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Nonlinear dynamics of DNA with topological constraints

A. S. Nikitiuk[1,†], E. A. Korznikova[2], S. V. Dmitriev[2,3], O. B. Naimark[1]

[†]nas@icmm.ru

[1]Institute of Continuous Media Mechanics Ural Branch of RAS, 1 Academika Koroleva str., Perm, 614013, Russia
[2]Institute for Metals Superplasticity Problems of RAS, 39 Khalturin str., Ufa, 450001, Russia
[3]Mirny Polytechnic Institute (branch) of North-Eastern Federal University, 5/1 Tikhonova str., Mirny, 678170, Sakha, Russia

The mechanical DNA model is developed to study the nonlinear dynamics, topological constrains of the helicoidal geometry DNA molecule, dissipation effects and influence of the external force. To construct the model of DNA the Peyrard-Bishop-Barbi approach has been applied. We have derived equations of motion for the DNA base pairs in the presence of a damping term and external driving force to follow the Caldirola-Kanai method. The analytical small localized solutions as the discrete breather and the antikink have been obtained by multiple scale expansion method for multicomponent lattices. The impact of the damping effect and external forces on the breather and the antikink propagation has been investigated. The prospects of using the helicoidal model of DNA with the energy dissipation and external force are discussed. The dissipative term and the external force term in the DNA motion equations follow from corresponding Hamiltonian energy representation. The advantage of this approach is the promising way to study both the thermodynamic properties and nonlinear dynamics of DNA system related to the types of the collective modes (breathers, antikinks) as new thermodynamic degrees of freedom. This result allows the formulation of the experimental strategy to analyze the qualitative changes in cell dynamics induced by mentioned collective modes.

Keywords: DNA, Peyrard-Bishop, helicoidal model, viscosity, mathematical modeling.

1. Introduction

Study of nonlinear dynamics of DNA molecule attracted interest of biologists and physicists as the key factor to link physical and biological properties of this "biological crystal" in the attempt to highlight the evolution of biological systems including the levels of cells and tissue. DNA belongs to the class of biopolymers and has an important biological function, which is the ability to store and transmit genetic information. It is a complex dynamic system consisting of many atoms and has a quasi-one-dimensional structure with specific symmetry, multiple degrees of freedom, many types of movements and a special distribution of internal interactions [1]. These functions of DNA are discussed in some DNA models to investigate the relationship of structural-dynamic and functional properties of the molecule [2 – 7]. However, most of these are ignoring the helicoidal geometry of DNA, damping effect and influence of external force.

Numerous researches have been devoted to the study of either the viscous dissipation effect and external force acting on DNA or the topological constraints to the helicoidal structure of the molecule. For instance, research by Sulaiman et al. [8] has used the Caldirola-Kanai approach [9] for the Peyrard-Bishop model [10] to consider the damping effect and external force. It was shown that the presence of viscosity is decelerated DNA breathing and on other hand the external force accelerates the breather propagation. Barbi et al. [11] modified the Peyrard-Bishop model to take into account helicoidal geometry of DNA molecule. The solitonic solution was obtained for the system consisting of nucleotides with two degrees of freedom (for radial one it was the breather, for angular one it was the kink).

New model of DNA is presented, which considers the helicoidal shape of DNA molecule taking into account the damping effect and external force. It is based on applying the Caldirola-Kanai approach for the Peyrard-Bishop-Barbi model to develop the motion equations for nucleotides.

The paper is organized as follows. In Section 2 DNA structure and the stabilizing forces are described. The Hamilton function of the model under consideration is explained in Section 3. The motion equations containing the dissipative term, external force and corresponding localized solution are described in Section 4.

2. DNA structure and forces stabilizing its

DNA consists of two polymer chains twisted around a common axis to form a double helix. The polymer chain is formed from monomers that are called nucleotides. A nucleotide consists of a phosphate group, a sugar ring and a nitrogenous base (adenine, thymine, guanine, cytosine). Nucleotides connect either with the sugar phosphate backbone or a nitrogen base.

Two polynucleotide chains are held together by hydrogen bonds between the bases. The hydrogen bases combined in pairs according to complementary principle. The forces stabilizing the structure of DNA include stacking interactions between adjacent bases along the DNA axis and provide long-range interactions inside and outside the sugar phosphate backbone (in particular covalent bonds).

3. Helicoidal model of DNA with damping and external force

The helicoidal model has been proposed by Barby et al. [11] to consider the helicoidal structure of the DNA molecule, base-base interactions in a pair and along the sugar-phosphate backbone coupling. Denaturation and melting transition [11] have been investigated by the model.

