Biophysical Reviews (2021) 13:315–338
https://doi.org/10.1007/s12551-021-00801-0

REVIEW

Ideas and methods of nonlinear mathematics and theoretical physics in DNA science: the McLaughlin-Scott equation and its application to study the DNA open state dynamics

Ludmila V. Yakushevich[1] · Larisa A. Krasnobaeva[2,3]

Received: 3 February 2021 / Accepted: 22 April 2021 / Published online: 13 May 2021

Abstract
The review is devoted to a new and rapidly developing area related to the application of ideas and methods of nonlinear mathematics and theoretical physics to study the internal dynamics of DNA and, in particular, the behavior of the open states of DNA. There are two main competing approaches to this research. The first approach is based on the molecular dynamics method, which takes into account the motions of all structural elements of the DNA molecule and all interactions between them. The second approach is based on prior selection of the main (dominant) motions and their mathematical description using a small number of model equations. This review describes the results of the study of the open states of DNA performed within the framework of the second approach using the McLaughlin-Scott equation. We present the results obtained both in the case of homogeneous sequences: *poly* (A), *poly* (T), *poly* (G) and *poly* (C), and in the inhomogeneous case when the McLaughlin-Scott equation has been used for studying the dynamics of open states activated in the promoters A_1, A_2 and A_3 of the bacteriophage T7 genome, in the genes IFNA17, ADRB2, NOS1 and IL-5, in the pBR322 and pTTQ18 plasmids. Particular attention is paid to the results concerning the effect of various external fields on the behavior of open states. In the concluding part of the review, new possibilities and prospects for the development of the considered approach and especially of the McLaughlin-Scott equation are discussed.

Keywords DNA open states · Sine-Gordon kinks · McLaughlin-Scott equation · IFNA17 · ADRB2 · NOS1 and IL-5 genes · pBR322 and pTTQ18 plasmids

Introduction

The penetration of the ideas of theoretical physics and nonlinear mathematics into various fields of science is a feature of modern research. The McLaughlin-Scott equation and its applications for studying the internal dynamics of DNA, to which this review is devoted, are a prime example of this trend.

Quite a long time has passed since John Scott Russel observed a single wave within the Union Canal (Scott-Rassel 1844). From that moment, the history of the study of solitary waves or solitons, propagating in nonlinear media, began. Numerous examples of the emergence and propagation of solitons in physical and then biological environments have been discovered. Basic equations describing these phenomena were obtained. The sine-Gordon equation (Rubinstein 1970), the Koteweg-deVries equation (Jeffrey and Kakutani 1972) and the nonlinear Schrödinger equation (Bochieri and Loinger 1970) were among them.

In 1980, to explain experimental data on hydrogen-deuterium exchange of DNA, Englander et al. (1980) demonstrated the existence of transiently open states (Fig. 1a) in DNA and synthetic polynucleotide double helices and proposed to describe them by kinks being one-soliton solutions of the nonlinear sine-Gordon equation.

The sine-Gordon equation is integrable (Ablowitz and Segur 1980; Rajaraman 1982). However, the perturbations to this equation associated with the effects of dissipation, external forces and inhomogeneities spoil its integrability, and the equation can not be solved exactly. If perturbations are

✉ Ludmila V. Yakushevich
kind-@mail.ru

[1] Institute of Cell Biophysics, Russian Academy of Sciences, Pushchino, Moscow Region, Russia

[2] Siberian State Medical University, Tomsk, Russia

[3] Tomsk State University, Tomsk, Russia

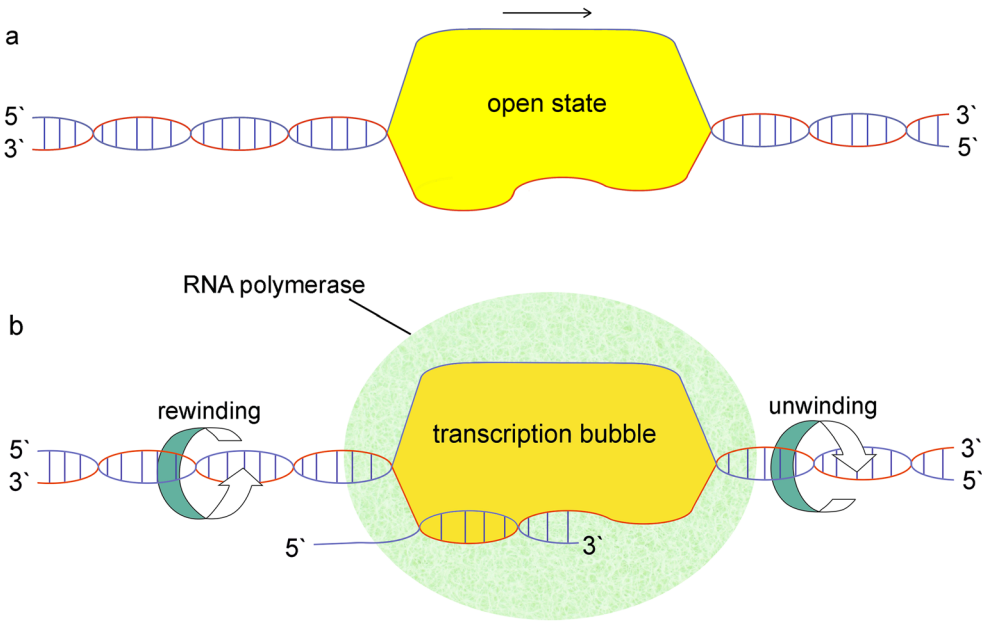

Fig. 1 Locally unwound regions: **a** open state and **b** transcription bubble that is formed at the initial stage of the transcription

small, the solution can be found with the help of the perturbation theory that was described in details by Keener and McLaughlin (1977). In addition, McLaughlin and Scott (1977) developed the perturbation analysis of the sine-Gordon equation and applied it to study the dynamics of vortices in Josephson contacts. In 1978, they (McLaughlin and Scott 1978a, b) derived the equation that allowed calculating the velocity of kinks being one-soliton solutions of the nonlinear sine-Gordon equation.

That time, the equation of McLaughlin and Scott was highly appreciated by physicists as one of the most effective approaches for solving the perturbed sine-Gordon equation that was used to explain many physical phenomena, including propagation of fluxons in long Josephson contacts (Kulik 1967; Nitta et al. 1984; Malomed 1988; Braun and Kivshar 1998), dislocations in crystals (Frenkel and Kontorova 1939; Braun and Kivshar 2004), nonlinear spin waves in superfluids (Kivshar and Malomed 1989), tectonic stress transfer (Bykov 2014), nonlinear geophysical processes in the earth's crust (Gerus and Vikulin 2016), the decay of a breather and pinning by a micro resistor (Gulevich and Kusmartsev 2006) and waves in ferromagnetic and antiferromagnetic materials (Zharnitsky et al. 1998a, b). Recent studies have shown, however, that the McLaughlin-Scott equation is a very convenient and effective tool not only in physics but also in biophysics related to the study of the internal dynamics of DNA.

The first works using the McLaughlin-Scott equation for DNA appeared in 2007–2008 (Yakushevich and Krasnobaeva 2007, 2008a, b; Krasnobaeva and Shapovalov 2008). Before that, in many publications, starting with the work of Englander et al. (1980) as well as in the works of Yomosa (1983, 1984), Takeno and Homma (1983), Homma and Takeno (1984), Krumhansl and Alexander (1983); Krumhansl et al. (1985), Fedyanin et al. (1986), Yakushevich (1987, 1989), Gaeta (1990, 1994, 2006, 2007), Cadoni et al. (2007), in the books and reviews (Gaeta et al. 1994; Peyrard 1995; Yakushevich 2004) and even in more recent works (Shapovalov and Krasnobaeva 2009; Derks and Gaeta 2011; Cadoni et al. 2011; Grinevich et al. 2015a, b; Chevizovich et al. 2020), studies of nonlinear DNA dynamics were carried out on the basis of the sine-Gordon equation (Scott 1969; Caudrey et al. 1975):

$$\varphi_{\tau\tau} - \varphi_{\xi\xi} + sin\varphi = 0 \tag{1}$$

of its modification that took into account the effects of dissipation and the effect of external fields (Quintero and Kevrekidis 2001; Cuenda and Sanchez 2004a; Ekomasov 2009; Ivancevic and Ivancevic 2013; Gumerov et al. 2015):

$$\varphi_{\tau\tau} - \varphi_{\xi\xi} + sin\varphi = -\alpha\varphi_{\tau} + F(\tau) \tag{2}$$

and of combined models which included Eq. (1) or (2) as a part of the system of coupled nonlinear differential equations (Zhou and Zhang 1991; Barbi et al. 2003; Barbi et al. 1999; Gaeta and Venier 2008a, b; Cadoni et al. 2009; Drobotenko et al. 2018). In Eqs. (1)–(2), $\varphi(\xi, \tau)$ is the angle of deviation of the nitrogenous base from the equilibrium position, α is the dimensionless dissipation coefficient and $F(\tau)$ is the dimensionless external field.

Equation (1) has a wide variety of solutions in the form of nonlinear solitary waves, including one-soliton solutions (kink and antikink), two-soliton solutions (breather, kink-kink, kink-antikink, antikink-antikink), three-soliton solutions, etc. (Scott et al. 1973). The kink solution:

$$\varphi_k(\xi, \tau) = 4\boldsymbol{arctg}\{exp[\gamma(\xi - v\tau - \xi_0)]\} \tag{3}$$

was successfully used by Englander et al. (1980) to explain experiments on hydrogen-deuterium exchange in DNA. Here,

v is the dimensionless kink velocity, ξ_0 is an arbitrary constant and $\gamma = (1 - v^2)^{-1/2}$.

Solutions of Eq. (2) have not yet been found. The approach proposed by McLaughlin and Scott (1978a, b) is one of the best for obtaining approximate solutions. To find the solutions, McLaughlin and Scott assumed that the terms on the right side of Eq. (2), simulating dissipation and external action, are small, which, in turn, enabled them to use the methods of perturbation theory. McLaughlin and Scott also suggested that, to first approximation, the kink shape is determined by formula (3) in which, however, the velocity is no longer a constant but a function that depends on time. The equation for velocity v obtained by McLaughlin and Scott as a result of all these assumptions turned out to be an ordinary first-order differential equation (see Appendix 1 for details):

$$\frac{dv}{d\tau} = -\alpha v\left(1-v^2\right) + \frac{\pi}{4} F(\tau)\left(1-v^2\right)^{3/2}. \quad (4)$$

In contrast to the modified sine-Gordon equation (2), Eq. (4) has analytical solutions with a simple and clear interpretation, which makes it more convenient for use in applications.

Equation (4) for the kink velocity is often supplemented by the equation for the kink coordinateξ:

$$\frac{d\xi}{d\tau} = v. \quad (5)$$

Equations (4) and (5) completely define the McLaughlin-Scott mathematical model.

In recent years, the model of McLaughlin and Scott has been actively used to study the behavior of transcriptional bubbles (Fig. 1b) (Shikhovtseva and Nazarov 2016; Grinevich et al. 2015b; Grinevich and Yakushevich 2018), which are locally unwound regions of the DNA double helix formed at the initial stage of the transcription process as a result of the interaction of RNA polymerase with DNA promoter regions (Forth et al. 2013; Severin 2016).

