

Nonlinearity-induced conformational instability and dynamics of biopolymers

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Abstract. – We propose a simple phenomenological model for describing the conformational dynamics of biopolymers via the nonlinearity-induced buckling and collapse instability. We describe the buckling instability analytically, and then demonstrate its role in the folding dynamics of macromolecules through the three-dimensional numerical simulations of long semiflexible chains.

Conformational flexibility is a fundamental property of polymers which differentiates them from small molecules and gives rise to their remarkable properties [1]. A distinctive feature of *biological* polymers is that their elementary sub-units have a complex structure and can carry long-lived nonlinear excitations [2,3]. The potentialities of the nonlinear excitations in biological functioning of proteins and DNA molecules are now intensively studied [3–7]. It is widely believed that nonlinear excitations may be responsible for *storage and transport of the energy* released during ATP hydrolysis [4,5]. It was also conjectured that the local opening of the DNA double helix, which is necessary for reading of the genetic code during transcription, is a result of *spontaneous localization of thermal energy* in the form of discrete breathers [3,4,6].

Here we suggest a *new role of nonlinear excitations* in one of the most important functionalities of biopolymers, their *conformational dynamics*. For the first time to our knowledge, we demonstrate that the nonlinear excitations may cause *local softening* of polymer bonds. That is the effective bending rigidity of a *semiflexible* biopolymer chain decreases nearby the nonlinear excitation as the amplitude of the excitation grows. When the amplitude exceeds some threshold value, the effective bending rigidity becomes negative, *i.e.* the nonlinear excitation, even in the absence of thermal fluctuations, causes a *buckling instability* of the chain. Moreover, on further increasing of the nonlinear excitation amplitude, the buckling instability is replaced by a *collapse instability*, which leads to folding of the chain into a compact coil. We verify that

all these effects survive in the presence of viscous damping, and thus they may play a part in the kinetics of conformational phase transitions of semiflexible biopolymers in solutions [8].

The importance of nonlinear excitations has already been emphasized in the modeling of biopolymers and conjugated polymers. In particular, it was suggested that solitons may provide a possible physical mechanism for the energy (or charge) transport and storage in proteins [4, 5] and conducting polymers [9]. The concept of nonlinear localized modes was also employed to explain some specific features of the DNA dynamics [3, 4, 6]. However, most of those studies were dealing with nonlinear properties of *straight* molecular chains. The study of nonlinear excitations [10] and discrete breathers [11, 12] in *curved chains* has been initiated only recently and it was shown, in particular, that the bending in a curved chain manifests itself as an effective trap for nonlinear localized modes [10]. Recently, it was also suggested [13] that Davydov solitons, propagating through the backbone of a protein, can mediate the transition of a protein from a metastable conformation to its ground-state conformation. In this letter, we make an important step forward and, taking into account a *bending flexibility* of biopolymer chains, we demonstrate that nonlinear excitations may induce *drastic change of the ground-state conformation* of the chain, and act as drivers giving impetus to *conformational dynamics* of biopolymers.

Let us consider a simple phenomenological model of a biopolymer consisting of particles with mass M , indexed by n , and located at the points $\mathbf{r}_n = \{x_n, y_n, z_n\}$. We assume that each particle represents a complex sub-unit of the biopolymer which, additionally to its position $\mathbf{r}_n(t)$, carries an internal excitation which can be characterized, in some approximation [4–7, 9], by the complex amplitude, $\psi_n(t)$. Such an internal mode can represent, for instance, a polaron state (an excess electron accompanied by phonons) or vibrational state (amide-I vibrations in proteins or base-pair vibrations in DNA). The Hamiltonian of such a chain is written as $H = T + U + V$, where $T = (M/2) \sum_n (d\mathbf{r}_n/dt)^2$ is the kinetic energy, $U(\mathbf{r}_n)$ is the potential energy of inter-particle interactions, and

$$V(\psi_n, \mathbf{r}_n) = \sum_n \left\{ W \left(2|\psi_n|^2 - \sum_{m \neq n} J_{nm} \psi_n^* \psi_m \right) - \frac{1}{2} \Delta |\psi_n|^4 \right\} \quad (1)$$

