Nonlinearity-induced conformational instability and dynamics of biopolymers

Serge F. Mingaleev\textsuperscript{1,2,3}, Yuri B. Gaididei\textsuperscript{2,3}, Peter L. Christiansen\textsuperscript{2}, and Yuri S. Kivshar\textsuperscript{1}
\textsuperscript{1} Nonlinear Physics Group, Research School of Physical Sciences and Engineering, Australian National University, Canberra ACT 0200, Australia
\textsuperscript{2} Department of Mathematical Modeling, The Technical University of Denmark, DK-2800 Lyngby, Denmark
\textsuperscript{3} Bogolyubov Institute for Theoretical Physics, 14-B Metrologichna St., 03143 Kiev, Ukraine

We propose a simple phenomenological model for describing the conformational dynamics of biopolymers via the nonlinearity-induced buckling and collapse (i.e. coiling up) instabilities. We describe the buckling instability analytically, and then demonstrate the role of both instabilities in the folding of biopolymers through the numerical simulations of the three-dimensional dynamics of a long semiflexible chain in the aqueous environment.

Conformational flexibility is a fundamental property of polymers which differentiates them from small molecules and gives rise to their remarkable properties. However, even the properties of polymers seem meagre when compared to the functionality of biopolymers. A distinctive feature of biopolymers is that, on the one hand, they are heterogeneous and, on the other, their elementary sub-units have a complex structure and can carry long-lived nonlinear excitations\textsuperscript{1–3}. While the significance of the heterogeneity gained wide recognition as being of fundamental importance for protein folding\textsuperscript{2},\textsuperscript{3}, the function of nonlinear excitations remains obscured, in spite of a large body of theoretical research\textsuperscript{2–5}.

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 nonlinear excitations can facilitate bending or folding of a semiflexible molecular chain via the buckling or collapse instability, and thus provide a possible scenario for the conformational dynamics of biopolymers. We consider a semiflexible chain that models a biopolymer and assume that its mechanical degrees of freedom are coupled to the internal degrees of freedom such as amide-I vibrations in proteins\textsuperscript{1–3}, base-pair vibrations in DNA\textsuperscript{2,4}, or polaron in proteins\textsuperscript{2,3}. This coupling provides the energy needed to overcome the potential barriers for folding, thus avoiding the need for stochastic thermal activation. We reveal that such a simple model describes the conformational dynamics as a deterministic controlled process: when the amplitude of the internal excitation becomes large, the chain displays the buckling or collapse instability that subsequently initiates the chain folding. We believe that such simple physics can also account for the kinetics of conformational phase transitions of semiflexible polymers in solutions\textsuperscript{2,3}.

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\textsuperscript{2,3} and conducting polymers\textsuperscript{3}. The concept of nonlinear localized modes was also employed to explain some specific features of the DNA dynamics\textsuperscript{2,4}. However, most of those studies were dealing with nonlinear properties of straight molecular chains and never discussed changes in their geometrical structure. The study of nonlinear properties of curved chains has been initiated only recently\textsuperscript{1,4} and, in particular, it was shown that the bending in a curved chain manifests itself as an effective trap for nonlinear localized modes. In this Letter, we make an important step forward and, taking into account flexibility of biopolymer chains, demonstrate that nonlinear excitations may 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 $r_n = \{x_n, y_n, z_n\}$. We assume that each particle represents a complex sub-unit of the biopolymer which, additionally to its position $r_n(t)$, carries an internal excitation which can be characterized, in some approximation\textsuperscript{2,4}, 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 $T = (M/2) \sum_n (dr_n/dt)^2$ is the kinetic energy, $U(r_n)$ is the potential energy of inter-particle interactions, and

$$V(\psi_n, r_n) = \sum_{n} \left\{ 2|\psi_n|^2 - \sum_{m \neq n} J_{nm} \psi_n^* \psi_m - \frac{1}{2} \chi |\psi_n|^4 \right\}$$

is the energy of the internal excitation. Here $\chi$ characterizes on-site self-trapping nonlinearity of the internal excitation, and $J_{nm}$ are the excitation transfer coefficients that depend on the distance in the embedding space between the particles $n$ and $m$: $J_{nm} = J(|r_n - r_m|) = (e^\alpha - 1) \exp(-\alpha |r_n - r_m|)\textsuperscript{2,4}$. From the Hamiltonian, we obtain the equations of motion

$$M \ddot{r}_n + \nu \frac{dr_n}{dt} + \frac{dU}{dr_n} - \sum_k \sum_{m \neq k} J_{km} \psi_k^* \psi_m = 0 \ ,$$
\[ i \frac{\partial \psi_n}{\partial t} - 2\psi_n + \sum_{m \neq n} J_{nm} \psi_m + \chi |\psi_n|^2 \psi_n = 0, \]  

(1)

where we allowed additionally for a viscous damping \( \nu \) of the aqueous environment. We assume that the number of excitations, \( \sum_n |\psi_n|^2 = 1 \), is conserved by Eq. (1). This approximation is fully justified for polaron states and should be fairly good for vibrational states, taking into account that in the case under study the lifetime of amide I vibrations is greatly increased as a result of their self-trapping localization [18, 19].