In the general case, the locally unwound regions of DNA are often named the open states. The term "open state" (or "open complex") was first used in 1974 by Chamberlin (1974). Besides experiments on hydrogen-deuterium exchange of DNA (Englander et al. 1980), the evidence was provided by Saucier and Wang (1972), who used a sensitive method for detecting DNA strand separation, based on the effect it has on supercoiling of plasmid DNA. The advent of chemical probes such as dimethyl sulphate and $KMnO_4$ for monitoring DNA strand separation (Siebenlist et al. 1980; Kirkegaard et al. 1983; Sasse-Dwight and Gralla 1989) made it possible to determine the region of strand separation with single bp resolution. In spite of this, there is still no consensus on the mechanisms of the formation of open states (Karpen and deHaseth 2015) and regulation of their movement along the DNA.

It is assumed that open states play an important role not only in the processes of transcription (Clark and Pazdernik 2015; He et al. 2016; Zuo and Steitz 2017) but also in replication (Bailey and Doherty 2017; Bleichert et al. 2017), denaturation (Sicard et al. 2015; Shi et al. 2016; Singh and Granek 2017) as well as in the transmission of structural changes and information along the DNA molecule (Dwiputra et al. 2017). The role of the dynamic properties of open states in the prediction of bacterial promoters has been recently considered by Ryasik et al. (2018).

In general, there are two main competing approaches to mathematical studying internal DNA mobility including open state dynamics. The first is based on the molecular dynamics method that takes into account the movements of all structural elements of a molecule and all interactions between them. The second method is based on prior selection of the main (dominant) motions, their mathematical description with the help of the model equations and the analysis of the solutions of the equations. The advantage of the first method lies in the maximum coverage and use of available information on the internal mobility of DNA, while the disadvantage is associated with the difficulties in interpreting the results obtained. The advantage of the second method is in the possibility of using not only computational but also analytical methods that simplifies the analysis and interpretation of the results. The disadvantage of this method is in the necessity to neglect a part of information which might be important and interesting in some special cases.

This review describes the results of the study of the open states of DNA performed within the framework of the second approach using the McLaughlin-Scott equation. In the first section of the review, we consider a homogeneous case where the McLaughlin-Scott equation is applied to DNA sequences consisting of identical nitrogenous bases. These are the sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C). The section begins with the necessary information about the predecessor of the McLaughlin-Scott equation—the sine-Gordon equation written in terms of DNA, about its one-soliton solutions (kinks), as well as data on the main dynamic characteristics of DNA kinks. Then, the McLaughlin-Scott equation for the kink velocity is considered directly. We present analytical and numerical solutions of this equation obtained in the absence of an external field, in the presence of a constant external field, a periodic external field with a constant frequency, a periodic external field with a slowly varying frequency and an external field with an "on/off" mode.

In the second part of the review, an inhomogeneous case is considered. New methods and approaches are presented that significantly expand the capabilities of the McLaughlin-Scott method in studies of nonlinear dynamics of DNA and in the construction of trajectories of motion of kinks in inhomogeneous DNA sequences. We demonstrate these new possibilities for both artificial and native sequences, in particular,

promoter regions of the T7 bacteriophage genome, the IFNA17, ADRB2, NOS1 and IL-5 gene sequences, and the pBR322 and pTTQ18 plasmid sequences. In conclusion, we discuss the prospects for using the McLaughlin-Scott model, as well as the limits of its applicability for DNA.

McLaughlin-Scott equation for homogeneous DNA

We begin our review with a brief description of the sine-Gordon equation, one-soliton solutions (kinks) and the main dynamic characteristics of the kinks written in terms of homogeneous DNA. These results are considered as a starting point for deriving the McLaughlin-Scott equation for DNA.

Sine-Gordon equation as a predecessor

Canonical sine-Gordon equation (1) is dimensionless, universal and can be applied to different nonlinear dynamical systems (not only to DNA). The sine-Gordon equation rewritten in terms of homogeneous DNA:

$$I\varphi_{tt} - K' a^2 \varphi_{zz} + V sin\varphi = 0 \tag{6}$$

and one-soliton solution in the form of the kink:

$$\varphi_k(z,t) = 4arctan\{exp[(\gamma_k/d_k)(z - \upsilon_k t - z_0)]\} \tag{7}$$

were first obtained by Englander et al. (1980) and later with refined parameters by Yakushevich et al. (2005).

Equation (6) is related to the canonical sine-Gordon equation (1) by a simple linear transformation:

$$\tau = \lambda t, \xi = \mu z, \tag{8}$$

where $\boldsymbol{\lambda = (V/I)^{1/2}}$, $\boldsymbol{\mu = a^{-1}(V/K')^{1/2}}$.

In formulas (6)–(8) υ_k is the kink velocity, $\boldsymbol{\gamma_k = \left(1 - \upsilon_k^2/C^2\right)^{-1/2}}$ is the Lorentz factor, $\boldsymbol{C = (K' a^2/I)^{1/2}}$ is the sound velocity in DNA, $\boldsymbol{d = (K' a^2/V)^{1/2}}$ is the kink size, $\boldsymbol{I = mR^2}$ is the moment of inertia of the base, m is mass of the base, R is the distance between the center of mass of the base and the nearest sugar-phosphate chain, V is the parameter that characterizes interaction between nitrogenous bases in pairs, $K' = KR^2$ is the coefficient of torsion rigidity of the sugar-phosphate chain, K is the stretch rigidity and a is the distance between the nearest base pairs.

Usually, considering the case of homogeneous (synthetic) DNA, many researchers are limited to only one set of parameters. In fact, there should be four such sets. One is for the sequence *poly* (A), the second for *poly* (T), the third for *poly* (G) and finally the fourth for *poly* (C). The values of all four parameter sets for different types of homogeneous DNA sequences were first gathered and estimated from experimental data by Yakushevich et al. (2005) and then refined by Yakushevich and Krasnobaeva (2016). The refined values are presented in Table 1.

In addition to the velocity, the total kink energy and rest energy:

$$E = \frac{E_0}{\sqrt{1 - \frac{\upsilon_k^2}{C^2}}}, \tag{9}$$

$$E_0 = 8\sqrt{K'V}, \tag{10}$$

are also important dynamic characteristics of the DNA kinks (Yakushevich and Ryasik 2012). Within the sine-Gordon model, both the total energy $\boldsymbol{E}$ and the velocity of the kink $\boldsymbol{\upsilon_k}$ are constants. There is one limitation on the velocity of the kink that is necessary to ensure the stability of the solution (7): $\boldsymbol{\upsilon_k < C}$.

In the case $\boldsymbol{\upsilon_k << C}$, formula (9) takes the form:

$$E = E_0 + \frac{8\sqrt{K'V}}{C^2}\frac{\upsilon_k^2}{2}, \tag{11}$$

whence follows the formula for the rest mass of a kink $\boldsymbol{m_0}$:

$$m_0 = \frac{8\sqrt{K'V}}{C^2}. \tag{12}$$

Formulas (11)–(12) indicate that, in the first approximation, the DNA kink can be considered as a quasiparticle with definite mass, velocity and rest energy.

Using formulas (10) and (12) and the parameter values from Table 1, the values of the kink rest energy, mass and size were obtained for four homogeneous DNA sequences: *poly* (A), *poly* (T), *poly* (G) and *poly* (C) (see Table 2).

McLaughlin-Scott equation for DNA kink velocity. Solution in the absence of external field

The McLaughlin-Scott equation in transformed parameters was obtained from the modified sine-Gordon equation having the following form (Yakushevich and Krasnobaeva 2007; Yakushevich et al. 2012; Zakiryanov and Yakushevich 2013):

$$I\varphi_{tt} - K' a^2 \varphi_{zz} + V sin\varphi = -\beta\varphi_t + M(t). \tag{13}$$

Table 1 Dynamic parameters of homogeneous DNA (Yakushevich and Krasnobaeva 2016)

Sequence	I (10^{-44} kg·m^2)	K'(10^{-18} N·m)	V (10^{-20} J)	a (10^{-10} m)
poly (A)	7.61	2.35	2.09	3.4
poly (T)	4.86	1.61	1.43	3.4
poly (G)	8.22	2.27	3.12	3.4
poly (C)	4.11	1.54	2.12	3.4

Table 2 Rest energy, mass and size of the DNA kinks activated in homogeneous DNA (Krasnobaeva and Yakushevich 2020)

Sequence	E_0 (10^{-20}·J)	m_0 (10^{-27}·kg)	d (10^{-10}·m)
poly (A)	177.13	495.88	36.09
poly (T)	121.32	316.97	36.09
poly (G)	212.88	666.56	29.00
poly (C)	144.74	333.14	29.00

There are two additional terms on the right side of this equation. The first term describes the effects of dissipation that is the energy loss due to resistance of the surrounding. The second term describes the action of an external field. It can be a constant torsion moment (for example, DNA torque) or periodic field (for example, terahertz field) (Swanson 2011; Bergues-Pupo et al. 2013).

Equation (13) is related to the dimensionless canonical equation (2) by linear transformation (8), $\boldsymbol{\beta = \alpha(IV)^{1/2}}$, $\boldsymbol{M(t) = VF((V/I)^{1/2}t)}$.

When obtaining the McLaughlin-Scott equation, it was assumed that the solution to Eq. (13) had the form of kink:

$$\varphi_k(z,t) = 4\boldsymbol{arctg}\{exp[(\gamma_k(t)/d_k)(z - \upsilon_k(t)\cdot t - z_{\boldsymbol{0}})]\}, \quad (14)$$

that was moving with the velocity $\upsilon_k(t)$ along the DNA molecule.

It was shown that the time dependence of the velocity was determined by the equation:

$$\frac{d\upsilon'(t)}{dt} = -\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right) + \frac{M(t)\pi}{4\sqrt{IV}}\left(1-\upsilon'^2(t)\right)^{3/2}. \quad (15)$$

Here, $\upsilon'(t) = \frac{\upsilon_k(t)}{C}$ is the relative kink velocity, $\boldsymbol{\gamma(t) = (1 - \upsilon'^2(t))^{-1/2}}$.

In the absence of an external force, Eq. (15) takes on a simpler form:

$$\frac{d\upsilon'(t)}{dt} = -\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right). \quad (16)$$

The solution of Eq. (16) was obtained by Yakushevich and Krasnobaeva (2007) by the method of direct integration:

$$\upsilon'(t) = \frac{C' exp\left(-\frac{\beta}{I}(t-t_0)\right)}{\sqrt{1 + C'^2 exp\left(-2\frac{\beta}{I}(t-t_0)\right)}}, \quad (17)$$

where C' is an arbitrary constant. The value of this constant was found then from the initial condition:

$$\upsilon'(t=0) = \frac{\upsilon_0}{C}, \quad (18)$$

where $\boldsymbol{\upsilon_0}$ is the kink initial velocity. Taking into account Eq. (18), the final formula for the kink velocity $\boldsymbol{\upsilon_k(t)}$ was obtained:

$$\upsilon_k(t) = \frac{\upsilon_0\gamma_0 exp\left(-\frac{\beta}{I}(t-t_0)\right)}{\sqrt{1 + \left(\frac{\upsilon_0}{C}\gamma_0\right)^2 exp\left(-2\frac{\beta}{I}(t-t_0)\right)}}, \quad (19)$$

where $\gamma_0 = \left(1-\frac{\upsilon_0^2}{C^2}\right)^{-1/2}$.