is the energy of the internal excitation, characterized by intensities of a linear excitation transfer, W , and nonlinear self-trapping interaction, Δ . The excitation transfer coefficients J_{nm} depend on the distance in the embedding space between the particles n and m : $J_{nm} \equiv J(|\mathbf{r}_n - \mathbf{r}_m|) = (e^\alpha - 1) \exp[-\alpha|\mathbf{r}_n - \mathbf{r}_m|]$ [14]. In what follows we use a dimensionless version of the potential energy (1) by rescaling the complex amplitude $\psi_n = \sqrt{W/\Delta} \bar{\psi}_n$ and expressing all energetic parameters in terms of the quantity W^2/Δ . From the Hamiltonian, we obtain the equations of motion

$$\begin{aligned} M \frac{d^2 \mathbf{r}_n}{dt^2} + \nu \frac{d\mathbf{r}_n}{dt} + \frac{dU}{d\mathbf{r}_n} - \sum_k \sum_{m \neq k} \frac{dJ_{km}}{d\mathbf{r}_n} \psi_k^* \psi_m &= 0, \\ i \frac{\partial \psi_n}{\partial t} - 2\psi_n + \sum_{m \neq n} J_{nm} \psi_m + |\psi_n|^2 \psi_n &= 0, \end{aligned} \quad (2)$$

where we allowed additionally for a viscous damping ν of the aqueous environment and omitted “bars” over ψ -functions. The equations of motion (2) conserve an important parameter

$$N = \sum_n |\psi_n|^2, \quad (3)$$

which is called the number of excitations and characterizes the nonlinearity of the chain. We consider the potential energy of inter-particle interactions as a sum, $U(\mathbf{r}_n) = U_S + U_B + U_R$, of the stretching energy $U_S = (\sigma/2) \sum_n (|\mathbf{r}_n - \mathbf{r}_{n-1}| - a)^2$, bending energy [15]

$$U_B = \frac{k}{2} \sum_n \frac{\theta_n^2}{1 - (\theta_n/\theta_{\max})^2}, \quad (4)$$

and (to describe correctly coiling up of the chain) the energy of short-range repulsive interactions between particles (considered as elastic balls of the diameter d):

$$U_R = \frac{\delta}{2} \sum_n \sum_{m \neq n} (d - |\mathbf{r}_n - \mathbf{r}_m|)^2, \quad (5)$$

for $|\mathbf{r}_n - \mathbf{r}_m| < d$, and $U_R = 0$, otherwise. Here a is the equilibrium lattice spacing, σ is the elastic modulus of the stretching rigidity of the chain, θ_n is the angle between neighboring bond vectors, $(\mathbf{r}_n - \mathbf{r}_{n-1})$ and $(\mathbf{r}_{n+1} - \mathbf{r}_n)$, that meet at the n -th particle (see fig. 1(a)), θ_{\max} is a maximum bending angle, and k is the dimensionless elastic modulus of the bending rigidity of the chain. Note that in polymer physics the flexibility of polymers is characterized by the quantity $k_B T l_p / a$, where T is the temperature, k_B is the Boltzmann constant and l_p is the persistence length in units of chain period [1]. In terms of these quantities the parameter k can be represented in the form

$$k = \frac{k_B T l_p \Delta}{a W^2}. \quad (6)$$

(in the following we let $a = 1$). First of all, we recall the properties of nonlinear localized modes in a curved chain, when the chain geometry is “frozen”. Such an analysis has been recently carried out in ref. [10], where it was found that the energy of the nonlinear excitation decreases as a square law of the chain curvature when the curvature is small. Thus, since the bending energy of the chain increases also as the square of the curvature, one can expect that there should exist a converse influence of the internal nonlinear modes on the conformational dynamics of the chain. Below, we confirm this conjecture by straightforward numerical calculations and find that not only the chain tends to bend, for small enough k , but it also collapses (*i.e.* coils up), for smaller k .

As the first step of our study in this letter, we analyze the stationary ground-state configurations of the chain described by the model introduced above. We assume that the chain is infinitely long, planar ($z_n = 0$), and inextensible ($\sigma \rightarrow \infty$), so that the distance between the neighboring sites of the chain remains constant. In this case, a spatial conformation of the chain is completely defined by the bending angles θ_n . We find the ground-state configurations of the chain looking for the stationary solutions of eq. (2) in the form $\psi_n(t) = e^{i\Delta t} \phi_n$ and $d\mathbf{r}_n/dt = 0$. The corresponding system of nonlinear algebraic equations has been solved by the Newton-Raphson iteration scheme. The results of these calculations are presented in fig. 2(a). The most interesting feature of this phase diagram is the existence of *three distinct types* of ground states.