We propose a modification of the helicoidal model of the DNA molecule, taking into account the effect of energy dissipation and external force. It is assumed that DNA consists of a sequence of N nucleotide pairs. The group consisting of a sugar ring and the associated base is treated as a point mass (without distinction between different types of bases). The phosphate backbone between the two base pairs is modeled as an elastic rod. The point masses within the pair move symmetrically about the axis of the molecule. Each point mass has two degrees of freedom: radial and angular. The radial degree of freedom is determined by the parameter r_n (distance between the center of symmetry and the point mass). Angular degree of freedom — angle φ_n, which is defined as the angle formed between the axis connecting the point masses inside the pair and the reference direction. Pairs of point masses move in parallel planes, the distance between them is fixed $h = 3.4$ Å (Fig. 1). Rotation is defined as the difference between the angles of adjacent point masses $\theta_n = \varphi_n - \varphi_{n-1}$ (Fig. 1). It is assumed that the DNA molecule is in-form, with the following geometric parameters $R_0 = 10$ Å, $\theta_0 = 36°$ (Fig. 1). The object of modeling is considered in the framework of nonlinear dynamics, because DNA is a dynamic object. The energy of the system is determined by the Hamiltonian. As the potential describing the interaction between point masses within the pair (which corresponds to the hydrogen bond between the bases), the Morse potential is chosen because it describes the interaction between atoms and molecules quite accurately. It is assumed that the relationship between adjacent point masses can be described by an elastic potential that considers the relationship between the radial and angular degrees of freedom. It is believed that the kinetic energy of the system decreases with time, while the potential energy increases. The rate of decrease and increase depends on the dissipation factor γ [8]. The system operates in an external conservative force F. Other external influences on the system are neglected.

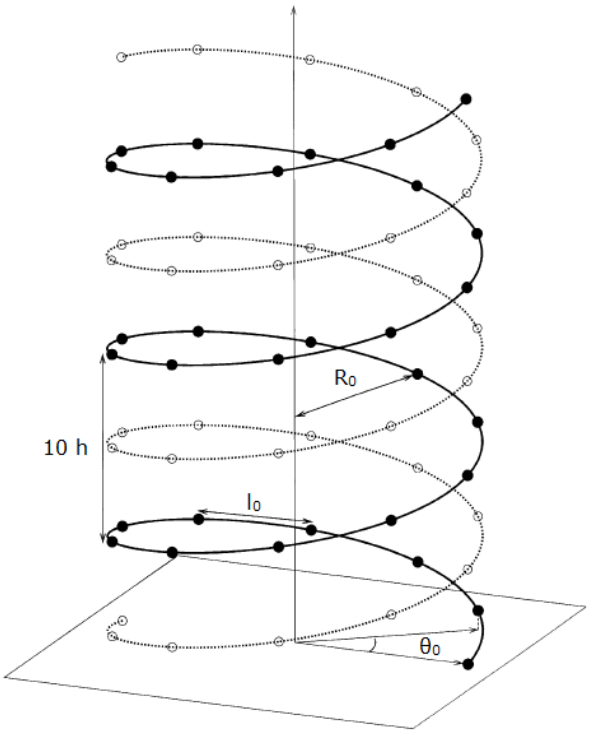

Fig. 1. Schematic view of the mechanical analogue of the DNA molecule [12].

Thus, the parameters describing the simulated system are the distance between the center of symmetry and the n-th point mass r_n and the rotation of the n-th point mass relative to $(n-1)$-th θ_n. To determine the parameters of the model at any time it is necessary to solve the system of equations of motion of point masses, determined from the Hamilton function.

4. Equations of motion of the DNA nucleotides and their approximate solution

The behavior of the modeling object is described by the Hamilton function

$$H\left(p_r, p_\varphi, r_n, \varphi_n\right) = e^{-\gamma t} E_{kin}\left(p_r, p_\varphi\right) + e^{\gamma t} U\left(r_n, \varphi_n\right) - e^{\gamma t} E_F, \quad (1)$$

where E_{kin} is the kinetic energy of the system, U is the potential energy of the system, E_F is the energy entering the system from an external source, p_r is the momentum of the point mass in a radial direction, p_φ the angular momentum of a point mass in the angular direction, γ is the damping constant.