In 2014, the McLaughlin-Scott approach received a new impetus for further development due to the fact that an analytical solution for the kink coordinate was found (Yakushevich et al. 2014):

$$z_k(t) = z_{01} - C\frac{I}{\beta}arcsinh\left(\frac{\upsilon_0}{C}\gamma_0 exp\left(-\frac{\beta}{I}(t-t_0)\right)\right) + C\frac{I}{\beta}arcsinh\left(\frac{\upsilon_0}{C}\gamma_0\right), \quad (20)$$

where $\boldsymbol{z_{01}}$ is the kink coordinate at the initial moment of time $\boldsymbol{t_0}$. The kink coordinate $\boldsymbol{z_k(t)}$ is determined by formula: $\upsilon_k(t) = \frac{dz_k(t)}{dt}$.

Formulas (19) and (20) made it possible to obtain the time dependence of the kink velocity and coordinate (Fig. 2a, b), as well as to draw the kink trajectories on the phase plane $\{\boldsymbol{\upsilon_k}, \boldsymbol{z_k}\}$ (Fig. 2c) and in 3D space $\{\boldsymbol{\upsilon_k}, \boldsymbol{z_k}, \boldsymbol{t}\}$ (Fig. 2d) (Yakushevich and Krasnobaeva 2019). The graphs were constructed for the sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C). When constructing them, the numerical values of the dissipation coefficients ($\beta_{poly(A)} = 4.25 \times 10^{-34}$ (J s), $\beta_{poly(T)} = 2.91 \times 10^{-34}$ (J s), $\beta_{poly(G)} = 4.10 \times 10^{-34}$ (J s), $\beta_{poly(C)} = 2.79 \times 10^{-34}$ (J s)) obtained by Yakushevich et al. (2011) were taken into account. The model value of the kink initial velocity υ_0 was chosen to be equal to 189 m/s, which was one-tenth of the sound velocity in *poly* (A).

In Fig. 2a, the velocity of the kinks decreases with time that is explained by the influence of dissipation effects, and the decrease occurs more sharply in the case of *poly* (T) and *poly* (C) sequences and more smoothly in the case of *poly* (G) and *poly* (A) sequences.

Later, Krasnobaeva and Yakushevich (2015) obtained an analytical formula determining the length of the path that the kink could travel to a complete stop:

$$s = \frac{IC}{\beta} ln\left[\frac{\upsilon_0\gamma_0}{C} + \sqrt{1 + \frac{\upsilon_0^2\gamma_0^2}{C^2}}\right]. \quad (21)$$

Using this formula and the parameter values from Table 1, it became possible to obtain the kink path lengths for four homogeneous DNA sequences: *poly* (A), *poly* (T), *poly* (G) and *poly* (C) (see Table 3).

From Table 3, it follows that the maximum kink path length is observed in the case of *poly* (G), and the minimum length, in the case of *poly* (C).

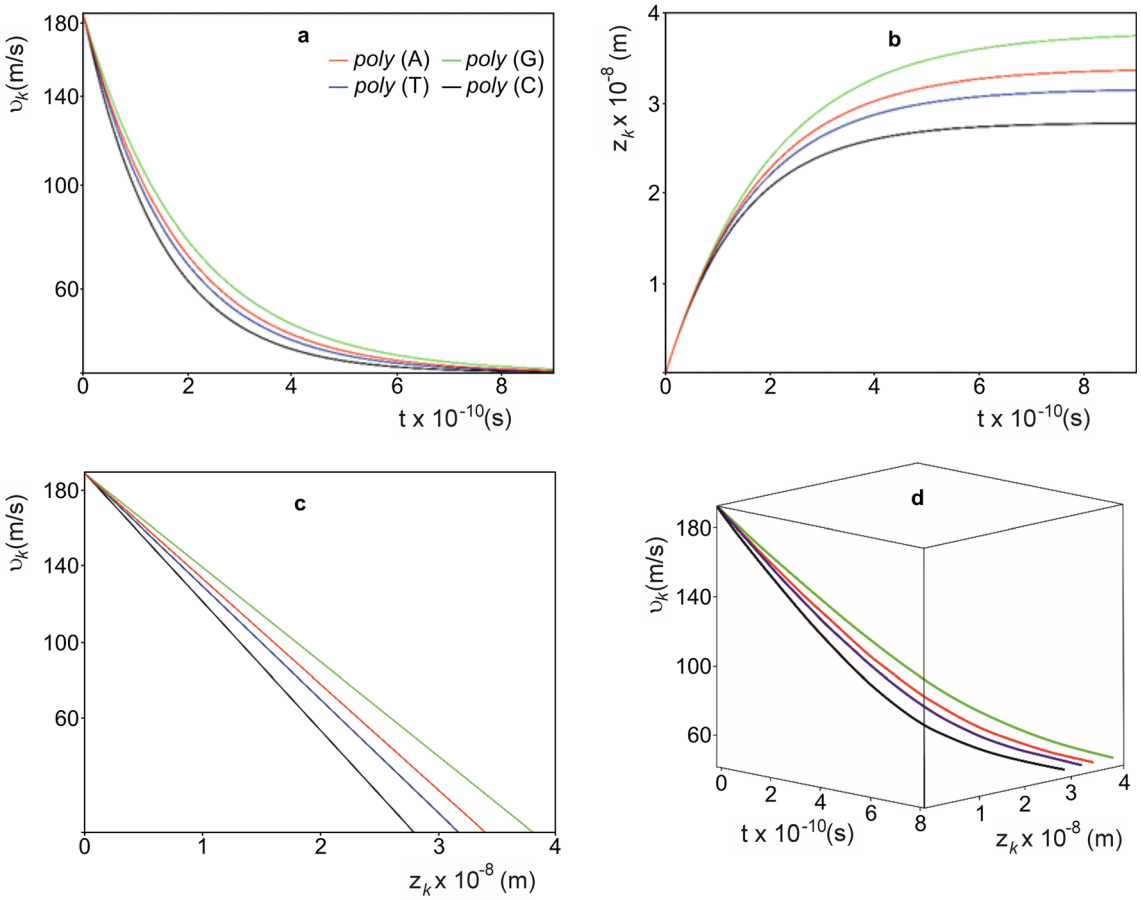

Fig. 2 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{v_k, z_k\}$ (**c**) and in 3D space $\{v_k, z_k, t\}$ (**d**). The graphs are constructed for four homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) and for the case of the absence of any external field. The initial velocity of the kinks is $v_0 = 189$ (m/s)

Solution in the presence of constant external field

It is believed that DNA torsion moment (DNA torque) can act as a mechanical regulator for many biological processes, including transcription and replication (Forth et al. 2013). However, the mechanisms of the influence of the torsion moment on the functional properties of the DNA molecule are still not clear enough, despite extensive discussion of this issue in the scientific literature (Derks and Gaeta 2011; Forth et al. 2013; Ma et al. 2013). This issue could be clarified with the help of new technologies for conducting experiments with single DNA, for example, using the methods of an optical torque wrench or an angle-dependent optical trap (AOT) (Porta and Wang 2004; Manoranjan et al. 2018), as well as the method of magnetic tweezers (Harada et al. 2001; Klaue and Seidel 2009; Lipfert et al. 2010), which allow direct investigation of the influence of such applied torque on the dynamic properties of the DNA molecule.

The solution of the McLaughlin-Scott equation in the case of constant torque $\boldsymbol{M_0}$ was obtained analytically by Yakushevich and Krasnobaeva (2007) and numerically in the work of Yakushevich et al. (2013, 2016). In this case, the McLaughlin-Scott equation has the form:

$$\frac{dv'(t)}{dt} = -\frac{\beta}{I}v'(t)\left(1-v'^2(t)\right) + \frac{M_0\pi}{4\sqrt{IV}}\left(1-v'^2(t)\right)^{3/2}, \quad (22)$$

and the analytical solution for the kink velocity is determined by:

$$v_k(t) = \frac{\left[\left(v_0\gamma_0 - \frac{CM_0\pi}{4\beta}\sqrt{\frac{I}{V}}\right)exp\left(-\frac{\beta}{I}t\right) + \frac{CM_0\pi}{4\beta}\sqrt{\frac{I}{V}}\right]}{\sqrt{1+\left[\left(\frac{v_0}{C}\gamma_0 - \frac{M_0\pi}{4\beta}\sqrt{\frac{I}{V}}\right)exp\left(-\frac{\beta}{I}t\right) + \frac{M_0\pi}{4\beta}\sqrt{\frac{I}{V}}\right]^2}}. \quad (23)$$

Table 3 Kink path lengths in homogeneous sequences

Sequence	s (10^{-7} m)
poly (A)	0.339
poly (T)	0.317
poly (G)	0.380
poly (C)	0.279

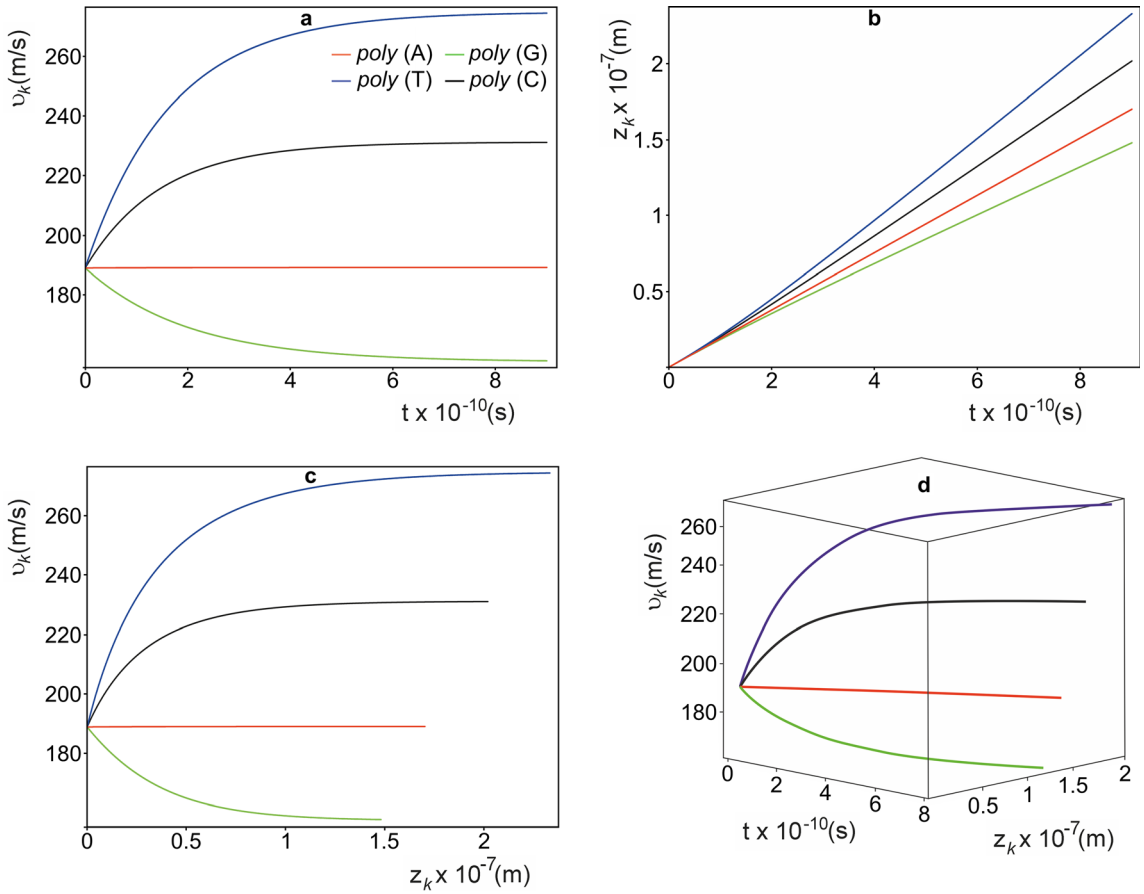

Fig. 3 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{\upsilon_k, z_k\}$ (**c**) and in 3D space $\{\upsilon_k, z_k, t\}$ (**d**). The graphs are constructed for four homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) and in the presence of a constant external field. The initial velocity of the kinks is $\upsilon_0 = 189$ (m/s)

In Fig. 3, the graphs of the time dependence of the kink velocity and coordinate, as well as 2D and 3D kink trajectories, are shown. These graphs were calculated for the sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) using the data of Table 1, as well as model values $M_0 = 2.85 \times 10^{-23}$ (J) and $\upsilon_0 = 189$ (m/s). The reasons for this choice of model values are as follows. As mentioned above, there is one important requirement for kink velocity: $\upsilon_k < C$ .Taking into account that the velocity of sound in DNA is equal to 1890 m/s, the initial value of the kink veocity was chosen equal to 189 m/s, which is 10 times less than C. The chosen model value M_0 coincides in order of magnitude with the data of Lui and Wang (1987) and Nelson (1999).

