{0,1} = 3.0\ \mathrm{N}m^{-1}$, and line 3 - $\chi_{0,1} = 25.0\ \mathrm{N}m^{-1}$.

Approximations (eqs. (10)-(12)), which we used at the description of the coupled PG chain and residue side-chain dynamics, are based on the experimental data obtained by site-directed spin labelling NMR, EPR and Raman spectroscopy on the side-chain mobility and the backbone order parameter (Lindorff-Larsen *et al.*, 2005), (Columbus and Hubbell, 2002), (Kuramochi *et al.*, 2019). This data particularly showed the tight coupling between backbone and side-chain dynamics in α-helical structures, but at the same time revealed the liquid-like dynamics of the side-chains that significantly contributes in the folded protein structures and functions.

3. Interaction of α-helical protein structure with water environment

Consider the interaction of the α-helical protein with its environment, surrounding water molecules which form a heat reservoir with a non-zero temperature *T*. The protein-water interaction defines dissipation processes in the system and contributes to the structure and functions of proteins (Bellissent-Funel *et al.*, 2016), (Kurian *et al.*, 2018a) . In the model, we represent surrounding water molecules by a large set of harmonic oscillators interacting with the protein molecule and suggest that this system possesses collective excitation modes with dynamics similar to that of an oscillators' ensemble. This approximation can be backed by the observation of the collective vibrational subpicosecond dynamics (phonons) of the hydrogen bond network of water molecules in hydration shells of protein in terahertz and IR spectra (Conti Nibali and Havenith, 2014).

Then the energy operator of the heat reservoir (surrounding water) can be written as a sum of energy operators for the independent oscillators through the operators of the creation $B_{p,t}^{+}$ and annihilation $B_{p,t}$ of phonons with the wave number p and frequencies dispersion relation $\omega_t(p)$

$$H_B = \sum_{p,t} \hbar\omega_t(p)\left(B_{p,t}^{+}B_{p,t} + \frac{1}{2}\right). \tag{14}$$

To calculate energy of the joint action of heat reservoir's oscillators on the protein macromolecule, W_B, we assumed that each oscillator contributes linearly to the energy W_B and interacts only with the residue side-chain of the α-helical protein. So, following Taneko's model (Takeno, 1984), we suggested that the PG chain interacts with the environment through amino acid residues R (Fig. 1). Then, interaction operator W_B can be written as

$$W_B = \hbar \sum_{p,gt,t\prime} \left\{\sigma_{tt\prime}(g,p)c_{g,t}^{+}B_{p,t\prime} + H.c.\right\}. \tag{15}$$

Parameter $\sigma_{tt\prime}(g,p)$ defines strength of the interaction between heat reservoir's oscillators of types t' and the residue side-chain oscillators of type *t*. Note that the operator (15) describes a wide class of relaxation mechanisms related to collective excitations (Lupichev, Savin and Kadantsev, 2015). The representation of the heat reservoir by a set of harmonic oscillators (Eq. 14) and protein interaction with the thermal reservoir in the form of Eq. (15) are commonly used in the modelling molecular chain dynamics particularly in the Wu-Austin Hamiltonian approximation (Columbus and Hubbell, 2002), (Vasconcellos *et al.*, 2012), (Wu and Austin, 1981).

For simplicity, let drop indexes which define phonon type, and indexes *s*, *t*, and *t'* of variables will below mean that the specific variable belongs either to the PG chain or the residue side-chain or heat reservoir, respectively.

4. Equation of motion

One of the features of a self-organisation behaviour of complex systems is the occurrence of system instability with respect to either one or several variables (dynamic modes) at the attainment of a critical condition (Haken, 1983). If the rest of the modes damp the different exclusion procedures of the stable variables can be applied that leads the system behaviour as a whole to be defined by the behaviour of a few unstable variables which govern all the damped modes. In real systems, a hierarchy of relaxation times takes place that allows applying adiabatic approximation for the exclusion of fast-relaxing variables. In the case of protein molecules, the fast-relaxing variables c_g^+ and c_g relate to the residue side-chain which directly interacts with the environment (structured water) surrounding a native protein and supporting stability of its structure. This approximation is based on the NMR experimental data on relaxation of order parameter and analysis of the time scale in backbone and side-chain dynamics (Columbus and Hubbell, 2002), (Wu and Austin, 1981). The experimental results revealed that the side chains exhibit faster sub-nanosecond dynamics than microsecond motions of the backbone.

To exclude fast-relaxing variables c_g^+ and c_g, we use Heisenberg equation for these operators

$$i\hbar \frac{dA}{dt} = [A, H], \tag{16}$$

where $\mathrm{A} = \{c_g^+, c_q\}$ and H is the energy operator of the macromolecule-heat reservoir system

$$H = H_P + H_C + H_B + W_P + W_B. \tag{17}$$

Substitution of H_P, H_C, H_B, W_P, and W_B in to eq. (17) and then to eq. (16) gives the equation of motion for the operator c_g

$$i\hbar \frac{dc_g}{dt} = \hbar\Omega_t(g)c_g + N\sum_k V_{k,g} b_{k-g}^+ b_k + \hbar\sum_p \sigma(p,q)B_p, \tag{18}$$

and the identical equation for the operator c_g^+. Then let require

$$\frac{dc_g}{dt} = \frac{dc_g^+}{dt} = 0. \tag{19}$$

The following relationship can be obtained for c_g^+ and c_g from eqs. (18) and (19)

$$c_g = -\frac{N}{\hbar\Omega_t(g)}\sum_k V_{k,g} b_{k-g}^+ b_k - \sum_p \frac{\sigma(p,q)}{\Omega_t(g)} B_p. \tag{20}$$

Using eq. (20) and commutation relations (4) for the Bose-operators, we get the energy operator in the form

$$H_S = H_P + H_B + H_{PB}, \tag{21}$$

where the energy operator of protein macromolecule is expressed only through the variables related to the PG chain

$$H_P = \sum_k \varepsilon_k b_k^+ b_k - \frac{N^2}{\hbar}\sum_{g,k,k'} \frac{V_{k,k'} V_{k',g}^*}{\Omega_t(g)} b_k^+ b_{k'-g}^+ b_{k-g} b_{k'}. \tag{22}$$

Here

$$\varepsilon_k = \hbar\Omega_t(k) - \frac{2N^3|V|^2}{\hbar\Omega_t(k)}. \tag{23}$$

Hamiltonian operator of the heat reservoir H_B is written in the form

$$H_B = \sum_p \varepsilon_p B_p^+ B_p\,, \tag{24}$$

where

$$\varepsilon_p = \hbar\omega(p) - \frac{\hbar N|\sigma|^2}{\Omega_t(p)}. \tag{25}$$