The potential energy of the system is given as

$$U = U_{hyd} + U_{\text{cov}} + U_{backbone}, \quad (2)$$

where U_{hyd} is the energy of hydrogen bonds between bases within one pair of nucleotides, U_{cov} is the energy of covalent bonds of nucleotides stacked one above the other, $U_{backbone}$ is the energy of sugar phosphate bonds responsible for the preservation of the helicoidal shape of the DNA molecule.

The energy of hydrogen bonds between the bases within one pair of nucleotides is described by the Morse potential, which has the following form

$$U_{hyd} = \sum_n \frac{D}{2}\left(e^{-\alpha(r_n - R_0)} - 1\right)^2, \quad (3)$$

where D and a are the depth and the width of the potential hole respectively.

We introduce a relation describing the covalent bond arising in the sugar phosphate backbone. Since the covalent bond is much stronger than the hydrogen bond, it can be taken as a harmonic approximation

$$U_{\text{cov}} = \sum_n \frac{K}{2}\left(l_{n-1,n} - l_0\right)^2, \quad (4)$$

where K is the stiffness coefficient of the covalent bonds, $l_{n-1,n}$

is the actual distance between $n-1$ and n points mass, l_0 is the equilibrium distance between $n-1$ and n points mass.

Since the energy of covalent bonds (8) tends to a minimum for arbitrarily oriented pairs of point masses, it is necessary to introduce an additional potential that determines the correct helix geometry of the simulated system

$$U_{backbone} = \sum_n \frac{G_0}{2}\left(\varphi_{n+1} + \varphi_{n-1} - 2\varphi_n\right)^2, \qquad (5)$$

where G_0 is the stiffness coefficient of the sugar phosphate backbone. Note that this potential does not contribute to the total energy of the system (vanishes) only when the base pairs form a spiral.

Substituting (2), (3), (4) and (5) into yields the final Hamiltonian

$$\begin{aligned} H = {} & e^{-\gamma t}\sum_n \frac{m}{2}\left(\left(\frac{p_r}{2m}\right)^2 + \left(\frac{p_\varphi}{2mr_n}\right)^2\right) + \\ & + e^{\gamma t}\left(\sum_n \frac{D}{2}\left(e^{-\alpha(r_n - R_0)} - 1\right)^2 + \sum_n \frac{K}{2}\left(l_{n-1,n} - l\right)^2\right) + \\ & + e^{\gamma t}\left(\sum_n \frac{G_0}{2}\left(\varphi_{n+1} + \varphi_{n-1} - 2\varphi_n\right)^2 - \sum_n F_n(t)\left(r_n + r_n\varphi_n\right)\right), \end{aligned} \qquad (6)$$

where m is the nucleotide mass.

For the convenience of studying the model, the dimensionless Hamilton function is obtained. To do this, we introduce the parameters Y_n and Φ_n denoting the displacement of the point mass relative to the equilibrium state in the radial and angular directions, respectively

$$Y_n = r_n - R_0, \quad \Phi_n = \varphi_n - n\theta_0. \qquad (7)$$

A limit on the amplitude of displacements of point masses in the radial $Y_n \ll 1$ and the angular $\Phi_n \ll 1$ directions is introduced. Then the Morse potential of U_{hyd} and the potential of U_{cov} can be written for small displacements in the following form

$$U_{hyd} \approx \frac{D}{2}\sum\left(\alpha^2 Y_n^2 - \frac{1}{2}\alpha^3 Y_n^3 + \frac{7}{8}\alpha^4 Y_n^4\right), \qquad (8)$$

$$\begin{aligned} U_{cov} \approx {} & \frac{K}{2}\sum_n \frac{R_0^4 \sin^2\theta_0}{l_0^2}\left(\Phi_n - \Phi_{n-1}\right)^2 + \\ & + \frac{K}{2}\sum_n \frac{R_0^2\left(1-\cos\theta_0\right)^2}{l_0^2}\left(Y_n + Y_{n-1}\right)^2 + \\ & + \frac{K}{2}\sum_n \frac{2R_0^3\left(1-\cos\theta_0\right)\sin\theta_0}{l_0^2}\cdot\left(\Phi_n - \Phi_{n-1}\right)\left(Y_n + Y_{n-1}\right). \end{aligned} \qquad (9)$$