A stiff chain (with $k > 0.183$) is always straight and, regardless of the value of N , it cannot be affected by the presence of a nonlinear excitation. However, for $k < 0.183$, there appears a finite domain of N , for which a straight chain becomes unstable in the presence of a nonlinear mode. Inside of this domain, the chain in its ground state *curves symmetrically* around the nonlinear excitation, with some finite overall buckling angle $\beta = \sum_n \theta_n$ (see fig. 1(b)). In fig. 2(b), we plot the dependence of the buckling angle β *vs.* N for different values of k . As

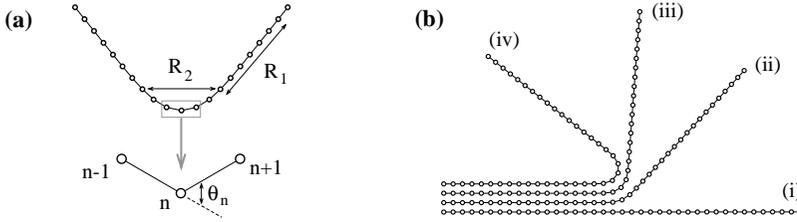


Fig. 1 – (a) Schematic representation of a buckled chain. The distance between the sites near the bend becomes smaller ($R_2 < R_1$) lowering the coupling energy of a nonlinear mode that works against the increased bending energy and lead to a buckling instability. (b) Ground-state spatial configurations of a semiflexible chain ($\alpha = 2$, $\theta_{\max} = \pi/3$, and $k = 0.125$) at different values of N : 2.13 (i), 2.26 (ii), 2.44 (iii), 2.88 (iv), 3.00 (iv), 3.13 (iii), 3.18 (ii), and 3.25 (i). As the nonlinearity N increases, the chain bending initially increases, reaches its maximum at $N \approx 2.96$, and then decreases.

is seen, for $0.124 < k < 0.183$ the buckling angle β is always finite and reaches its maximum at $N \simeq 3$. When the bending rigidity of the chain decreases further, *i.e.* for $k < 0.124$, a new type of ground state, a *collapsed chain*, emerges (see fig. 2). In this case, the distance between particles which belong to different legs of the chain (see fig. 1(b)) decreases to an extent that the growing interaction between the tails of the nonlinear excitation turns buckling into collapse causing coiling up of the chain. The conformation of the chain in the collapsed state (which is usually a three-dimensional compact globule, see fig. 3) is sensitive to the peculiarities of the potentials (4)-(5) and initial conditions.

To gain better insight into the physical mechanism of the buckling instability, we have developed an analytical approach, details of which will be presented elsewhere. Brief mention should be made of the main conclusion that the physical mechanism of buckling instability implies softening of polymer bonds which are occupied by nonlinear excitations. In the vicinity of such excitations one can introduce an *effective bending rigidity* of the chain $k_{\text{eff}} = k - f(N)$, where $f(N)$ is depicted in fig. 2(a) by the dashed curve. For nonlinear excitations with $f(N) > k$ we obtain negative k_{eff} and the straight conformation of the chain becomes unstable.

An important question is how the buckling and collapse instabilities manifest themselves