In the work of Yakushevich and Krasnobaeva (2007), it was shown that for each type of homogeneous DNA, it is possible to find a value of the constant external field M_0^{crit}, for which the velocity of the kink movement remained constant and equal to the initial value. To prove this, it was enough to assume that the derivative in Eq. (22) was equal to zero. Then, the McLaughlin-Scott equation transformed to:

$$\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right) = \frac{M_0\pi}{4\sqrt{IV}}\left(1-\upsilon'^2(t)\right)^{3/2}, \tag{24}$$

whence the formula for M_0^{crit} was found

$$M_0^{crit} = \frac{4\beta}{\pi}\frac{\upsilon_0\gamma_0}{C}\sqrt{\frac{V}{I}}, \tag{25}$$

where

$$\gamma_0 = \left(1-(\upsilon_0/C)^2\right)^{-1/2}. \tag{26}$$

Numerical estimates of M_0^{crit} that we calculated for four types of homogeneous polynucleotide chains are presented in the second column of Table 4.

Another important feature in the DNA kink behavior was noted in the computer experiments: after a short initial period, the kink velocity always reached a constant (stationary) value

Table 4 Critical values of M_0^{crit} in the case $\upsilon_0 = 189$ (m/s) and stationary kink velocity calculated in the case of constant external field $M_0 = 2.85 \times 10^{-23}$ (J)

Sequence	M_0^{crit} (10^{-23} J)	υ_{st} (m/s)
poly (A)	2.85	189.05
poly (T)	1.95	274.68
poly (G)	3.43	157.49
poly (C)	2.33	231.10

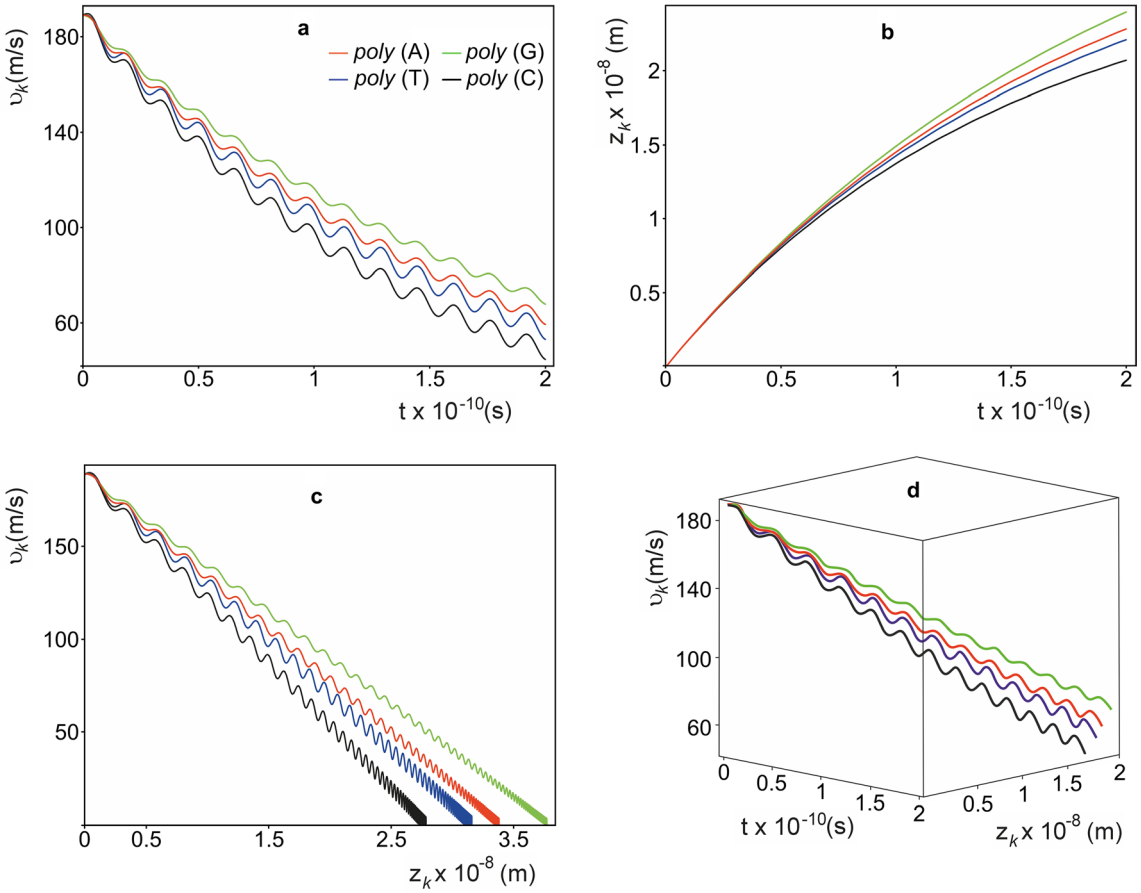

Fig. 4 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{v_k, z_k\}$ (**c**) and in 3D space $\{v_k, z_k, t\}$ (**d**). The graphs are constructed for four homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) and in the presence of a periodic external field with constant frequency. The initial velocity of the kinks is $\upsilon_0 = 189$ (m/s)

(Yakushevich and Krasnobaeva 2007; Yakushevich et al. 2016). It was shown that the stationary velocity did not depend on the value of the initial velocity. This was confirmed via development of an analytical formula which permitted the calculations of values of the stationary kink velocity for different types of homogeneous polynucleotide chains:

$$\upsilon_{st} = C\left[1 + \frac{16V\beta^2}{\pi^2 I M_0^2}\right]^{-1/2}. \tag{27}$$

The calculation results for four types of homogeneous polynucleotide chains are presented in the third column of Table 4.

Solution in the presence of periodic external field with constant frequency

The action of periodic fields on living systems is a frequently encountered problem in modern biophysics. This is due to the growing number and variety of electronic devices and their influence on the basic fundamental life processes and, therefore, on human health. It has been suggested that external periodic fields with a frequency of the terahertz range can cause a change in the physicochemical property of DNA (Alexandrov et al. 2010a, b).

The McLaughlin-Scott equation gives a possibility to demonstrate one of the mechanisms of the influence of this field on the dynamics of open states in DNA. In the case of a periodic external field with a constant frequency Ω, the McLaughlin-Scott equation has the form (Yakushevich et al. 2012):

$$\frac{d\upsilon'(t)}{dt} = -\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right) + \frac{M_0 cos(\Omega t)\pi}{4\sqrt{IV}}\left(1-\upsilon'^2(t)\right)^{3/2}. \tag{28}$$

An analytical solution of Eq. (28) was found by Krasnobaeva and Shapovalov (2009):

$$\upsilon_k(t) = \frac{\left(\upsilon_0\gamma_0 - \frac{C_0 bh}{h^2+\Omega^2}\right)exp(-ht) + \frac{C_0 b}{h^2+\Omega^2}(hcos\Omega t + \Omega sin\Omega t)}{\sqrt{1+\left\{\left(\frac{\upsilon_0}{C_0}\gamma_0 - \frac{bh}{h^2+\Omega^2}\right)exp(-ht) + \frac{b}{h^2+\Omega^2}(hcos\Omega t + \Omega sin\Omega t)\right\}^2}}, \tag{29}$$

where $b = \frac{M_0\pi}{4\sqrt{IV}}$, $h = \frac{\beta}{I}$.

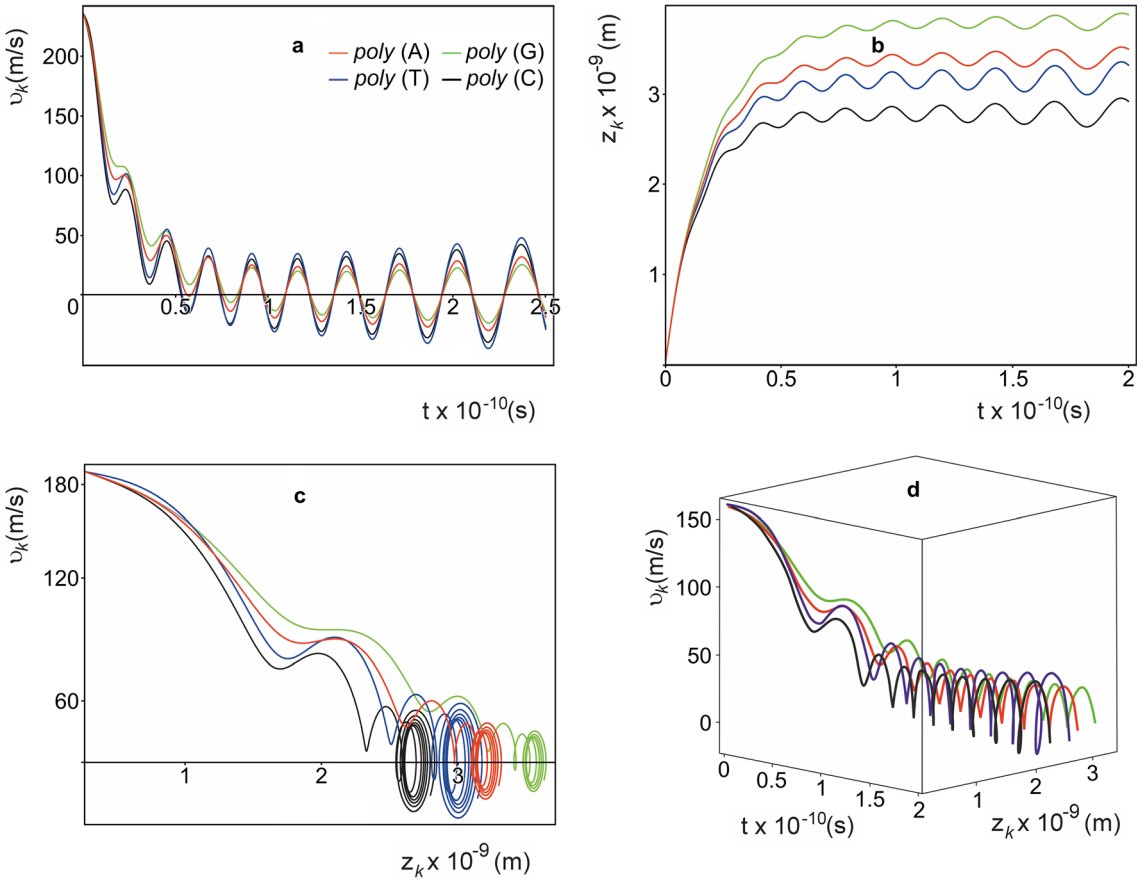

Fig. 5 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{\upsilon_k, z_k\}$ (**c**) and in 3D space $\{\upsilon_k, z_k, t\}$ (**d**). The graphs are constructed for four homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) and in the presence of a slowly varying periodic external field: $M_0 \cos(\Omega t - \alpha t^2/2)$. The initial kink velocity is $\upsilon_0 = 189$ (m/s)

In Fig. 4, the graphs of the time dependence of the kink velocity and coordinate, as well as 2D and 3D kink trajectories, are shown. These graphs were calculated for the homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) using the data in Table 1, as well as model values $M_0 = 2.85 \times 10^{-23}$ (J), $\upsilon_0 =$ **189** (m/s) and $\Omega = 0.4 \times 10^{12}$ (s^{-1}). Due to the lack of experimental data, the obtained results on the influence of this periodic field on the dynamics of open states are so far only predictive.