We introduce the dimensionless quantities

$$\begin{aligned} & y_n = \alpha Y_n, \quad \varphi_n = \alpha R_0 \Phi_n, \quad K \to K / D\alpha^2, \quad R_0 \to R_0\alpha, \\ & h \to h\alpha, \quad G_0 \to G_0 / D, \quad l_0 \to \alpha l_0, \\ & \gamma \to \gamma\sqrt{m / D\alpha^2}, \quad t \to t\sqrt{D\alpha^2 / m}, \quad H \to H / D. \end{aligned} \qquad (10)$$

As result we have the dimensionless Hamiltonian

$$\begin{aligned} H = {} & e^{-\gamma t}\sum_n \frac{1}{2}\left(p_y^2 + \frac{p_\phi^2}{\left(1 + y_n / R_0\right)^2}\right) + \\ & + e^{\gamma t}\left(\sum_n \frac{1}{2}\left(y_n^2 - \frac{1}{2}y_n^3 + \frac{7}{8}y_n^4\right) + \sum_n \frac{K_{yy}}{2}\left(y_n + y_{n-1}\right)^2\right) + \\ & + e^{\gamma t}\left(\sum_n \frac{K_{y\phi}}{2}\left(y_n + y_{n-1}\right)\left(\phi_n - \phi_{n-1}\right) + \right. \\ & \left. + \sum_n \frac{K_{\phi\phi}}{2}\left(\phi_n - \phi_{n-1}\right)^2 + \sum_n \frac{G_0}{2}\left(\phi_{n+1} + \phi_{n-1} - 2\phi_n\right)^2\right) - \\ & - e^{\gamma t}\sum_n CF_n(t)\left(y_n + R_0\right)\left(1 + \left(\phi_n / R_0 + n\theta_0\right)\right), \end{aligned} \qquad (11)$$

where

$$\begin{aligned} & K_{yy} = \frac{KR_0^2}{D\alpha^2 l_0^2}\left(1-\cos\theta_0\right)^2, \quad K_{\phi\phi} = \frac{KR_0^2}{D\alpha^2 l_0^2}\sin^2\theta_0, \\ & K_{y\phi} = \frac{KR_0^2}{D\alpha^2 l_0^2}\sin\theta_0\left(1-\cos\theta_0\right), \; G = \frac{G_0}{D\alpha^2 R_0^2}, C = \frac{1}{D\alpha}. \end{aligned} \qquad (12)$$

From the Hamiltonian in, one can obtain the canonical coordinates,

$$\dot{y}_n = \frac{\partial H}{\partial p_y}, \; \dot{\phi}_n = \frac{\partial H}{\partial p_\phi}, \; \dot{p}_y = -\frac{\partial H}{\partial y_n}, \; \dot{p}_\phi = -\frac{\partial H}{\partial \phi_n}. \qquad (13)$$

Substituting $(13)_1$ and $(13)_2$ into $(13)_3$ and $(13)_4$, respectively, yields a system of differential equations with the initial conditions

$$\begin{cases} \ddot{y}_n = e^{-2\gamma t}\dfrac{2}{R_0}\dfrac{\dot{\phi}_n^2}{\left(1 + y_n / R_0\right)} - \left(y_n - \dfrac{3}{4}y_n^2 + \dfrac{7}{4}y_n^3\right) - \\ \quad - \dfrac{K_{y\phi}}{2}\left(\phi_{n+1} - \phi_{n-1}\right) - K_{yy}\left(y_{n-1} + 2y_n + y_{n+1}\right) - \\ \quad - \gamma\dot{y}_n + CF_n(t)\left(1 + \left(\phi_n / R_0 + n\theta_0\right)\right) \\ \ddot{\phi}_n = -\dfrac{2}{R_0}\dot{y}_n\dot{\phi}_n - \dfrac{2}{R_0}y_n\ddot{\phi}_n - \dfrac{2}{R_0^2}y_n\dot{y}_n\dot{\phi}_n - \dfrac{1}{R_0^2}y_n^2\ddot{\phi}_n + \\ \quad + \dfrac{K_{y\phi}}{2}\left(y_{n+1} - y_{n-1}\right) + K_{\phi\phi}\left(\phi_{n+1} + \phi_{n-1} - 2\phi_n\right) - \\ \quad - G_0\left(\phi_{n+2} + \phi_{n-2} - 4\phi_{n+1} - 4\phi_{n-1} + 6\phi_n\right) - \\ \quad - \gamma\dot{\phi}_n - \dfrac{2}{R_0}\gamma y_n\dot{\phi}_n - \dfrac{1}{R_0^2}\gamma y_n^2\dot{\phi}_n + \dfrac{C}{R_0}F_n(t)\left(y_n + R_0\right) \\ y_n(0) = Y_0, \; \phi_n(0) = \Phi_0 \end{cases} \qquad (14)$$