The energy of interaction of the α-helical protein with the heat reservoir H_{PB} after exclusion of the variables related to the residue side-chain is defined by

$$H_{PB} = -\sum_{k,p}\{G(k,p) b_k^+ b_{k-p}^+ B_p + H.c.\}, \tag{26}$$

where

$$G(k,p) = \frac{\sigma(k,p)VN}{\Omega_t}. \tag{27}$$

Equation of motion for dynamic variables of the PG chain and heat reservoir can be derived using Heisenberg equation (16) for the operators $b_k, b_k^+, B_p,$ and b_p^+, the Hamiltonian operator (21), and eqs. (22)-(27)

$$i\hbar\frac{db_k}{dt} = \varepsilon_k b_k - \frac{N^2}{\hbar}\sum_{g,k\prime}\frac{V_{k,k\prime}V^*_{k\prime,g}}{\Omega_t(g)} b^+_{k\prime-g} b_{k-g} b_{k\prime} - \sum_p G(k,p) b^+_{k-p} B_p \tag{28}$$

and

$$i\hbar\frac{dB_p}{dt} = \varepsilon_p B_p - \sum_k G^*(k,p) b_{k-p} b^+_k. \tag{29}$$

At the next step, we use the obtained eqs. (28) and (29) to derive the motion equation for the growing modes and define system dynamics near unstable stationary points. Moreover, we describe dissipation in the system and express fluctuating forces which are coursed by the interaction of the protein macromolecule with the environment.

5. The Langevin equation for generalized coordinates of the protein macromolecule

As known, all basic (microscopic) equations of motion are invariant with respect to time reversal, that is the motion is entirely reversal. Although dissipative forces, violating this invariance, cannot be expressed in the original equations, under certain assumptions the Langevin equations can be derived from the Heisenberg equation for a system interacting with a heat reservoir which is represented by a set of harmonic oscillators (Shibata and Hashitsume, 1978).

Heretofore, we considered the model of α-helical protein interacting with the heat reservoir as the systems of interacting quantum oscillators. However, this molecular system can be considered as the classical one that can be justified by that a number of phonons in strongly exciting modes in the protein and a number of oscillators in the heat reservoir are significantly larger than unity. This allows us to represent phonon amplitudes by c-numbers and substitute operators b_k, b_k^+, B_k , and B_k^+ in eqs. (28) and (29) for c-numbers β_k, β_k^*, B_k, and B_k^* respectively. Amplitude $\beta_k(t)$ can be considered as the generalised coordinates with corresponding generalised momentum $i\hbar\beta_k^*$. Moreover, coefficients, defining intensity of phonon interaction of the different subsystems in the model, are assumed to weakly depend on the phonon momentum. Then, eqs. (28) and (29) can be integrated as the classical ones that gives the solution of eq. (29) in the form:

$$B_p(t) = B_p(0)e^{-i\frac{\varepsilon_p}{\hbar}t} + i\int_{-\infty}^{t}\sum_k \frac{G^*(k,p)}{\hbar}\beta_{k-p}(\tau)\beta_k^*(\tau)e^{-i\frac{\varepsilon_p}{\hbar}(t-\tau)}d\tau\,, \tag{30}$$

where $B_p(0)$ is the initial value of amplitude $B_p(t)$ at t=0.

Introduce a new variable $\widetilde{\beta_k}(t)$

$$\beta_k(t) = \widetilde{\beta_k}(t)e^{-i\Omega_k t} \tag{31}$$

and use below the previous notation $\beta_k(t)$ for $\widetilde{\beta_k}(t)$. Then apply adiabatic approximation commonly used in the modelling of cooperative systems, i.e. the relaxation times of the strong exciting phonon modes become longer in comparison with the typical relaxation times for the heat reservoir variables. This allows factoring out the preexponential term in eq. (30) and obtain it in the form

$$B_p(t) = B_p(0)e^{-i\frac{\varepsilon_p}{\hbar}t} + \\ +i\sum_k \frac{G^*(k,p)}{\hbar}\beta_{k-p}(t)\beta_k^*(t)\int_{-\infty}^{t} exp\left\{-i\left[\frac{\varepsilon_p}{\hbar} - \Omega_{k-p} + \Omega_k\right](t-\tau)\right\}d\tau\,. \tag{32}$$

Integrals in eq. (32) gives

$$\int_{-\infty}^{t} exp\left\{-i\left[\frac{\varepsilon_p}{\hbar} - \Omega_{k-p} + \Omega_k\right](t-\tau)\right\}d\tau = -\frac{i}{\frac{\varepsilon_p}{\hbar} - \Omega_{k-p} + \Omega_k} = -\frac{i}{\Lambda} = \\ = -i\left[P\left(\frac{1}{\Lambda}\right) + i\pi\delta(\Lambda)\right], \tag{33}$$

where P is a symbol of principal value. Finally, $B_p(t)$ is obtained in the form

$$B_p(t) = B_p(0)e^{-i\frac{\varepsilon_p}{\hbar}t} + i\sum_k \frac{G^*(k,p)}{\hbar\Lambda(k,p)}\beta_{k-p}(t)\beta_k^*(t). \tag{34}$$

Substitution of eq. (34) into eq. (28) gives us equation for $\beta_k(t)$

$$\frac{d\beta_k(t)}{dt} = -i\frac{\varepsilon_k}{\hbar}\beta_k(t) + iN^2\sum_{g,k'}\frac{V_{k,g}V_{k',g}^*}{\hbar^2\Omega_t}\beta_{k-g}(t)\beta_{k'-g}(t)\beta_{k'}^*(t) - \\ - i\sum_{g,k'}\frac{G(k,p)G^*(k',p)}{\hbar^2\Lambda}\beta_{k-p}(t)\beta_{k'-p}(t)\beta_{k'}^*(t) + \\ + i\sum_p \frac{G(k,p)}{\hbar}\beta_{k-p}(t)B_p(0)e^{-i\frac{\varepsilon_p}{\hbar}t}\,. \tag{35}$$

Eq. (35) is the Langevin equation for phonon amplitudes $\beta_k(t)$

$$\frac{d\beta_k(t)}{dt} = -\frac{i}{\hbar}(\varepsilon_k + e_k)\beta_k(t) + \frac{iN^2|V_k|^2}{\hbar^2\Omega_t}\sum_{g,k\prime}\beta_{k-g}(t)\beta_{k\prime-g}(t)\beta^*_{k\prime}(t) - \\ -\frac{1}{2}\gamma_k\beta_k(t) + iF_p(t)\,, \tag{36}$$

where the following variables are introduced

$$e_k = \frac{1}{\hbar}\sum_{p,k\prime} G(k,p)G^*(k',p)\beta_{k\prime-p}\beta^*_{k\prime}P\left(\frac{1}{\Lambda}\right), \tag{37}$$

$$\gamma_k = \frac{2\pi}{\hbar^2}\sum_{p,k\prime} G(k,p)G^*(k',p)\beta_{k\prime-p}\beta^*_{k\prime}\delta(\Lambda) \tag{38}$$

and

$$F_k(t) = \widetilde{F_k}(t)e^{-i\Omega_k t} = \frac{1}{\hbar}\sum_p G(k)\beta_{k-p}(t)B_p(0)e^{-i\frac{\varepsilon_p}{\hbar}t}. \tag{39}$$