Solution in the presence of periodic external field with a slowly varying frequency

The case of periodic external field with a slowly varying frequency was considered by Yakushevich et al. (2012, 2013). The McLaughlin-Scott equation takes in this case the following form:

$$\frac{d\upsilon'(t)}{dt} = -\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right) + \frac{\pi}{4\sqrt{IV}}M_0 cos(\Omega t - \alpha t^2/2)\left(1-\upsilon'^2(t)\right)^{3/2}. \quad (30)$$

Here, M_0 and Ω are the amplitude and frequency of the external field, and α is the coefficient characterizing the velocity of decrease (or increase) of the frequency.

An analytical solution of Eq. (30) has not yet been found. Numerical solutions for the velocity, coordinates and phase trajectory of the kink were obtained in the works of Krasnobaeva and Yakushevich (2015) and Yakushevich et al. (2013). Figure 5 shows the results obtained using the revised values of the DNA dynamic parameters from Table 1, the initial kink velocity (m/s), as well as model values characterizing the external field: $M_0 = 2.85 \times 10^{-19}$ (J), $\Omega = 0.4 \times 10^{12}$ (s^{-1}) and $\alpha = 1 \times 10^{21}$ (s^{-2}) (Yakushevich et al. 2013).

Solution in the presence of on/off external field

In the case of an on/off external field, the McLaughlin-Scott equation has the form (Yakushevich et al. 2018a, b):

$$\frac{d\upsilon'(t)}{dt} = -\frac{\beta}{I}\upsilon'(t)\left(1-\upsilon'^2(t)\right) + \frac{\pi}{4\sqrt{IV}}M_0\left(1-\upsilon'^2(t)\right)^{3/2}$$
$$\left(\frac{1}{1+\exp\left((t_1-t)/\bar{\sigma}\right)} - \frac{1}{1+\exp\left((t_2-t)/\bar{\sigma}\right)}\right) + + \frac{\pi}{4\sqrt{IV}}M_1\cos(\Omega t) \quad (31)$$
$$\left(\frac{1}{1+\exp\left((t_3-t)/\bar{\sigma}\right)} - \frac{1}{1+\exp\left((t_4-t)/\bar{\sigma}\right)}\right)\left(1-\upsilon'^2(t)\right)^{3/2}$$

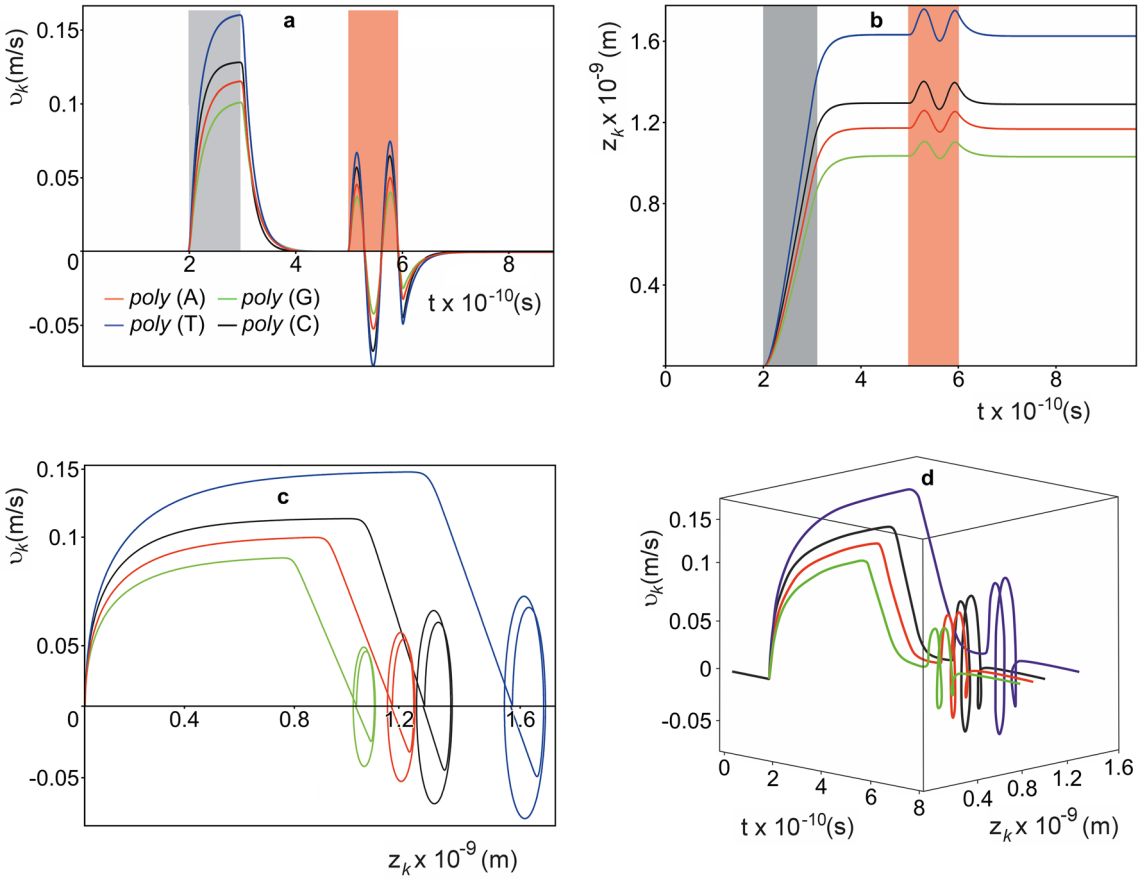

Fig. 6 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{v_k, z_k\}$ (**c**) and in 3D space $\{v_k, z_k, t\}$ (**d**). The graphs are constructed for four homogeneous sequences *poly* (A), *poly* (T), *poly* (G) and *poly* (C) and in the presence of an on/off external field. The initial kink velocity is $v_0 = 189$ (m/s)

Here, M_0 denotes a constant external field, $M_1\cos(\Omega t)$ models a periodic external field, $\sigma = \widetilde{\sigma}\sqrt{V/I}$, and $\widetilde{\sigma}$ is the parameter characterizing the slope of the sigmoid function.

Numerical solutions of Eq. (31) for the velocity and coordinates of the kink, as well as two-dimensional and three-dimensional trajectories of the kink, are shown in Fig. 6. The results presented correspond to the case when initially the constant external field is switched on/off, and after a pause, the periodic external field is switched on/off. The time intervals during which the external fields are turned on are indicated by stripes. The results presented in Fig. 6 were obtained using the values of the dynamic parameters of DNA from Table 1 and model values $v_0 = 0$, $M_0 = 2.85 \times 10^{-23}$ (J), $M_1 = 2.85 \times 10^{-23}$ (J) and $\widetilde{\sigma} = \mathbf{5}$.

McLaughlin-Scott equation for inhomogeneous DNA

Natural DNA is inhomogeneous (Watson and Crick 1953; Crick and Watson 1954). It contains four types of nitrogenous bases: adenine (A), thymine (T), guanine (G) and cytosine (C), arranged in a certain order, unique for each living organism. Therefore, when modeling the internal dynamics of inhomogeneous DNA, it is necessary to take into account that the values of the dynamic parameters are not constant but depend on the location of nitrogenous bases in the sequence.

This approach was used for simulation of bubble dynamics in artificial inhomogeneous (random, periodic, aperiodic) sequences (Dominguez-Adame et al. 1995; Yakushevich et al. 2002) and natural DNA sequences such as the sequence of the A_1 promoter of bacteriophage T7 (Salerno 1991), sequences of the A_3 and D promoter of bacteriophage T7 (Salerno 1992), the promoter sequence of the pBR322 plasmid (Salerno 1995), the complete genome of the bacteriophage T7 (Lennholm and Hornquist 2003), some regions of the human genome (coding region 114 000–115 000 and non-coding region 50000–51000) (Cuenda and Sanchez 2004a, b). In these works, different modifications of the sine-Gordon equation were used.

Sine-Gordon equations for inhomogeneous DNA

One of the first modifications of the sine-Gordon equation, taking into account DNA inhomogeneity, was proposed by

Table 5 Coefficients of the McLaughlin-Scott equation for the IFNA17 gene and the kink dynamic characteristics (Krasnobaeva and Yakushevich 2015)

Sequence	Coefficients of the McLaughlin-Scott equation				Dynamic characteristics of kinks		
IFNA17	$\overline{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K}'$ (10^{-18} N·m)	V (10^{-20} J)	α (10^{-34} J s)	E_0 (10^{-20} J)	$\overline{m}_0$ (10^{-27} kg)	$\overline{d}$ (10^{-10} m)
	6.11	1.93	2.08	3.49	1.60	438.78	32.75

Salerno (1991). For this purpose, a discrete version of Eq. (5) was used:

$$I_n \frac{d^2\varphi_n}{dt^2} - K_n'(\varphi_{n+1} - 2\varphi_n + \varphi_{n-1}) + V_n sin\varphi_n = 0, \quad (32)$$

where the first two coefficients (I_n and K_n') were assumed to be constants, and the third coefficient (V_n), characterizing the interaction between complementary bases within pairs, was replaced by:

$$V_n = \frac{\lambda_n \eta}{2}, \quad (33)$$

where $\lambda_n = 2$ in the case of an AT base pair, and $\lambda_n = 3$ in the case of a GC base pair.