In order to look for approximate localized solution of the equations of motion of the DNA nucleotides, we use the multiple scale technique for multicomponent lattices [12]. The method amounts to looking for wave-packet like solution. At the first step of the method, we determine the carrier vector as a phonon mode of the linearized system, increasing progressively the space and time scales. Next, we deduce the partial differential equation that identifies the envelope velocity with the wave-packet group velocity. Finally, we derive the nonlinear Schrodinger equation for the envelope, whose diffusion coefficient is in fact the wave packet group velocity dispersion. The complete solution obtained the method has the following form

$$\begin{cases} y_n = 2\varepsilon V_1^- \mathrm{Asech}\left[\eta\left(x-V_e t\right)\right]\cos\left(\mathrm{Kx}-\Omega t\right)+ \\ +\varepsilon^2 V_1^{(1)} \mathrm{Asech}\left[\eta\left(x-V_e t\right)\right]\cdot \\ \cdot\left[\dfrac{-2-2\sqrt{D^2-G^2}}{L_e}\,\mathrm{th}\left(\eta\left(x-V_e t\right)\right)\sin\left(\mathrm{Kx}-\Omega t\right)+\dfrac{u_e}{P}\cos\left(\mathrm{Kx}-\Omega t\right)\right]+ \\ +2\varepsilon^2\gamma_{1c}\mathrm{A}^2\,\mathrm{sech}^2\left[\eta\left(x-V_e t\right)\right]\cos\left(2\mathrm{Kx}-2\Omega t\right)+ \\ +\mu_{1c}\varepsilon^2\mathrm{A}^2\,\mathrm{sech}^2\left[\eta\left(x-V_e t\right)\right]+O\left(\varepsilon^3\right) \\ \phi_n = \varepsilon\left(\sigma_{2c}+\varepsilon\mu_{2c}\right)L_e\mathrm{A}^2\,\mathrm{th}\left(\eta\left(x-V_e t\right)\right)- \\ -2\varepsilon\mathrm{A}\left|V_2^-\right|\mathrm{sech}\left[\eta\left(x-V_e t\right)\right]\sin\left(\mathrm{Kx}-\Omega t\right)+ \\ +\varepsilon^2 V_2^{(1)}\mathrm{Asech}\left[\eta\left(x-V_e t\right)\right]\cdot \\ \cdot\left[\dfrac{2+2\sqrt{D^2-G^2}}{L_e}\,\mathrm{th}\left(\eta\left(x-V_e t\right)\right)\cos\left(\mathrm{Kx}-\Omega t\right)+\dfrac{u_e}{P}\sin\left(\mathrm{Kx}-\Omega t\right)\right]+ \\ +2\varepsilon^2\left|\gamma_{1c}\right|\mathrm{A}^2\,\mathrm{sech}^2\left[\eta\left(x-V_e t\right)\right]\sin\left(2\mathrm{Kx}-2\Omega t\right)+O\left(\varepsilon^3\right) \end{cases} \quad (15)$$

with

$$\mathrm{A}=\sqrt{\frac{\left(u_e-G/D\left(x-\omega_-^{(1)}t\right)\right)^2-2\left(u_e-G/D\left(x-\omega_-^{(1)}t\right)\right)u_c}{2PQ}} \quad (16)$$

$$L_e=\frac{2P}{\sqrt{\left(u_e-G/D\left(x-\omega_-^{(1)}t\right)\right)^2-2\left(u_e-G/D\left(x-\omega_-^{(1)}t\right)\right)u_c}} \quad (17)$$

$$\begin{aligned} G &= \omega_-\left(V_1^{-*}\gamma V_1^- + V_1^{-*}\gamma V_2^- + V_2^{-*}\gamma V_1^- + V_2^{-*}\gamma V_2^-\right), \\ D &= \omega_-\left(V_1^{-*}CF + V_1^{-*}CF + V_2^{-*}CF + V_2^{-*}CF\right) \end{aligned} \quad (18)$$

where A and L_e are the amplitude and the width of the soliton, respectively, ε, V_1^-, V_2^-, η, V_e, K, Ω, $V_1^{(1)}$, $V_2^{(1)}$, u_e, P, Q, γ_{1c}, μ_{1c}, μ_{2c}, σ_{2c}, ω_-, $\omega_-^{(1)}$, V_1^-, V_2^- are solution parameters which determines in [13].