Function $F_k(t)$ (39) can be considered as a random force with the correlator:

$$< F^*_k(t)F_k(\tau) >= \\ = \frac{1}{\hbar^2}\sum_{p,p\prime}|G(k)|^2 < \beta^*_{k-p}(0)\beta_{k-p\prime}(0) >< B^*_p(0)B_p(0) > e^{-i(\Lambda(k,p)t-\Lambda(k,p\prime)\tau)}. \tag{40}$$

Assume that at the initial time, amplitudes $\beta(0)$ and $B(0)$ are not correlated, i.e.

$$< \beta^*_{k-p}(0)\beta_{k-p\prime}(0) >= n_p\delta_{pp\prime} \tag{41}$$

and

$$< B^*_p(0)B_{p\prime}(0) >= N_p\delta_{pp\prime}\,, \tag{42}$$

where

$$n_p = \left(e^{\theta\hbar\Omega_p} - 1\right)^{-1} \tag{43}$$

and

$$N_p = \left(e^{\theta\hbar\omega_p} - 1\right)^{-1}. \tag{44}$$

Here $\theta = 1/k_BT$.

Substitute eqs. (41)-(44) into eq. (40) and take into consideration that the main contribution in a sum (40) is given by terms $\Lambda(k,p) = 0$ at not too small values of a difference $(t-\tau)$. Then finally obtain

$$< F^*_k(t)F_k(\tau) >= \frac{2\pi}{\hbar^2}|G(k)|^2 n_p N_p \delta(t-\tau) = D_k\delta(t-\tau). \tag{45}$$

It can be shown that after averaging in eq. (38) for γ_k with consideration of eq. (44) and substituting this result into eq. (45), the value D_k can be written in the form

$$D_k = \hbar^2 \gamma_k N_p. \tag{46}$$

6. Vibrational dynamics of α-helical protein in a long wave approximation

Consider vibrational modes in the α-helical protein at the various parameters characterising its interaction with the environment. We applied a long-wave approximation to derive the equation for undamped modes which build up to macroscopic values and investigate system dynamics in the vicinity of an unstable point. For small values $ka \ll 1$, phonon frequencies according to eq. (8) can be written in the form

$$\Omega_s(k) = \Omega_{0s} + I_s k^2 a^2, \tag{47}$$

where

$$I_s = (-1)^{s+1} \frac{\chi_{1,2}\chi_{2,1}}{4m_1 m_2 \Omega_{0s}\sqrt{A^2 - B(0)}}. \tag{48}$$

Here Ω_{0s} and $B(0)$ are defined by eq. (8) at k=0. Note that the value

$$\sqrt{A^2 - B(0)} = \frac{1}{2}(\Omega_{02}^2 - \Omega_{01}^2) \tag{49}$$

can be found from the dependence of frequencies Ω_{0s} on the elastic constants shown in Fig. 2.

As in the long-wave approximation, the value $\Lambda(k,p) = \Lambda(p)$ does not depend on k, we turn to continuum limit in eq. (36) after Fourier transformation by multiplication of all terms in eq. (36) by $N^{-1/2}e^{ikz}$ and summing up over k according to eq. (47). In continuum limit, eq. (36) for photon modes with the dispersion relation (47) takes the form

$$i\hbar \frac{\partial \beta_s(x,t)}{\partial t} + \hbar a^2 I_s \frac{\partial^2 \beta_s(x,t)}{\partial z^2} - E_s \beta_s(x,t) + Q_s |\beta_s(x,t)|^2 \beta_s(x,t) = F_s(x,t), \tag{50}$$

where

$$E_s = \varepsilon_{0s} - e_{0s} - \frac{i\hbar\gamma_s}{2} = E_{0s} - \frac{i\hbar\gamma_s}{2} \tag{51}$$

and

$$Q_s = \frac{N^2 |V_s|^2}{\Omega_s}.$$

A solution of eq. (50) can be represented in the form

$$\beta_s(z,t) = \Phi_s(\rho) exp\left\{i(q_s z - \omega_s t) - \frac{\gamma_s}{2} t\right\}, \tag{52}$$

where $\rho = z - z_0 - V_s$, V_s is the velocity of excitation motion along the PG chain, and the real amplitude $\Phi_s(\rho)$ satisfies the following normalization condition

$$\frac{1}{a} \int_{-\infty}^{+\infty} \Phi_s^2(\rho)\, d\rho = N_0 \,. \tag{53}$$

Consider solutions of eq. (50) at weak damping, i.e. when $\gamma_s \approx 0$. The reasonable mechanism of the reduced relaxation of protein collective motion may be linked to the interaction of macromolecules with their environment, for example with ordered water clusters possessing slow dynamics (Xie, van der Meer and Austin, 2002; Squire *et al.*, 2013). Another mechanism of slow relaxation of the collective modes was suggested to be based on the experimental observation of vibrational wave packets of a long lifetime over 500 picoseconds in bacteriorhodopsin exposed by picosecond far IR sources (Xie, van der Meer and Austin, 2002). Authors discussed a possible mechanism of slow relaxation due to quantum effects of restricted interaction of the low-frequency collective modes with solvent and suggested a link between undamped collective vibration and the conformational transitions in proteins enriched by α-helical structures.