Salerno solved the problems (32)–(33) numerically and used the solutions (kinks) to simulate the movement of the DNA open states in a small (168 base pairs) fragment of the T7 bacteriophage sequence:

```
ttgtctttattaatacaactcactataagg
agagacaacttaaagagacttaaaagatta
atttaaaatttatcaaaaagagtattgact
taaagtctaacctataggatacttacagcc
atcgagagggacacggcgaatagccatccc
aatcgacaccggggtcaa
```

The bacteriophage T7 genome is one of the most studied genomes. It is also one of the first genomes to be fully sequenced (Dunn et al. 1983, Genome of bacteriophage T7, n.d.). An important area of application of bacteriophages is antibacterial therapy, as well as genetic engineering. Salerno and Kivshar Yu (1994) suggested that the kinklike solutions of Eq. (32) can be thought of as quasiparticles moving in the effective potential of the T7 bacteriophage.

It seemed quite natural that further development of this direction would follow the path of a simple generalization of the Salerno model, and that for this it would be sufficient to take into account the dependence of all three coefficients from the sequence of bases. However, Grinevich et al. (2013) showed that a model generalized in this way led to contradictory results. The reason for these contradictions was explained later (Grinevich et al. 2015a, b). It was shown that the more accurate derivation of the sine-Gordon equation for an inhomogeneous DNA led to the following model equation:

$$I_n \frac{d^2\varphi_n}{dt^2} - KR_n\left(R_{n+1}\varphi_{n+1} - 2R_n\varphi_n + R_{n-1}\varphi_{n-1}\right) + V_n sin\varphi_n = 0, \quad (34)$$

which in the continuum limit took the form:

$$I(z)\frac{\partial^2\varphi}{\partial t^2} - KR(z)\frac{\partial^2(R(z)\varphi)}{\partial z^2} + V(z)sin\varphi_n = 0. \quad (35)$$

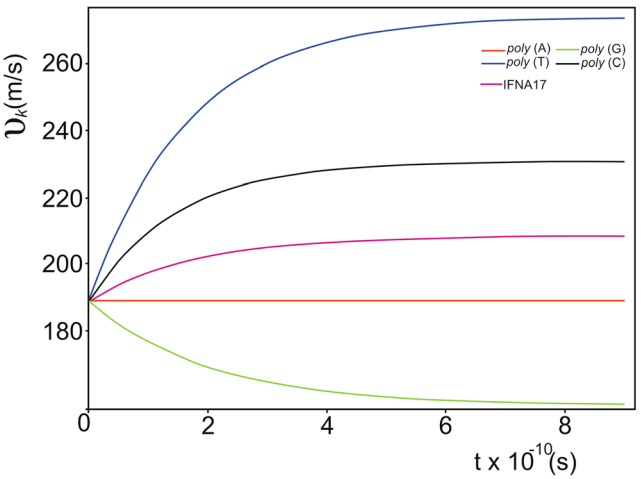

Fig. 7 Time dependence of the velocity of kinks activated in the IFNA17 gene and in homogeneous chains. The graphs were constructed for $M_0 = 2.85 \times 10^{-23}$ (J), $\upsilon_0 = 189$ (m/s)

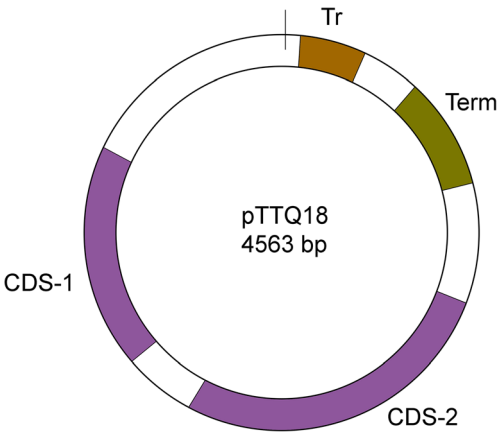

Fig. 8 Schematic representation of the pTTQ18 plasmid containing four functional regions: promoter (Pr), terminator (Term) and two coding regions (CDS-1 and CDS-2)

Table 6 Coefficients of the McLaughlin-Scott equation for the pTTQ18 plasmid and the kink dynamic characteristics (Yakushevich et al. 2018a)

Sequence	Coefficients of the McLaughlin-Scott equation				Dynamic characteristics of kinks		
	$\overline{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K'}$ (10^{-18} N·m)	V (10^{-20} J)	α (10^{-34} J s)	E_0 (10^{-20} J)	m_0 (10^{-27} kg)	$\overline{d}$ (10^{-10} m)
pTTQ18	6.21	1.95	2.21	3.51	1.66	457.87	31.91

Problem (35) has not yet been solved analytically. However, Yakushevich and Krasnobaeva (2008a, b) proposed an approximate method, called the method of concentrations method, which made it possible to reduce the inhomogeneous problem (35) to a quasi-homogeneous one and thus to solve it using the methods applied for solving homogeneous problems.

Method of concentrations

In the method of concentrations, the idea of Dominguez-Adame et al. (1995) was used whereby they proposed replacing the coefficient $V(z)$ in Eq. (35) by a linear function of the concentrations of AT and GC base pairs in the double polynucleotide chain:

$$V \rightarrow V(C_{AT}, C_{GC}) = C_{AT}V_{AT} + C_{GC}V_{GC}, \tag{36}$$

where C_{AT} and C_{GC} are the concentrations of AT and GC base pairs, respectively. V_{AT} and V_{GC} are the values of the coefficient V in the double strand consisting of only AT base pairs and of only GC base pairs, respectively. This idea was developed by Yakushevich and Krasnobaeva (2008a). They suggested that three coefficients (I, K' and V) of the inhomogeneous sine-Gordon equation depended on the concentrations of A-, T-, G- and T-bases (C_A, C_T, C_G and C_C) in the DNA sequence:

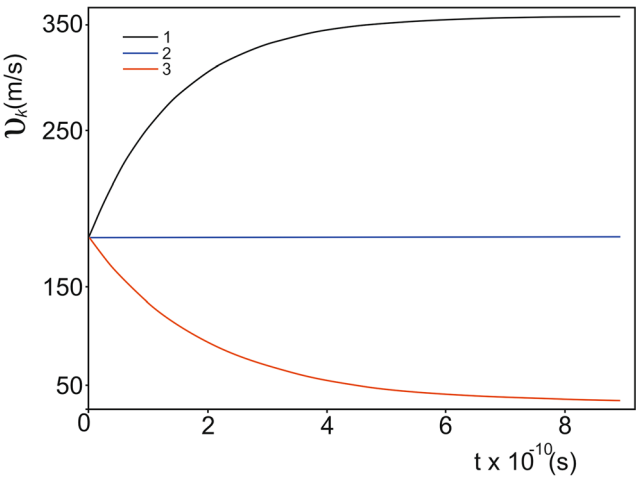

Fig. 9 Time dependence of the velocity of kinks activated in the pTTQ18 plasmid. Curve 1 corresponds to $M_{01} = 5.37 \times 10^{-23}$ (J), curve 2—$M_{02} = 2.67 \times 10^{-23}$ (J), curve 3—$M_{03} = 2.77 \times 10^{-24}$ (J). $\upsilon_0 = 189$ (m/s)

$$\begin{aligned} \overline{I} &= I_A C_A + I_T C_T + I_G C_G + I_C C_C, \\ \overline{K}' &= K'_A C_A + K'_T C_T + K'_G C_G + K'_C C_C, \\ \overline{V} &= V_A C_A + V_T C_T + V_G C_G + V_C C_C. \end{aligned} \tag{37}$$

Here I_A, I_T, I_G and I_C are the moments of inertia of adenine, thymine, guanine and cytosine, respectively; K'_A, K'_T, K'_G and K'_C are the torsion rigidity constants in homogeneous DNA; V_A, V_T, V_G and V_C are the constants that characterize interaction between nitrogenous bases in pairs AT, TA, GC and CG. Concentrations are determined by formulas:

$$C_A = \frac{N_A}{N}, C_T = \frac{N_T}{N}, C_G = \frac{N_G}{N}, C_C = \frac{N_C}{N}, \tag{38}$$

$$C_A + C_T + C_G + C_C = 1, \tag{39}$$

where N_A, N_T, N_G, N_C are the number of adenines, thymines, guanines and cytosines, respectively; N is the total number of the bases in the sequence.

Then, Eq. (35) takes the following form:

$$\overline{I}\varphi_{tt} - \overline{K'}a^2\varphi_{zz} + \overline{V}sin\varphi = 0, \tag{40}$$

and the complex inhomogeneous problem (35) is reduced to the simpler homogeneous problem (39) with renormalized coefficients.

After taking into account the effects of dissipation and external field, Eq. (39) transforms to:

$$\overline{I}\varphi_{tt} - \overline{K'}a^2\varphi_{zz} + \overline{V}sin\varphi = -\overline{\beta}\varphi_t + M(t), \tag{41}$$

where $\beta = \beta_A C_A + \beta_T C_T + \beta_G C_G + \beta_C C_C$. The one-soliton solution of Eq. (41) has the form:

$$\varphi_k(z,t) = 4arctg\{exp[(\gamma_k(t)/d_k)(z - \upsilon_k(t) \cdot t - z_0)]\}. \tag{42}$$

Table 7 Details of the structure of the ADRB2, NOS1 and IL-5 gene sequences

Sequence	N_A	N_T	N_G	N_C	N
ADRB2	466	529	498	520	2013
NOS1	3028	2833	3135	3295	12,291
IL-5	589	584	419	460	2052

Table 8 Coefficients of the McLaughlin-Scott equation for the ADRB2, NOS1 and IL-5 genes and the kink dynamic characteristics (Krasnobaeva et al. 2012)

Sequence	Coefficients of the McLaughlin-Scott equation				Dynamic characteristics of kinks		
	$\overline{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K'}$ (10^{-18} N·m)	V (10^{-20} J)	$\overline{\alpha}$ (10^{-34} J s)	E_0 (10^{-20} J)	m_0 (10^{-27} kg)	$\overline{d}$ (10^{-10} m)
ADRB2	6.13	1.93	2.18	3.49	163.91	451.09	31.99
NOS1	6.19	1.94	2.21	3.51	165.67	456.69	31.90
IL-5	6.17	1.94	2.12	3.51	162.25	445.51	32.56

Here, $\gamma(t) = \left(1-v'^2(t)\right)^{-1/2}$, $C = (K'a^2/I)^{1/2}$, $d = (K'a^2/V)^{1/2}$. Within this approach, the total kink energy is determined as:

$$E(t) = E_0\gamma(t), \tag{43}$$

where $E_0 = 8\sqrt{K'V}$ is the rest energy. The rest mass is determined as:

$$\overline{m}_0 = \frac{8\sqrt{\overline{K'}\,\overline{V}}}{\overline{C}^2}. \tag{44}$$

Solution of the McLaughlin-Scott equation for the IFNA17 gene by the method of concentrations

The McLaughlin-Scott equation derived from the sine-Gordon equation (41) has the form:

$$\frac{dv'(t)}{dt} = -\frac{\overline{\beta}}{\overline{I}}v'(t)\left(1-v'^2(t)\right) + \frac{M(t)\pi}{4\sqrt{\overline{I}\,\overline{V}}}\left(1-v'^2(t)\right)^{3/2}. \tag{45}$$

where $v'(t) = \frac{v_k(t)}{\overline{C}}$ is the relative kink velocity.