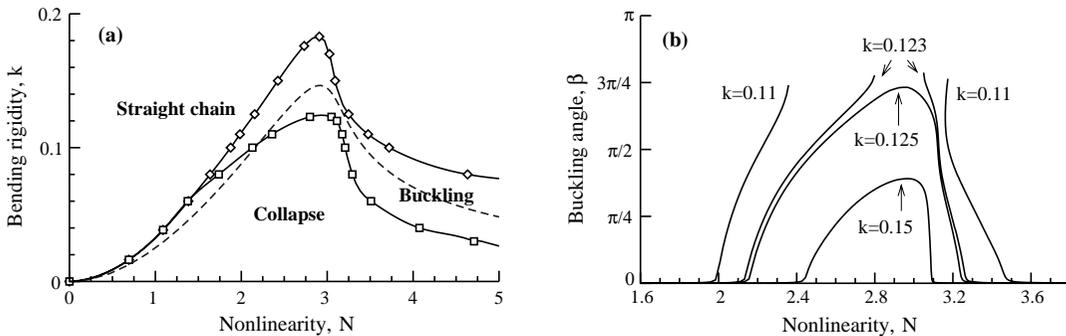


Fig. 2 – (a) Phase diagram of the ground states of a semiflexible biopolymer chain calculated numerically for $\alpha = 2$, $\theta_{\max} = \pi/3$, and $\sigma = \infty$ (solid curves with diamonds and squares) and analytically (dashed curve). (b) Buckling angle β vs. the nonlinearity N for $\alpha = 2$, $\theta_{\max} = \pi/3$, $\sigma = \infty$, and varying k .

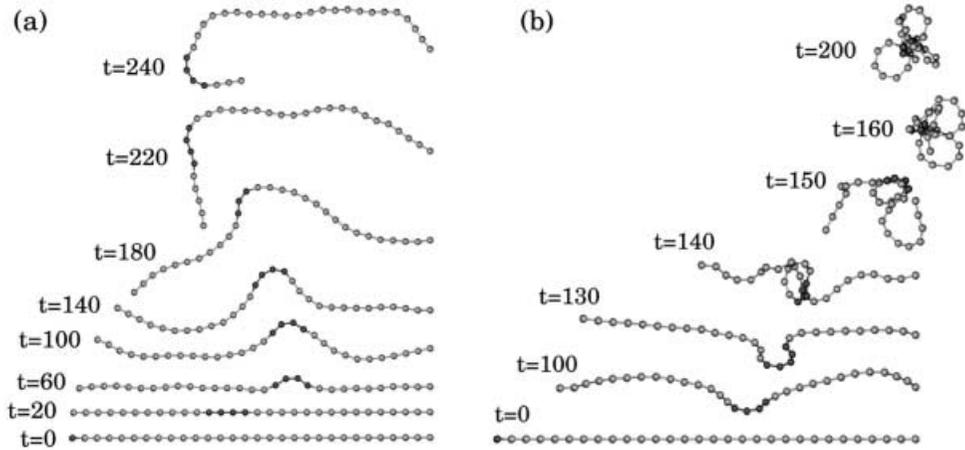


Fig. 3 – Dynamics of a semiflexible biopolymer chain due to (a) buckling ($k = 0.10$) and (b) collapse ($k = 0.08$) instabilities produced by a moving nonlinear mode generated from the single-particle excitation at the left end of the chain. The chain consists of 30 particles, with the right end fixed. Marked particles indicate location of the moving excitation (for these particles, $|\psi_n|^2 > 0.25$). Other parameters are: $N = 3.2$, $\nu = 0$, $\sigma = 10^3$, $\alpha = 2$, $\theta_{\max} = \pi/3$, $M = 0.5$, $\delta = 10^2$, and $d = 0.6$.

in the dynamics of semiflexible biopolymer chains. To clarify this issue, we consider a simple (but physically important) case of an initially straight chain of a finite length whose left end is free whereas the right end is fixed. First, we excite a single particle at the left end of the chain, and then keep track of how this excitation propagates along the chain and how it modifies the chain geometry. For small values of N , such a single-particle excitation disperses and spreads out, whereas for very large values of N it does not propagate and remains completely trapped at the end of the chain. However, for the intermediate values of N (in our model, for $2.5 < N < 3.5$), such a single-particle drive applied at the end of the chain generates a *moving localized mode*. It is remarkable that this interval of nonlinearity parameter N matches closely the region in which the bending capability of the nonlinear mode reaches its maximum.

For a stiff biopolymer chain (*i.e.*, for $k > 0.183$), the propagation of the generated nonlinear mode does not produce any conformational change of the chain. However, when k decreases, the nonlinear mode generates a local chain bending. In this case the nonlinear mode propagates along the chain *being accompanied by a local bending*, as is seen in fig. 3(a). The amplitude of such a bending decreases as the viscous damping ν increases. Thus, the buckling instability we have described above appears to be physically visible, and it is responsible, in particular, for large-amplitude localized bending waves.