In this condition ($\gamma_s \approx 0$), according to eq. (46) and fluctuation-dissipation theorem, fluctuations are small and can be neglected. Then eq. (50) takes the form:

$$\left[\Xi_s + \hbar a^2 I_s \frac{\partial^2}{\partial z^2} + Q_s |\Phi_s(\rho)|^2\right] \Phi_s(\rho) = 0, \tag{54}$$

where Ξ_s is a spectral parameter connected with phonon energy by the equation:

$$\hbar\omega_s = \Xi_s + E_s + \hbar q^2 a^2 I_s \,. \tag{55}$$

Eq. (54) has solution $\Phi_s(\rho) = const$:

$$\Phi_s(\rho) = 0 \quad \text{at } \lambda_s = \frac{\Xi_s}{Q_s} > 0 \tag{56}$$

and

$$\Phi_s(\rho) = 0 \text{ and } \Phi_s(\rho) = (-\lambda_s)^{1/2} \quad \text{at } \lambda_s < 0, \tag{57}$$

where parameter λ_s defines interaction of the PG chain with its environment. At changing λ_s the oscillation modes become unstable and their amplitudes $\Phi_s(\rho)$ play a role of the order parameters of the system. Note that solutions (56) and (57) obtained under conditions of the smallness of dissipation in the system and absence of fluctuations. Thus, living time τ_s of the

dynamic modes of the PG chain corresponding to nontrivial solutions (57) is less than the inverse-time of relaxation

$$\tau_s < \gamma_s^{-1} . \tag{58}$$

Thus, dynamics of this system is defined by weak damped (long-living) phonon modes. More detailed analysis of the dynamic equation of the type (50) is given in (Glauber, 2006), where it was shown in particular that the right-hand side of this equation can be obtained from the potential

$$U(|\Phi_s|) = \Xi_s|\Phi_s|^2 - \frac{1}{2}Q_s|\Phi_s|^4 . \tag{59}$$

This allows writing and solving the corresponding Fokker-Planck equation and then finding a distribution function for the phonons in a coherent excitation state

$$\Psi(\Phi_s) \sim exp\left\{-\frac{2U(|\Phi_s|)}{D_s}\right\}, \tag{60}$$

where parameter D_s defines intensity of fluctuating force according to eqs. (45) and (46) at $k = 0$ for both phonon branches. From eq. (60) follows that fluctuations enable the system to switch to a new state. The role of fluctuations is much significant at the transition of the system to an unstable mode at $\lambda_s \leq 0$ when, as known, fluctuations sharply increase (Haken, 1983). At the sign change of parameter λ_s, solution $\Phi_s(\rho) = 0$ remains one of the solutions of eq. (54). Transition of the system to the new states, corresponding to nontrivial solutions $\Phi_s(\rho) \neq 0$, is possible as a result of an action of external factors including fluctuations.

Eq. (54), being nonlinear Schrodinger equation, besides the solutions considered above has a solution in the form of solitary wave (soliton) travelling along the z-axis and satisfying normalisation condition (53). For any positive values Q_s, eq. (54) has the normalised partial solution in the form

$$\Phi(\rho) = \left(\frac{a\Theta_0 N_0}{2}\right)^{1/2} \frac{1}{ch[\Theta_0(z - z_0 - V_{sol}t)]}, \tag{61}$$

where z_0 is the soliton centre, V_{sol} is soliton velocity, and

$$\Theta_0 = \frac{Q_s N_0}{4\hbar a I_s} . \tag{62}$$

In the presence of dissipation, when $\gamma_s \neq 0$, a solution of eq. (50) in view of eqs. (51) and (52) is written in the form:

$$\beta(x,t) = \left(\frac{a\Theta_0 N}{2}\right)^{1/2} \frac{e^{i(q_s z - \omega_s t)}}{ch[\Theta_0 e^{-\gamma_s t}(z - z_0 - V_{sol}t)]}, \tag{63}$$

where

$$N = N_0 e^{-\gamma_s t}.$$

The region occupied by soliton, soliton's width, is defined by equation

$$d(t) = \frac{\pi}{\Theta_0} e^{\gamma_s t}. \tag{64}$$

7. Discussion: Vibrational modes and self-organization in α-helical protein structures

In the present paper, we further developed the quantum dynamic model of the collective excitations in α-helical protein structures (Davydov, 1977), (Kadantsev, Lupichov and Savin, 1987; Lupichev, Savin and Kadantsev, 2015), (Takeno, 1984) and extended this approach to taking into account the dynamics of the side-chains of residues responsible for the protein interaction within the environment. In the model, we considered a side-chain-dependent coupling of the vibration excitations in the PG chain and surrounding hydrogen bond network of water molecules. The model development was based on a series of approximations which are either the typical ones in the theoretical modelling of molecular chains or based on the experimental data on protein dynamics. Main parameters of the model were extracted from experimental data on the structure and strength of peptide bonds of the α-helix.

The investigation of the dynamics of the α-helical proteins interacting with water environment in the framework of the developed model showed that the equation for phonon dynamics of the PG chain can be considered as the equation for the order parameter that admits a bifurcation of its solutions. Thus, this molecular system can function in different dynamic modes, which are defined by the order parameter. Transition of protein behaviour between different states occurs at a change in the bifurcation parameter λ_s which, according to eq. (37), determines the interaction of the macromolecule with its environment. The PG chain dynamics below and above of the switching threshold are significantly different. At the parameter $\lambda_s > 0$, the system is characterised by the absence of excited modes, and the PGs fluctuate that

results in a zero-mean amplitude of the phonon modes.

At the parameter $\lambda_s < 0$, the behaviour of the system changes so that either one or several vibrational modes become unstable and their amplitudes can grow to macroscopic values. At this transition, the vibration energy is condensated in a set of low-frequency vibrational modes that can lead to the excitation of coherent vibrations of α-helical proteins in the terahertz frequency range. Thus, the dynamic behaviour of the macromolecule in our model is defined by a) fluctuations governed by dissipation in the system and b) switching behaviours as a result of an order parameter change that is controlled by the strength of protein interaction with the environment.

According to our model, the emergence of space-temporal structures in the form of solitary waves (Davydov regime) are possible in the PG chain. Analysis of the soliton mode showed that first, soliton formation is governed by phonon-phonon interaction of the PGs with radical chains in α-helical proteins and second, the Davydov regime realises at the bifurcation parameter value corresponding to the excitation of collective vibrational modes (Fröhlich-like regime). This result which shows the coexistence of the Frohlich vibration and Davydov soliton excitations in the same region of the control parameters of the PG chain agrees with similar conclusion obtained by other research groups in different approaches such as kinetic approach of the Fröhlich rate equations, the Wu-Austin Hamiltonian approach and others (Del Giudice *et al.*, 1986; Bolterauer and Tuszyński, 1989; Bolterauer, Tuszyński and Satarić, 1991; Mesquita, Vasconcellos and Luzzi, 2004). Some experimental data supporting Davidov soliton formation in proteins was obtained by IR and Raman spectroscopy as results of the observation of an anomalous line close to the amide I excitation in IR spectrum of the hydrogen-bonded chains in polymer macromolecules and α-helical protein structures (Christiansen and Scott, 1990), (Cruzeiro, 2009).