One of the first examples of the application of the method of concentrations for solving the McLaughlin-Scott equation in the case of inhomogeneous DNA was presented in the work of Krasnobaeva and Yakushevich (2015). An analytical solution was obtained there for the IFNA17 gene coding interferon alpha 17 (human), which is known in medicine as an antiviral and antitumor drug (Dubois et al. 2009; Bychkov et al. 2011). The IFNA17 gene was identified by Lawn et al. (1983). The sequence of nucleotides in this gene (Homo sapiens interferon alpha 17 (IFNA17) n.d.) is the following:

```
   1 gttcaaggtt acccatctca agtagcctag caacatttgc aacatcccaa tggccctgtc
  61 cttttcttta ctgatggccg tgctggtgct cagctacaaa tccatctgtt ctctaggctg
 121 tgatctgcct cagacccaca gcctgggtaa taggagggcc ttgatactcc tggcacaaat
 181 gggaagaatc tctcctttct cctgcctgaa ggacagacat gactttggac ttccccagga
 241 ggagtttgat ggcaaccagt tccagaagac tcaagccatc tctgtcctcc atgagatgat
 301 ccagcagacc ttcaatctct tcagcacaga ggactcatct gctgcttggg aacagagcct
 361 cctagaaaaa ttttccactg aactttacca gcaactgaat aacctggaag catgtgtgat
 421 acaggaggtt gggatggaag agactcccct gatgaatgag gactccatcc tggctgtgag
 481 gaaatacttc caaagaatca ctctttatct aacagagaag aaatacagcc cttgtgcctg
 541 ggaggttgtc agagcagaaa tcatgagatc tctctctttt tcaacaaact tgcaaaaaat
 601 attaaggagg aaggattgaa aactggttca acatggcaat gatcctgatt gactaataca
 661 ttatctcaca ctttcatgag ttcctccatt tcaaagactc acttctataa ccaccacgag
 721 ttgaatcaaa attttcaaat gttttcagca gtgtaaagaa gcgtcgtgta tacctgtgca
 781 ggcactagta ctttacagat gaccatgctg atgtctctgt tcatctattt atttaaatat
 841 ttatttaatt atttttaaga tttaaattat ttttttatgt aatatcatgt gtacctttac
 901 attgtggtga atgtaacaat atatgttctt catatttagc caatatatta atttcctttt
 961 tcattaaatt tttactatac
```

The sequence contains 282 adenines, 303 thymines, 181 guanines and 214 cytosines. The total number of bases in the IFNA17 gene sequence is equal to 980. With the help of formula (37), the coefficients of the McLaughlin-Scott equation were obtained. Using formulas (43) and (44), the values of the main dynamic characteristics of the kink propagating in the IFNA17 gene were obtained. The results of these calculations are presented in Table 5.

Then, with the help of formula (23), the model values $M_0 = 2.85 \times 10^{-23}$ (J) and $v_0 = 189$ (m/s), the dependence of the kink velocity on time was constructed (Fig. 7)

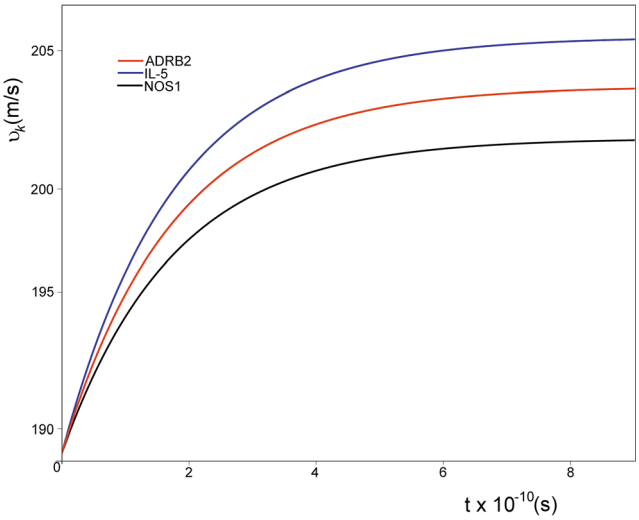

Fig. 10 Time dependence of the velocity of kinks activated in the genes ADRB2, NOS1 and IL-5

Figure 7 shows that the velocity of the kink activated in the IFNA17 gene (solid line) first increases and then reaches a stationary value $\upsilon_{st} = 208.65$ m/s. The increase of the velocity at the initial stage is explained by the fact that the model value of the constant external field $M_0 = 2.85 \times 10^{-23}$ (J) exceeds the critical value $M_0^{\text{crit}} = 2.58 \times 10^{-23}$ (J). Curves calculated for homogeneous sequences *poly* (T) and *poly* (C) behave in a similar way. However, in the case of *poly* (A), the velocity curve remains straight, and in the case of *poly* (G), it decreases.

Solution of the McLaughlin-Scott equation for the pTTQ18 plasmid by the method of concentrations

The method of concentrations was applied by Yakushevich et al. (2018a) to solve the McLaughlin-Scott equation for the case of a small circular DNA molecule, the pTTQ18 plasmid (Stark 1987) (Fig. 8). This plasmid was originally intended for the expression of cloned genes in *Escherichia coli* under the control of the tac promoter (Amann et al. 1983). It is widely used now in genetic engineering for genetic information transfer and for genetic manipulations (Bishop et al. 2003). The sequence length of the plasmid is 4563 bases (Plasmid pTTQ18, complete sequence, n.d.). Of these, 1105 are adenines, 1090 are thymines, 1193 are guanines and 1175 are cytosines (see Appendix 2).

Table 9 Stationary kink velocities in the genes ADRB2, NOS1 and IL-5 (Krasnobaeva et al. 2012)

Sequence	υ_{st} (m/s)
ADRB2	204.16
NOS1	206.23
IL-5	202.01

Table 10 Details of the structure of A_1, A_2 and A_3 promoters

Sequence	N_A	N_T	N_G	N_C	N
A_1	25	19	7	9	60
A_2	27	11	12	10	60
A_3	26	9	13	12	60

The coefficients of the McLaughlin-Scott equation, calculated with the help of Eq. (37), as well as the dynamic characteristics of the kink (rest energy, mass and size), obtained using formulas (43)–(44), are presented in Table 6. The curves of the kink velocity versus time, calculated for three different values of the external field, are shown in Fig. 9.

Figure 9 shows the time dependence of the kink velocity for three different values of constant external field. In the case $M_{01} = 5.37 \times 10^{-23}$ (m /s) > M_0^{crit}, the kink velocity increases and reaches a stationary value $\upsilon_{st} = 369.08$ (m/s) (curve 1). At $M_{02} = M_0^{\text{crit}} = 2.70 \times 10^{-23}$ (J), the kink velocity practically does not change and remains equal to $\upsilon_{st} = 187.37$ (m/s) (curve 2). At $M_{03} = 2.67 \times 10^{-24}$ (m/s) < M_0^{crit}, the kink velocity decreases and goes to the stationary value $\upsilon_{st} = 18.83$ (m/s) (curve 3).

Solution of the McLaughlin-Scott equation for the ADRB2, NOS1 and IL-5 genes by the method of concentrations

Krasnobaeva et al. (2012) used the method of concentrations to solve the McLaughlin-Scott equation for three genes: the ADRB2, NOS1 and IL-5 genes of the human genome with an established effect on the course of bronchial asthma (Lammers et al. 1992). The ADRB2 gene encodes a beta-2-adrenergic receptor that is an ionic protein channel built into the cytoplasmic membrane of a cell, which has a high affinity for adrenaline and provides an increase or decrease in the activity of an innervated tissue or organ (Israel et al. 2000; Bengtsson et al. 2001; Dallongeville et al. 2003; Contopoulos-Ioannidis et al. 2005). The NOS1 gene encodes nitric oxide synthase, which in turn catalyzes the production of nitric oxide (NO). The latter plays an important role in the body of mammals, participating in neurotransmission, regulation of blood circulation and the development of lung pathology (Grasemann et al. 1999; Alderton et al. 2001; Shinkai et al. 2002; Reif et al. 2006). The IL-5 gene encoding interleukin-5 (IL-5) belongs to an extensive family of cytokines that are information molecules secreted by cells of the immune system (Stark et al. 2007). In turn, cytokines mediate intercellular and intersystem interactions, regulating cell survival, stimulation or suppression of their growth, differentiation, functional activity and apoptosis, ensuring the coordination of the action of the immune, endocrine and nervous systems (Mordvinov and Furman 2009).

The sequences of these genes (Homo sapiens adrenoceptor beta 2 (ADRB2) n.d.; Homo sapiens nitric oxide synthase 1 (NOS1) n.d.; Homo sapiens interleukin 5 (IL5) n.d.) are presented in Appendixes 3–5. After calculating the number of A-, T-, G- and C-bases in these sequences (see Table 7) and applying formula (37), the values of the coefficients of the McLaughlin-Scott equation were obtained (see Table 9).

With the help of formulas (37), (43) and (44), the coefficients of the McLaughlin-Scott equation and the main dynamic characteristics of the kinks propagating in the ADRB2, NOS1 and IL-5 genes were obtained (see Table 8).

Table 8 shows that the kink activated in the IL-5 gene has the lowest rest energy, and the kink activated in the NOS1 gene has the highest rest energy. The difference is 3.42 J. Thus, it can be argued that from an energetic point of view, it is easiest to excite a kink in the IL-5 gene, and most difficult in the NOS1 gene. Note also that the mass of the kink activated in the NOS1 gene is the largest, and the size is the smallest.

With the help of formula (23), parameters presented in Table 8, the model values of the external field $M_0 = 2.85 \times 10^{-23}$ (J) and the initial velocity $\upsilon_0 = 189$ (m/s), the time dependence of the kink velocity was constructed (Fig. 10).

Figure 10 shows that the velocity of the kink for each sequence reaches a stationary value. Numerical estimates of the values of stationary velocities are presented in Table 9.

Solution of the McLaughlin-Scott equation for three promoters of bacteriophage T7 by the method of concentrations

Yakushevich and Krasnobaeva (2008b) solved the McLaughlin-Scott equation for three promoters: A_1, A_2 and A_3:

A_1: tttaaaatttatcaaaaagagtattgacttaaagtctaacctataggatacttacagcca
A_2: taagtcgcacgaaaaacaggtattgacaacatgaagtaacatgcagtaagatacaaatcg
A_3: gcacataaggtgaaacaaaacggttgacaacatgaagtaaacacggtacgatgtaccaca

which produce early mRNAs and are located near the left end of the T7 bacteriophage sequence (Genome of bacteriophage T7, n.d.) (Table 10).

With the help of formulas (37), (43) and (44), the values of the coefficients of the McLaughlin-Scott equation and the main dynamic characteristics of the kinks propagating in the A_1, A_2 and A_3 promoters were obtained (see Table 11).

Table 11 shows that the rest energy of the kink activated in the promoter A_1 is less than the rest energy of the kink activated in the promoters A_2 and A_3. Thus, it is more energetically advantageous to activate kink in the A_1 promoter than in the A_2 and A_3 promoters. This conclusion is consistent with the fact that the A_1 promoter is a "strong" promoter, while the A_2 and A_3 promoters are weak.

Yakushevich and Krasnobaeva (2008a) were limited themselves to consideration of A_1, A_2 and A_3 promoters. However, the methods described above make it possible to consider a wider class of sequences having the same values of the coefficients of the McLaughlin-Scott equation as in the case of promoters A_1, A_2 and A_3.