Let us consider now a flexible biopolymer chain with even smaller k , for which the nonlinear mode should produce a collapse instability (see fig. 2(a)). In this case, the evolution of the chain clearly demonstrates a collapse dynamics (see fig. 3(b)), and the chain folds into a compact coil with several loops consisting of 7–10 particles each [16]. Importantly, even for large values of the damping parameter ν the collapse of the chain is only delayed but not prevented. For instance, for the parameters used in fig. 3 and $k = 0.06$, the collapse-on time t_c grows almost linearly with ν : $t_c \approx 87 + 1290\nu + 283\nu^2$ for $\nu \leq 1$. Besides, increasing of ν leads to decreasing of the distance between the place of the collapse nucleation and the left end of the chain. Usually the dynamics of polymer chains, moving in a viscous medium, is studied neglecting the inertial term [1], *i.e.*, assuming $M = 0$ in eq. (2). We have verified that

all above-discussed effects remain qualitatively the same in this approximation, too.

In conclusion, we have predicted analytically and demonstrated numerically a new role played by nonlinear excitations in the conformational dynamics of biopolymers. Taking into account coupling between the internal and mechanical degrees of freedom of a semiflexible biopolymer chain, we have found that the presence of nonlinear excitations leads to local softening of polymer bonds and may even cause the buckling and collapse instabilities of an initially straight chain. These instabilities remain latent in a straight infinitely long chain, because the bending of such a chain would require an infinite energy. However, as we have demonstrated above, they manifest themselves as soon as we consider more realistic cases and take into account a finite length of the chain. In this case, a nonlinear localized mode, once generated at the end of the chain, propagates along the chain *accompanied by a local chain bending*, for intermediate values of the bending rigidity k , and it *causes the chain folding*, for smaller k . In the case of collapse instability, the viscous damping of the aqueous environment only slows down the chain folding (coiling up), but does not stop it even for relatively large damping ($\nu \simeq 1$). It should be stressed that these instabilities are most pronounced for *intermediate values* of the nonlinearity N , and they vanish completely in the linear limit as well as in the strong-nonlinearity limit. We find that this effect is only weakly affected by the peculiarities of the interaction potentials [14,15], and thus it should be generic for different models of nonlinear semiflexible chains.

As an example, let us estimate the possibility of the coupling of polarons and the bending in DNA-like polymers. Here the nonlinearity parameter Δ is determined by the coupling between a charge carrier (an extra electron or hole) and phonons. Following estimates presented in [17] we chose $\Delta = 0.4$ eV and $W = 0.3$ eV. Inserting these values into eqs. (3) and (6) for $k_B T \approx 0.02$ eV (room temperature) we get $N = \Delta/W \sim 1$ and $k \approx 10^{-1} l_p/a$. For example, the double-stranded DNA molecule has a persistence length $l_p \approx 50$ nm. Taking into account that the distance between base pairs is $a \approx 0.34$ nm, we see that the dimensionless bending constant $k \sim 10$ and, in accordance with the phase diagram presented in fig. 2(a), the polaron cannot bend the molecule. However, in the case of single-stranded DNA (or RNA) molecules, where the persistence length $l_p \sim 1.4$ nm was found for poly-(dT) strands [18], the dimensionless bending constant $k \sim 10^{-1}$ and nonlinearity-induced bending may be energetically favorable. We also believe that the nonlinearity-induced buckling and collapse instabilities may be of a considerable importance in the conformational dynamics of the globular macromolecules with a multitude of quasi-isoenergetic conformations [19], where nonlinear modes excited even inside the chain should cause *conformational transitions* between different types of globular states of the same or similar topology. Presumably, another related problem is the energy transduction in molecular motors, for which it was recently suggested that the free energy from ATP hydrolysis is initially converted into the hinge-bending motion of the motor sub-unit [20]. However, to approach reality some more credible models of biopolymers should be studied. In particular, it should be important to account for a helical structure and heterogeneity of biopolymers which may decrease an effective bending rigidity of a chain. Since thermal fluctuations provide an alternative mechanism for effective softening of polymer bonds, they also may not be neglected in realistic simulations. We believe that our work will stimulate further theoretical and experimental progress in this promising direction.

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