Following the Fröhlich's hypothesis, cooperative behaviour of the PG chain can lead to the formation of a giant oscillating dipole (Fröhlich, 1968a) due to a large dipole moment of the PG. Its formation is suggested to be associated with protein functions such as selective forces, protein-ligand interaction, molecular recognition, and catalytic enzyme activity. On the other hand, soliton formation (including acoustic solitons (Davydov, 1985)) can lead to energy/charge transport along α-helical protein structures due to either exciton or electron-phonon interaction (Kadantsev, Lupichcv and Savin, 1994; Kadantsev and Savin, 1997). A similar mechanism was explored in the theoretical description of collective vibrational mode excitation (Cifra *et al.*, 2010; Craddock *et al.*, 2014) and resonance energy transfer (Kurian, Obisesan and Craddock, 2017) in microtubules.

The obtained results on the dynamics of α-helical protein interacting with water environment showed that instability of vibrational modes, induced by a change in the parameter of protein-environment interaction, can cause a formation of new macroscopic space-temporal structures in the system. The joint action of random and deterministic forces can lead to the switching of the system to a dynamic state, characterised by cooperative behaviour of its subsystems (subunits). As shown, one of the factors defining self-organisation process in the protein is the non-linear interaction of three subsystems, i.e. the regular chains of hydrogen bonds, amino acid side-chain, and hydrogen bond networks of surrounding water molecules.

Note, that the developed model of the ideal α-helix interacting with its environment needs in the further development to build a more realistic model by considering tertiary interactions of α-helical structures in native proteins. As the α-helical structure is not stable in solution and gets stable within the hydrophobic core of the folded proteins due to electrostatic interactions of the side-chains with neighbouring residues. The developed model of vibration excitations in the ideal α-helix can be extended to the folded proteins enriched by α-helical structures buried in the hydrophobic core of proteins. In this case, the role of the α-helix environment responsible for dissipation and fluctuation processes is played by electrostatic interaction of the side-chains with surrounding amino acids, which participate in the vibrational motion of the protein as a whole. Moreover, in folded proteins, α-helical structures form more complex structures such as the coiled-coil ones, supercoils (a superhelix) as well as α-helix barrel structures due to hydrophobic interaction of the non-polar side-chains (Lupas and Bassler, 2017). Thus, the extension of our model to these superhelix structures should include the interaction of water molecules with the polar side-chains of the superhelix facing outward, toward surrounding water.

The amphipathic α-helical coiled-coil structures are stable in solution due to sequence repetition of hydrophobic and polar residues and play a significant role in molecular recognition and protein-protein interaction. For example, the leucine zipper (coiled coil) structures are responsible for recognition and binding of the transcription factors with the DNA promoter regions of about short (~20) nucleotide sequence (Lupas and Bassler, 2017). Excitation of the vibrational modes in superhelices can be applied to explain the mechanism of molecular recognition, long-range protein-protein (Fröhlich, 1968a) and protein-DNA interaction (Kurian *et al.*, 2018b).

The developed approach can also be extended to the modelling of vibrational excitation in other quasi-linear superhelix protein structures, such as amyloid-like fibres that are formed by the backbones of cross-beta-structures and exhibit most stable protein structures in solution

under physiological conditions (Baldwin *et al.*, 2011), (del Mercato *et al.*, 2007). Again, hydrogen bonds between neighbouring β-sheets and trapped water molecules play a similar role in vibrational energy dissipation as suggested in our model of the ideal α-helix. The quantum dynamic model of soliton dynamics in the α-helical structures discussed above can be also extended to the modelling of intrapeptide excitation dynamics in β-sheet structures (Lupichev, Savin and Kadantsev, 2015). This development can help to describe the unique properties of self-assembled amyloid-like fibres such as intrinsic fluorescence and emergence of delocalized electron transport along the fibre backbone facilitated by long-range hydrogen bonds of the PGs as well as their cytotoxicity related to Alzheimer's and Parkinson's diseases (del Mercato *et al.*, 2007).

Progress in terahertz spectroscopic techniques and their combination with other spectroscopic methods led to a revival of interest in the experimental observation of Fröhlich coherent excitation in biological structures (Pokorný, 2004; Weightman, 2014). Recently, a search for experimental evidence of long-range quantum coherent states in the proteins was undertaken in experiments on the investigation of biomolecule interaction with microwave and terahertz irradiation (Lundholm *et al.*, 2015). Authors used X-ray crystallographic methods to visualise structural changes in the lysozyme protein crystal induced by 0.4 THz electromagnetic radiation (Lundholm *et al.*, 2015). They observed the excitation of longitudinal compression modes of microsecond lifetime in the protein α-helix that is significantly longer than femto- and nanosecond time scale of the intramolecular vibration decay due to protein interaction with the environment (thermalisation). Authors attributed this underdamped low-frequency collective vibration modes to the Fröhlich condensation mode, excited by terahertz radiation. The existence of these persisting motions indicates that damping and intermode coupling are weaker than previously assumed (Acbas *et al.*, 2014).

Experimental investigation of the coherent vibrational dynamics in proteins was intensified by the observation of long-lived coherent excitonic states in light-harvesting proteins in photosynthetic bacteria (Engel *et al.*, 2007). The results of 2D IR coherent spectroscopy suggests that the coherent vibrations in photosynthetic pigment–protein complexes contribute to the effective electron and energy transport due to the electron-vibrational couplings (Kolli *et al.*, 2012; Chenu *et al.*, 2013; Duan *et al.*, 2017; Rolczynski *et al.*, 2018). It is notable that Fröhlich in 1968 proposed the role of coherent longitudinal electric modes (polarization waves) of low frequency (0.01 THz – 1 THz) in the storage of light energy in photosynthesis (Fröhlich, 1968b).

In recent intriguing work, the joint theoretical and experimental investigation of out-of-

equilibrium collective oscillation of the Fröhlich type was carried out in the bovine serum albumin (BSA), the protein mainly composed of α-helical structures (Nardecchia *et al.*, 2018). Authors recreated in their experimental setup the conditions close to the Fröhlich model i.e. they transferred energy to the protein and created far from the thermal equilibrium state in the macromolecule by optical pumping through the excitation of fluorochromes (at wavelength of 488 nm) bonded at the lysine residues to each BSA molecule. Using complementary THz spectroscopy, the strong resonance around 0.3 THz in absorption spectrum was observed, when optical pumping to the vibrational modes of the BSA took place through excitation of fluorochromes. To theoretically analyse the experimental results, authors developed a classical version of the Fröhlich model and showed that phonon condensation is possible in nonequilibrium state of the protein, when energy flows from an external energy source to the protein and dissipates then through protein interaction with the environment. Authors treated a threshold like collective vibrational modes as non-equilibrium phase transition in open dynamic systems.

Note, that the resonance absorption spectrum in the terahertz frequency region for α-helical protein structures was defined by one of the authors (VNK) in the framework of the quantum mechanical model which describes the direct transfer of electron captured by the moving acoustic soliton (electrsoliton) along the molecular chain (Kadantsev and Savin, 1997).