We consider the potential energy of inter-particle interactions as a sum, \( U(R_n) = U_S + U_B + U_R \), of the stretching energy \( U_S = (\sigma/2) \sum_n (|r_n - r_{n-1} - a|^2) \), bending energy \( U_B = \kappa \sum_n \frac{\theta_n^2}{1 - (\theta_n/\theta_{\text{max}})^2} \),

(2)

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 \( d \)):

\[ U_R = \frac{\delta}{2} \sum_{n \neq m} (d - |r_n - r_m|)^2, \]

(3)

for \( |r_n - r_m| < d \), and \( U_R = 0 \), otherwise. Here \( a \) is the equilibrium lattice spacing (we take \( a = 1 \)), \( \sigma \) is the elastic modulus of the stretching rigidity of the chain, \( \theta_n \) is the angle between neighboring bond vectors, \( (r_n - r_{n-1}) \) and \( (r_{n+1} - r_n) \), that meet at the \( n \)-th particle [see Fig. 1(a)], \( \theta_{\text{max}} \) is a maximum bending angle, and \( \kappa \) is the elastic modulus of the bending rigidity of the chain.

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. [12], where it was shown that the chain curvature affects strongly the properties of nonlinear modes, creating an effective double-well potential around the bending point, which is responsible for the symmetry-breaking effect: as the nonlinearity \( \chi \) increases above some threshold, a symmetric stationary mode becomes unstable, and it transforms into an energetically more favorable asymmetric stationary mode. In that study, it was also found that the energy of a nonlinear mode decreases as a square-law of the 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 \( \kappa \), but it also collapses (i.e. coils up), for smaller \( \kappa \).

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 \( (\sigma \to \infty) \), 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 \( \theta_n \).

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

\[ \text{FIG. 2. Phase diagram of the ground states of a semiflexible biopolymer chain calculated numerically (solid curves with squares) and analytically from Eqs. (1) - (3) (dashed curve), at} \ \alpha = 2, \ \theta_{\text{max}} = \pi/3, \ \text{and} \ \sigma = \infty. \]

We find the ground-state configurations of the chain looking for the stationary solutions of Eq. (1) in the form \( \psi_n(t) = e^{i\lambda t} \phi_n \) and \( d \psi_n/dt = 0 \). 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. The most interesting feature of this phase diagram is the existence of three distinct types of the ground states.

A stiff chain (with \( \kappa > 0.183 \)) is always straight and, regardless of the value of \( \chi \), it cannot be affected by the presence of a nonlinear excitation. However, for \( \kappa < 0.183 \), there appears a finite domain of \( \chi \), 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. 3b)]. In Fig. 3 we plot the dependence of the buckling angle \( \beta \) vs. \( \chi \) for different values of \( \kappa \). As is seen, for \( 0.124 < \kappa < 0.183 \) the buckling angle \( \beta \) is always finite and reaches its maximum at \( \chi \approx 3 \).

When the bending rigidity of the chain decreases further, i.e. for \( \kappa < 0.124 \), a new type of the ground state, a collapsed chain, emerges (see Figs. 2 and 3). In this case, the distance between the complementary particles of the chain [see Fig. 1b)] decreases to an extent that the growing interaction between the tails of the nonlinear excitation turns buckling into collapse causing the coiling up of the chain. The conformation of the chain in the collapsed state (which is usually a three-dimensional compact globule, see Fig. 4) is sensitive to the peculiarities of the potentials (2)–(3) and initial conditions.

To gain a better insight into the physical mechanism of the buckling instability, we have developed a simple variational approach. We assume that the chain bending occurs only at the center of the excitation (\( n = 0 \)). In this case, the chain is composed of two semi-infinite lines with the overall buckling angle \( \beta \equiv \theta_0 \) between them. Obviously, such a geometry cannot describe the chain collapse because \( \beta \) is restricted by the maximum angle \( \theta_{\text{max}} \), but it should be valid as long as we are not interested in the collapsed phase but study only a threshold between the straight and buckled chain phases.