Fig. 2 shows analytical solution in displacement and time variable, as function of base pairs and time, obtained by the multiple scale technique for multicomponent lattices. The approximate localized solution of the equations of motion of the DNA nucleotides derived with the following model parameters $D=0.04$ eV, $a=4.45$ Å^{-1}, $K=0.04$ eV Å^{-2}, $G_0=0.5KR_0^2$, $m=300$ a.m.u., $\gamma=0.05$ kg/s, $F=15$ pN. The radial motion has the shape of discrete breather (Fig. 2a, c) and angular motion exhibits an antikink structure (Fig. 2b, d). Also, according to the results, we can conclude that the presence of viscosity decelerated DNA breathing, and the influence of the external force accelerates the breather propagation. This result is consistent with the study [8].

5. Conclusion

The main objective of the present work was to propose a new model of DNA which considers its helicoidal shape, the damping and external force. Current models take into account either the viscous dissipation effect and external force acting on DNA or the topological constraints to the helicoidal structure of the molecule. To solve this problem, two approaches were used together: the Peyrard-Bishop-Barbie model and the Caldirola-Kanai approach.

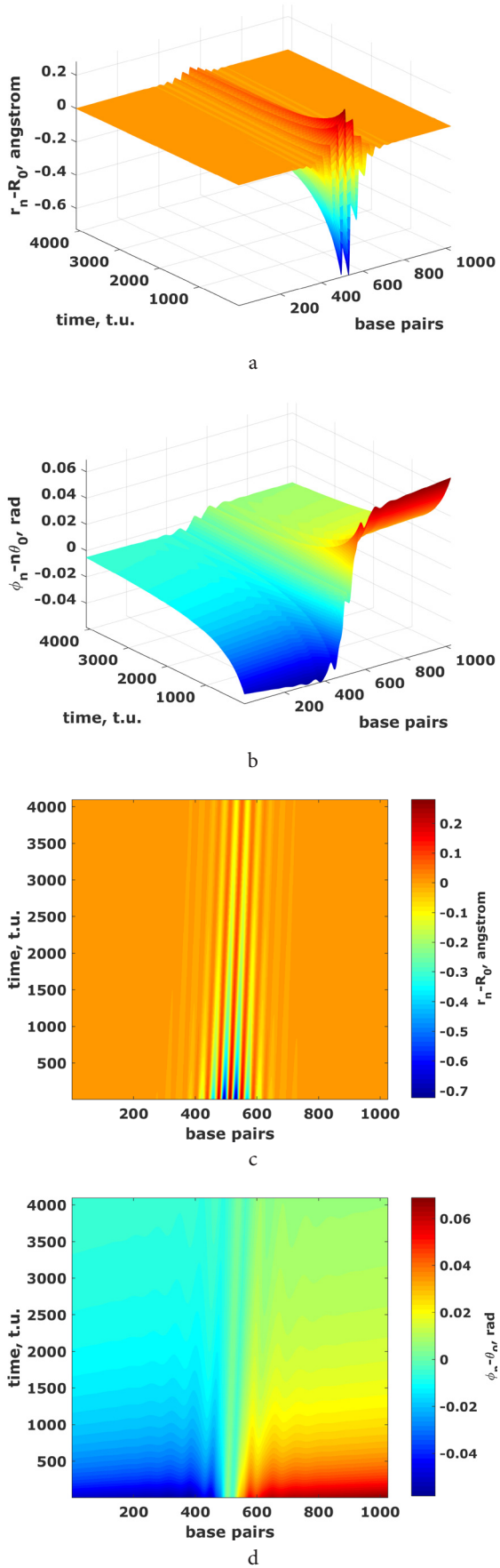

Fig. 2. Analytical solution of the DNA helicoidal model with the damping and constant external force. The radial displacement $r_n(t)-R_0$ in 3D (a) and 2D (c). The corresponding angular displacement in 3D (b) and 2D (d). The chain length is of 1024 cites. The total time is 4096 t.u.

We derived the dissipative term and the external force term of equations of motion of the DNA nucleotides directly from the Hamilton function. The main advantage of this approach is able to calculate the thermodynamic behaviors of the system under consideration for future studies. Future research will concentrate on the looking for approximate localized solution at different types of external force and different values of the damping constant and their following investigation.

Molecular aspects of topological constraints were analyzed in this study in the conceptual spirit to construct the bridge between dynamic and thermodynamic behavior of multiscale mesoscopic modes of open complex that was proposed in [2].

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