In conclusion, the developed quantum dynamics model of the α-helical structure interacting with water environment can be useful in the analysis of the current experimental data on the molecular mechanisms of the long-lived, low-frequency collective vibrations in α-helical protein structures. The further expansion of the model to describe the dynamics of α-helix in native proteins, protein-membrane systems, superhelix structures such amiloids fibers, and microtubules might support experimental investigation of the role of quasi-linear dynamical structures in extraordinary effectiveness of protein functions such as energy storage, transport and transformation.

Acknowledgments

AG acknowledges Scottish Informatics and Computer Science Alliance (SICSA) for partial funding his post at Abertay University.

Conflict of interest

The authors report no conflict of interest.

References

Acbas, G. *et al.* (2014) 'Optical measurements of long-range protein vibrations', *Nature Communications*. Nature Publishing Group, 5(1), p. 3076. doi: 10.1038/ncomms4076.

Baldwin, A. J. *et al.* (2011) 'Metastability of Native Proteins and the Phenomenon of Amyloid Formation', *Journal of the American Chemical Society*. American Chemical Society, 133(36), pp. 14160–14163. doi: 10.1021/ja2017703.

Balu, R. *et al.* (2008) 'Terahertz Spectroscopy of Bacteriorhodopsin and Rhodopsin: Similarities and Differences', *Biophysical Journal*, 94(8), pp. 3217–3226. doi: 10.1529/biophysj.107.105163.

Bellissent-Funel, M.-C. *et al.* (2016) 'Water Determines the Structure and Dynamics of Proteins', *Chemical Reviews*. American Chemical Society, 116(13), pp. 7673–7697. doi: 10.1021/acs.chemrev.5b00664.

Bolterauer, H. and Tuszyński, J. A. (1989) 'Fröhlich's condensation in a biological membrane viewed as a Davydov soliton', *Journal of Biological Physics*. Kluwer Academic Publishers, 17(1), pp. 41–50. doi: 10.1007/BF00393325.

Bolterauer, H., Tuszyński, J. A. and Satarić, M. V. (1991) 'Fröhlich and Davydov regimes in the dynamics of dipolar oscillations of biological membranes', *Physical Review A*. American Physical Society, 44(2), pp. 1366–1381. doi: 10.1103/PhysRevA.44.1366.

Chenu, A. *et al.* (2013) 'Enhancement of Vibronic and Ground-State Vibrational Coherences in 2D Spectra of Photosynthetic Complexes', *Scientific Reports*. Nature Publishing Group, 3(1), p. 2029. doi: 10.1038/srep02029.

Christiansen, P. L. and Scott, A. C. (eds) (1990) *Davydov's Soliton Revisited*. Boston, MA: Springer US (NATO ASI Series). doi: 10.1007/978-1-4757-9948-4.

Cifra, M. *et al.* (2010) 'Electric field generated by axial longitudinal vibration modes of microtubule', *Biosystems*. Elsevier, 100(2), pp. 122–131. doi: 10.1016/J.BIOSYSTEMS.2010.02.007.

Columbus, L. and Hubbell, W. L. (2002) 'A new spin on protein dynamics.', *Trends in*

biochemical sciences, 27(6), pp. 288–95. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12069788 (Accessed: 14 April 2019).

Conti Nibali, V. and Havenith, M. (2014) 'New Insights into the Role of Water in Biological Function: Studying Solvated Biomolecules Using Terahertz Absorption Spectroscopy in Conjunction with Molecular Dynamics Simulations', *Journal of the American Chemical Society*. American Chemical Society, 136(37), pp. 12800–12807. doi: 10.1021/ja504441h.

Craddock, T. J. A. *et al.* (2014) 'The feasibility of coherent energy transfer in microtubules.', *Journal of the Royal Society, Interface*. The Royal Society, 11(100), p. 20140677. doi: 10.1098/rsif.2014.0677.

Cruzeiro, L. (2009) 'The Davydov/Scott Model for Energy Storage and Transport in Proteins', *Journal of Biological Physics*. Springer, 35(1), p. 43. doi: 10.1007/S10867-009-9129-0.

Davydov, A. S. (1977) 'Solitons and energy transfer along protein molecules', *Journal of Theoretical Biology*. Academic Press, 66(2), pp. 379–387. doi: 10.1016/0022-5193(77)90178-3.

Davydov, A. S. (1985) *Solitons in Molecular Systems*. Dordrecht: Springer Netherlands (Mathematics and Its Applications). doi: 10.1007/978-94-017-3025-9.

Duan, H.-G. *et al.* (2017) 'Nature does not rely on long-lived electronic quantum coherence for photosynthetic energy transfer.', *Proceedings of the National Academy of Sciences of the United States of America*. National Academy of Sciences, 114(32), pp. 8493–8498. doi: 10.1073/pnas.1702261114.

Engel, G. S. *et al.* (2007) 'Evidence for wavelike energy transfer through quantum coherence in photosynthetic systems', *Nature*. Nature Publishing Group, 446(7137), pp. 782–786. doi: 10.1038/nature05678.

Foletti, A. *et al.* (2013) 'Bioelectromagnetic medicine: The role of resonance signaling', *Electromagnetic Biology and Medicine*, 32(4), pp. 484–499. doi: 10.3109/15368378.2012.743908.

Fröhlich, H. (1968a) 'Long-range coherence and energy storage in biological systems',

International Journal of Quantum Chemistry. John Wiley & Sons, Inc., 2(5), pp. 641–649. doi: 10.1002/qua.560020505.

Fröhlich, H. (1968b) 'Storage of Light Energy and Photosynthesis', *Nature*. Nature Publishing Group, 219(5155), pp. 743–744. doi: 10.1038/219743a0.

Fröhlich, H. (1970) 'Long range coherence and the action of enzymes.', *Nature*, 228(5276), p. 1093. Available at: http://www.ncbi.nlm.nih.gov/pubmed/5483165 (Accessed: 7 June 2019).

Fröhlich, H. (1980) 'The Biological Effects of Microwaves and Related Questions', *Advances in Electronics and Electron Physics*. Academic Press, 53, pp. 85–152. doi: 10.1016/S0065-2539(08)60259-0.

Fröhlich, H. (Herbert) (1988) *Biological Coherence and Response to External Stimuli*. Springer Berlin Heidelberg.

Del Giudice, E. *et al.* (1986) 'Collective Properties of Biological Systems', in *Modern Bioelectrochemistry*. Boston, MA: Springer US, pp. 263–287. doi: 10.1007/978-1-4613-2105-7_9.

Glauber, R. J. (2006) *Quantum Theory of Optical Coherence*. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA. doi: 10.1002/9783527610075.