In such a simplified model, the ground state of the chain is determined by the dependence of the system energy on \( \beta \). We use a variational ansatz for the localized mode in the form \( \phi_n = \sqrt{\tanh \gamma} \exp(-\gamma |n|) \), which satisfies the constraint \( \sum_n \phi_n^2 = 1 \), and we minimize \( H \) with respect to \( \beta \) and \( \gamma \). Thus, we can show that the straight configuration of the chain (\( \beta = 0 \)) corresponds to the energy maximum (i.e., the straight chain is unstable) for \( \kappa < \kappa_{\text{cr}} \), where the critical value of the bending stiffness is given by the following analytical expression

\[
\kappa_{\text{cr}} = \chi \alpha (e^\alpha - 1) \frac{3 e^{\alpha+\gamma} - 1}{3 (e^{\alpha+\gamma} - 1)^3} \tanh \gamma ,
\]

and \( \gamma \) is determined from the equations

\[
\chi = \frac{8 \cosh^4 \gamma}{(4 \cosh^2 \gamma - 3)} \frac{\partial Q(\gamma)}{\partial \gamma} ,
\]

\[
Q(\gamma) = \frac{e^\alpha (e^\gamma - 1)^2(e^{\alpha+2\gamma} + 1)}{(e^{2\gamma} + 1)(e^\alpha + \gamma - 1)^2} .
\]

In Fig. 4 we compare the threshold curve that separates the phases of the straight and buckled conformations predicted by the analytical formula (4)–(5), with the same dependence calculated numerically. One can see that the variational method provides reasonably fair analytical results for the phase diagram.

An important question is how the buckling and collapse instabilities manifest themselves 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 \( \chi \), such a single-particle excitation disperses and spreads out, whereas for very large values of \( \chi \) it does not propagate and remains completely trapped at the end of the chain. However, for the intermediate values of \( \chi \) (in our model, for \( 2.5 < \chi < 3.5 \)), 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 \( \chi \) matches closely the region in which the bending capability of the nonlinear mode reaches its maximum.

For a stiff biopolymer chain (i.e., for \( \kappa > 0.183 \)), the propagation of the generated nonlinear mode does not produce any conformational change of the chain. However, when \( \kappa \) 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; the amplitude of such a bending decreases as the viscous damping \( \nu \) 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 \( \kappa \), for which the nonlinear mode should produce a collapse instability (see Fig. 3). In this case, the evolution of the chain clearly demonstrates a collapse dynamics (see Fig. 4), and the chain folds into a compact coil with several loops consisting of 7–10 particles each. Importantly, even for large values of the damping parameter \( \nu \) the collapse of the chain is only delayed, but not prevented. For instance, for the parameters used in Fig. 4 the collapse-on time \( t_c \) grows almost linearly with \( \nu : t_c \approx 87 + 1290\nu + 283e^{2\nu} \) for \( \nu \leq 1 \). Besides, increasing of \( \nu \) leads to decreasing of the distance between the place of the collapse nucleation and the left end of the chain.

It should be mentioned that the instability we discuss in this Letter remains 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, the instability manifests itself 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 $\kappa$, and it causes the chain folding, for smaller $\kappa$.

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 the coupling between the internal and mechanical degrees of freedom of a semiflexible biopolymer chain, we have found that it may produce the buckling and collapse instabilities of an initially straight chain, because the bending of such a chain would require an infinite energy. However, as we have demonstrated above, the instability manifests itself 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 $\kappa$, and it causes the chain folding, for smaller $\kappa$.

We believe that the nonlinearity-induced buckling and collapse instabilities may be of a considerable importance in the conformational dynamics of the globular macro-molecules with a multitude of quasi-isoeenergetic conformations [1], where nonlinear modes excited even far from the chain ends should cause conformational transitions between different types of the 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 [2].

The authors are indebted to M. Peyrard, K. Rasmussen, S. Takeno, J. Tuszyński, and A. Zolotaryuk for useful and encouraging comments. S. M. and Yu. G. acknowledge support from the European Commission RTN project LOCNET (HPRN-CT-1999-00163) and the MIDIT center at the Technical University of Denmark, S. M. acknowledges supports from the the Performance and Planning Fund of the Institute for Advanced Studies, the Australian National University, and Yu. G. from the DLR Project No. UKR-002-99 and the SRC “Vidhuk” (Kiev).

FIG. 4. Dynamics of a semiflexible biopolymer chain due to the collapse instability 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, $|\psi_n|^2 > 0.25$). The parameters are: $\chi = 3.2$, $\kappa = 0.06$, $\nu = 0.3$, $\sigma = 10^3$, $\alpha = 2$, $\theta_{\text{max}} = \pi/3$, $M = 0.5$, $\delta = 10^2$, and $d = 0.6$.

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 the coupling between the internal and mechanical degrees of freedom of a semiflexible biopolymer chain, we have found that it may produce the buckling and collapse instabilities of an initially straight chain. In the case of collapse instability, the viscous damping of the aqueous environment only slows down the folding (coiling up) of the chain, 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 self-trapping nonlinearity, and they vanish completely in the linear limit (i.e., for $\chi = 0$). We find that this effect is only weakly affected by the peculiarities of the interaction potentials [1,2], and thus it should be generic for different models of nonlinear semiflexible chains.

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