Go, N., Noguti, T. and Nishikawa, T. (1983) 'Dynamics of a small globular protein in terms of low-frequency vibrational modes.', *Proceedings of the National Academy of Sciences of the United States of America*. National Academy of Sciences, 80(12), pp. 3696–700. doi: 10.1073/PNAS.80.12.3696.

Goncharuk, V. V. *et al.* (2017) 'On the possibility of chiral structure-density submillimeter inhomogeneities existing in water', *Journal of Water Chemistry and Technology*. Pleiades Publishing, 39(6), pp. 319–324. doi: 10.3103/S1063455X17060029.

Haken, H. (1983) *Synergetics : an introduction : nonequilibrium phase transitions and self-organization in physics, chemistry, and biology*. Springer. Available at: https://books.google.co.uk/books?id=KHn1CAAAQBAJ&source=gbs_similarbooks (Accessed: 14 January 2018).

Kadantsev, V. N. and Goltsov, A. N. (2018) 'Collective excitations in α-helical protein structures', *Russian Technological Journal*, 6(2), pp. 32–45. doi: 10.32362/2500-316X-2018-6-2-32-45.

Kadantsev, V. N., Lupichcv, L. N. and Savin, A. V. (1994) 'Electrosoliton dynamics in a thermalized chain', *physica status solidi (b)*. Wiley-Blackwell, 183(1), pp. 193–199. doi: 10.1002/pssb.2221830115.

Kadantsev, V. N., Lupichov, L. N. and Savin, A. V. (1987) 'Intramolecular Excitation Dynamics in a Thermalized Chain. I. Formation of Autolocalized States in a Cyclic Chain', *physica status solidi (b)*. Wiley-Blackwell, 143(2), pp. 569–579. doi: 10.1002/pssb.2221430217.

Kadantsev, V. and Savin, A. (1997) 'Resonance Effects of Microwaves are Caused by their Interaction with Solitons in A-Helical Proteins', *Electro- and Magnetobiology*. Taylor & Francis, 16(2), pp. 95–106. doi: 10.3109/15368379709009835.

Kamerlin, S. C. L. and Warshel, A. (2010) 'At the dawn of the 21st century: Is dynamics the missing link for understanding enzyme catalysis?', *Proteins: Structure, Function, and Bioinformatics*, 78(6), p. NA-NA. doi: 10.1002/prot.22654.

Kolli, A. *et al.* (2012) 'The fundamental role of quantized vibrations in coherent light harvesting by cryptophyte algae', *The Journal of Chemical Physics*. American Institute of Physics, 137(17), p. 174109. doi: 10.1063/1.4764100.

Kuramochi, H. *et al.* (2019) 'Fifth-order time-domain Raman spectroscopy of photoactive yellow protein for visualizing vibrational coupling in its excited state', *Science Advances*. American Association for the Advancement of Science, 5(6), p. eaau4490. doi: 10.1126/sciadv.aau4490.

Kurian, P. *et al.* (2018a) 'Water-mediated correlations in DNA-enzyme interactions', *Physics Letters A*. North-Holland, 382(1), pp. 33–43. doi: 10.1016/J.PHYSLETA.2017.10.038.

Kurian, P. *et al.* (2018b) 'Water-mediated correlations in DNA-enzyme interactions', *Physics Letters A*. North-Holland, 382(1), pp. 33–43. doi: 10.1016/J.PHYSLETA.2017.10.038.

Kurian, P., Obisesan, T. O. and Craddock, T. J. A. (2017) 'Oxidative species-induced

excitonic transport in tubulin aromatic networks: Potential implications for neurodegenerative disease', *Journal of Photochemistry and Photobiology B: Biology*, 175, pp. 109–124. doi: 10.1016/j.jphotobiol.2017.08.033.

Lambert, N. *et al.* (2013) 'Quantum biology', *Nature Physics*. Nature Publishing Group, 9(1), pp. 10–18. doi: 10.1038/nphys2474.

Lawrence, A. F. *et al.* (1987) 'The nature of phonons and solitary waves in alpha-helical proteins', *Biophysical Journal*. Cell Press, 51(5), pp. 785–793. doi: 10.1016/S0006-3495(87)83405-7.

Lindorff-Larsen, K. *et al.* (2005) 'Simultaneous determination of protein structure and dynamics', *Nature*. Nature Publishing Group, 433(7022), pp. 128–132. doi: 10.1038/nature03199.

Liu, D. *et al.* (2008) 'Studies of Phononlike Low-Energy Excitations of Protein Molecules by Inelastic X-Ray Scattering', *Physical Review Letters*, 101(13), p. 135501. doi: 10.1103/PhysRevLett.101.135501.

Lundholm, I. V *et al.* (2015) 'Terahertz radiation induces non-thermal structural changes associated with Fröhlich condensation in a protein crystal.', *Structural dynamics (Melville, N.Y.)*. American Institute of Physics, 2(5), p. 054702. doi: 10.1063/1.4931825.

Lupas, A. N. and Bassler, J. (2017) 'Coiled Coils – A Model System for the 21st Century', *Trends in Biochemical Sciences*, 42(2), pp. 130–140. doi: 10.1016/j.tibs.2016.10.007.

Lupichev, L. N., Savin, A. V. and Kadantsev, V. N. (2015) *Synergetics of Molecular Systems*. Cham: Springer International Publishing (Springer Series in Synergetics). doi: 10.1007/978-3-319-08195-3.

Markov, M. (Marko S. . (2015) *Electromagnetic Fields in Biology and Medicine*, *Electromagnetic Fields in Biology and Medicine*. doi: 10.1201/b18148.

del Mercato, L. L. *et al.* (2007) 'Charge transport and intrinsic fluorescence in amyloid-like fibrils', *Proceedings of the National Academy of Sciences*, 104(46), pp. 18019–18024. doi: 10.1073/pnas.0702843104.

Mesquita, M. V., Vasconcellos, Á. R. and Luzzi, R. (2004) 'Considerations on undistorted-

progressive X-waves and Davydov solitons, Fröhlich-Bose-Einstein condensation, and Cherenkov-like effect in biosystems', *Brazilian Journal of Physics*. Sociedade Brasileira de Física, 34(2a), pp. 489–503. doi: 10.1590/S0103-97332004000300028.

Mohseni, M. *et al.* (eds) (2014) *Quantum Effects in Biology*. Cambridge: Cambridge University Press. doi: 10.1017/CBO9780511863189.

Nardecchia, I. *et al.* (2018) 'Out-of-Equilibrium Collective Oscillation as Phonon Condensation in a Model Protein', *Physical Review X*. American Physical Society, 8(3), p. 031061. doi: 10.1103/PhysRevX.8.031061.

Niessen, K. A. *et al.* (2017a) 'Moving in the Right Direction: Protein Vibrations Steering Function', *Biophysical Journal*. Cell Press, 112(5), pp. 933–942. doi: 10.1016/J.BPJ.2016.12.049.

Niessen, K. A. *et al.* (2017b) 'Moving in the Right Direction: Protein Vibrations Steering Function', *Biophysical Journal*, 113(11), p. 2573. doi: 10.1016/j.bpj.2017.10.038.

Pokorný, J. (1999) 'Conditions for coherent vibrations in the cytoskeleton', *Bioelectrochemistry and Bioenergetics*. Elsevier, 48(2), pp. 267–271. doi: 10.1016/S0302-4598(99)00016-1.

Pokorný, J. (2004) 'Excitation of vibrations in microtubules in living cells', *Bioelectrochemistry*, 63(1–2), pp. 321–326. doi: 10.1016/j.bioelechem.2003.09.028.

Preto, J. (2017) 'Semi-classical statistical description of Fröhlich condensation', *Journal of Biological Physics*, 43(2), pp. 167–184. doi: 10.1007/s10867-017-9442-y.

Prigogine, I. and Lefever, R. (1973) 'Theory of Dissipative Structures', in *Synergetics*. Wiesbaden: Vieweg+Teubner Verlag, pp. 124–135. doi: 10.1007/978-3-663-01511-6_10.

Reimers, J. R. *et al.* (2009) 'Weak, strong, and coherent regimes of Fröhlich condensation and their applications to terahertz medicine and quantum consciousness.', *Proceedings of the National Academy of Sciences of the United States of America*. National Academy of Sciences, 106(11), pp. 4219–24. doi: 10.1073/pnas.0806273106.

Rolczynski, B. S. *et al.* (2018) 'Correlated Protein Environments Drive Quantum Coherence Lifetimes in Photosynthetic Pigment-Protein Complexes', *Chem*. Cell Press, 4(1), pp. 138–

149. doi: 10.1016/J.CHEMPR.2017.12.009.

Salari, V. *et al.* (2011) 'Plausibility of quantum coherent states in biological systems', *Journal of Physics: Conference Series*. IOP Publishing, 306(1), p. 012075. doi: 10.1088/1742-6596/306/1/012075.

Shibata, F. and Hashitsume, N. (1978) 'Generalized Phase-Space Method in the Langevin-Equation Approach', *Journal of the Physical Society of Japan*. The Physical Society of Japan, 44(5), pp. 1435–1448. doi: 10.1143/JPSJ.44.1435.

Siegel, P. H. (2004) 'Terahertz Technology in Biology and Medicine', *IEEE Transactions on Microwave Theory and Techniques*, 52(10), pp. 2438–2447. doi: 10.1109/TMTT.2004.835916.

Sivaramakrishnan, S. *et al.* (2008) 'Dynamic charge interactions create surprising rigidity in the ER/K -helical protein motif', *Proceedings of the National Academy of Sciences*, 105(36), pp. 13356–13361. doi: 10.1073/pnas.0806256105.

Squire, R. H. *et al.* (2013) 'Comparison of various types of coherence and emergent coherent systems', *International Journal of Quantum Chemistry*. Wiley-Blackwell, 113(19), pp. 2181–2199. doi: 10.1002/qua.24423.

Takeno, S. (1984) 'Vibron Solitons in One-Dimensional Molecular Crystals', *Progress of Theoretical Physics*. Oxford University Press, 71(2), pp. 395–398. doi: 10.1143/PTP.71.395.

Turton, D. A. *et al.* (2014) 'Terahertz underdamped vibrational motion governs protein-ligand binding in solution', *Nature Communications*. Nature Publishing Group, 5, p. 3999. doi: 10.1038/ncomms4999.

Vasconcellos, Á. R. *et al.* (2012) 'Fröhlich Condensate: Emergence of Synergetic Dissipative Structures in Information Processing Biological and Condensed Matter Systems', *Information*. Molecular Diversity Preservation International, 3(4), pp. 601–620. doi: 10.3390/info3040601.

Weightman, P. (2014) 'Investigation of the Frohlich hypothesis with high intensity terahertz radiation', in Jansen, E. D. et al. (eds) *Optical Interactions with Tissue and Cells XXV; and Terahertz for Biomedical Applications*, p. 89411F. doi: 10.1117/12.2057397.

Wu, T. M. and Austin, S. J. (1981) 'Fröhlich's model of bose condensation in biological systems', *Journal of Biological Physics*. Kluwer Academic Publishers, 9(2), pp. 97–107. doi: 10.1007/BF01987286.

Xie, A., van der Meer, L. and Austin, R. H. (2002) 'Excited-State Lifetimes of Far-Infrared Collective Modes in Proteins', *Journal of Biological Physics*. Kluwer Academic Publishers, 28(2), pp. 147–154. doi: 10.1023/A:1019986321524.

Xie, L., Yao, Y. and Ying, Y. (2014) 'The Application of Terahertz Spectroscopy to Protein Detection: A Review', *Applied Spectroscopy Reviews*. Taylor & Francis, 49(6), pp. 448–461. doi: 10.1080/05704928.2013.847845.

Figure legends

Fig. 1. (a) A polypeptide chain with amino acid residues (R). (b) The chain of hydrogen-bonded peptide groups. (c) Structure of α-helical protein, where one of the three hydrogen-bonded PG chains with the side-chains of amino acid residues are shown. Hydrogen-bonds are depicted by dots.

Fig. 2. Dispersion curves for the chain of hydrogen-bounded PGs calculated at the following elastic constants (Lupichev, Savin and Kadantsev, 2015). (a) s=1, $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$, $\chi_{0,1} = 5.0\ \mathrm{N}m^{-1}$, $\chi_{0,2} = 0\ \mathrm{N}m^{-1}$. (B) s=2, $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$, $\chi_{0,1} = 5.0\ \mathrm{N}m^{-1}$, $\chi_{0,2} = 0\ \mathrm{N}m^{-1}$. (b) Dependence of the frequency Ω_{01} (C) and Ω_{02} (D) (k=0) on constant χ_{02} at the fixed values of elastic constants $\chi_{1,2} = 13.0\ \mathrm{N}m^{-1}$, $\chi_{2,1} = 17.0\ \mathrm{N}m^{-1}$ and different constant $\chi_{0,1}$: line 1 - $\chi_{0,1} = 0.0\ \mathrm{N}m^{-1}$, line 2 - $\chi_{0,1} = 3.0\ \mathrm{N}m^{-1}$, and line 3 - $\chi_{0,1} = 25.0\ \mathrm{N}m^{-1}$.