Let us call such sequences the promoter-like sequences and denote them as $\overline{A}_1$, $\overline{A}_2$ and $\overline{A}_3$. Figure 11 shows the time dependence of the velocity and coordinates of the kinks moving under the action of a constant external field M_0, as well as the kink trajectories on the phase plane $\{\upsilon, z\}$, calculated using the dynamic parameters from Table 11 and the model $M_0 = 2.85 \times 10^{-23}$ (J) and $\upsilon_0 = 189$ (m/s).

Figure 11a shows that the kink velocity calculated for each promoter-like sequence reaches a stationary value. Numerical estimates of the stationary velocities are presented in Table 12.

Table 11 Coefficients of the McLaughlin-Scott equation and the kink dynamic characteristics, calculated for A_1, A_2 and A_3 promoters (Yakushevich and Krasnobaeva 2008b)

Sequence	Coefficients of the McLaughlin-Scott equation				Dynamic characteristics of kinks		
	$\overline{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K'}$ (10^{-18} N·m)	V (10^{-20} J)	α (10^{-34} J s)	E_0 (10^{-20} J)	m_0 (10^{-27} kg)	$\overline{d}$ (10^{-10} m)
A_1	6.28	1.99	2.00	3.59	159.56	436.82	33.85
A_2	6.64	2.06	2.18	3.73	169.61	472.16	33.10
A_3	6.63	2.06	2.22	3.73	171.03	475.84	32.77

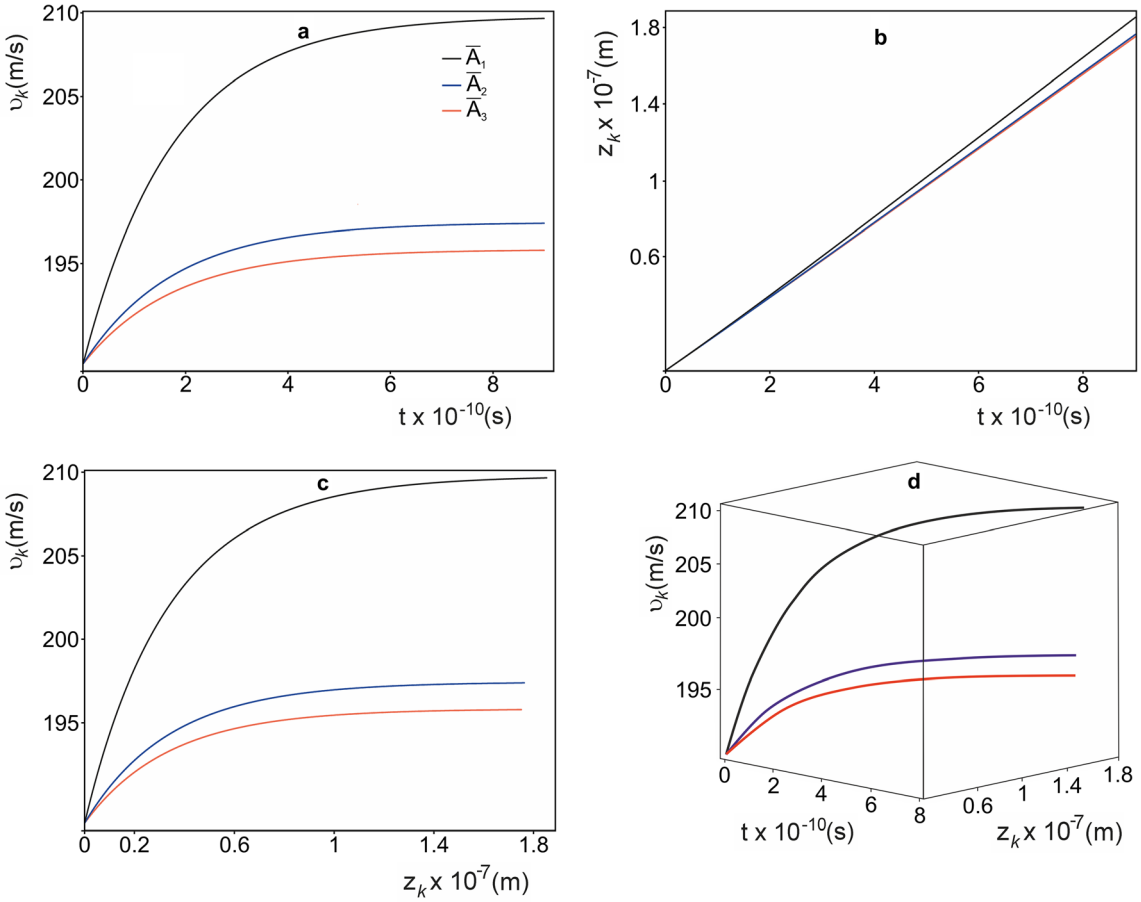

Fig. 11 Time dependence of the kink velocity (**a**) and coordinate (**b**), as well as the kink trajectories on the phase plane $\{\upsilon_k, z_k\}$ (**c**) and in 3D space $\{\upsilon_k, z_k, t\}$ (**d**). The graphs are constructed for promoter-like sequences $\overline{A}_1$, $\overline{A}_2$ and $\overline{A}_3$ in the presence of a constant external field $M_0 = 2.85 \times 10^{-23}$ (J). The initial velocity of the kinks is $\upsilon_0 = 189$ (m/s)

Method of blocks

In contrast to the method of concentrations, the method of blocks proposed by Grinevich et al. (2015a) makes it possible to take into account inhomogeneity of the DNA molecule.

According to this method, an inhomogeneous DNA sequence is first divided into several regions or blocks. Usually, such blocks are functionally significant regions and areas between them. Secondly, for each of the blocks, the solutions of the McLaughlin-Scott equation are found with the help of the method of concentrations. Then, these solutions are stitched at the boundaries between the blocks.

This approach allows calculating the energy profile of the sequence and constructing the trajectories of kinks moving in a potential field with such a profile.

Table 12 Stationary kink velocities calculated for promoter-like sequences (Yakushevich and Krasnobaeva 2008a)

Sequence	υ_{st} (m/s)
$\overline{A}_1$	209.67
$\overline{A}_2$	197.35
$\overline{A}_3$	195.74

Solution of the McLaughlin-Scott equation for the IFNA17 gene by the method of blocks

The solution of the McLaughlin-Scott equation for the IFNA17 gene has been obtained by Yakushevich and Krasnobaeva *(2017) using the method of blocks. In contrast to the method of concentrations, the method of blocks takes into account the internal structure of the sequence, which, according to the GenBank data (Homo sapiens interferon alpha 17 (IFNA17) n.d.) contains three blocks: one CDS region (50..619) and two regions (1..49) and (620..980) with unknown functional properties (Fig. 12).*

The details of the gene structure are presented in Table 13. There, N_j is the total number of nitrogenous bases in the j-th block, $N_{j,A}$, $N_{j,T}$, $N_{j,G}$ and $N_{j,C}$ are the numbers of adenines, thymines, guanines and cytosines in the j-th block, $j = 1, 2, 3$.

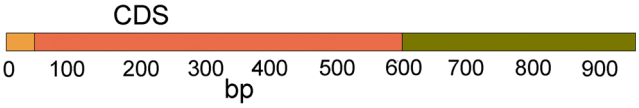

Fig. 12 Three blocks in the IFNA17 gene sequence

The coefficients of the McLaughlin-Scott equation and the kink rest energy averaged over the length of each of the three blocks are presented in Table 14.

Using the data of Table 14, the energy profile of the IFNA17 gene was constructed (Fig. 13). It turned out that the profile contained one barrier corresponding to the CDS region.

The solution of the McLaughlin-Scott equation in the first block has the following form (Yakushevich and Krasnobaeva 2017):

$$\upsilon_{1,k}(t) = \frac{\left[\left(\upsilon_{01}\widetilde{\gamma}_{01}\right) exp\left(-\frac{\widetilde{\beta}_1}{\widetilde{I}_1}t\right)\right]}{\sqrt{1+\left[\left(\frac{\upsilon_{01}}{\widetilde{C}_{01}}\widetilde{\gamma}_{01}\right) exp\left(-\frac{\widetilde{\beta}_1}{\widetilde{I}_1}t\right)\right]^2}}, \tag{46}$$

where υ_{01} is the initial kink velocity, $\widetilde{I}_1$ is the moment of inertia averaged over the first block, $\widetilde{C}_{01}$ is the sound velocity in the first block, $\widetilde{\gamma}_{01} = \left(1-\left(\upsilon_{01}/\widetilde{C}_{01}\right)^2\right)^{-1/2}$ and $\widetilde{\beta}_1$ is the coefficient of dissipation.

In the second and third blocks, the kink velocity is determined by similar formulas (Yakushevich and Krasnobaeva 2017):

$$\upsilon_{2,k}(t) = \frac{\left[\left(\upsilon_{02}\widetilde{\gamma}_{02}\right) exp\left(-\frac{\widetilde{\beta}_2}{\widetilde{I}_2}(t-t_1)\right)\right]}{\sqrt{1+\left[\left(\frac{\upsilon_{02}}{\widetilde{C}_{02}}\widetilde{\gamma}_{02}\right) exp\left(-\frac{\widetilde{\beta}_2}{\widetilde{I}_2}(t-t_1)\right)\right]^2}} \tag{47}$$

$$\upsilon_{3,k}(t) = \frac{\left[\left(\upsilon_{03}\widetilde{\gamma}_{03}\right) exp\left(-\frac{\widetilde{\beta}_3}{\widetilde{I}_3}(t-t_2)\right)\right]}{\sqrt{1+\left[\left(\frac{\upsilon_{03}}{\widetilde{C}_{03}}\widetilde{\gamma}_{03}\right) exp\left(-\frac{\widetilde{\beta}_3}{\widetilde{I}_3}(t-t_2)\right)\right]^2}} \tag{48}$$

where υ_{02} and υ_{03} are the initial velocities of the DNA kink in the second and the third blocks, $\widetilde{I}_2$ and $\widetilde{I}_3$ are the moments of inertia of nitrogenous bases averaged over the second and third blocks, respectively, $\widetilde{C}_{02}$ and $\widetilde{C}_{03}$ are the sound velocities in the second and in the third blocks, $\widetilde{\gamma}_{02} = \left(1-\left(\upsilon_{02}/\widetilde{C}_{02}\right)^2\right)^{-1/2}$, $\widetilde{\gamma}_{03} = \left(1-\left(\upsilon_{03}/\widetilde{C}_{03}\right)^2\right)^{-1/2}$, $\widetilde{\beta}_2$ and $\widetilde{\beta}_3$ are the coefficients of dissipation, t_1 and t_2 are the times of crossing the boundaries between the first and second blocks and between the second and third blocks, respectively.

Defining the kink coordinate in the i-th block by formula: $\upsilon_{ki}(t) = \frac{dz_{ki}(t)}{dt}$, the formulas for time dependence of the kink coordinate for each of the blocks were found:

$$z_{1,k}(t) = \int_0^t \upsilon_{1,k}(\tau)d\tau. \tag{49}$$

$$z_{2,k}(t) = \int_{t_1}^t \upsilon_{2,k}(\tau)d\tau \tag{50}$$

$$z_{3,k}(t) = \int_{t_2}^t \upsilon_{3,k}(\tau)d\tau \tag{51}$$

With the help of formulas (49)–(51) and of the data of Table 14, the kink trajectories in the plane {t, z} for different values of the initial velocity υ_{01} were constructed (Fig. 14).

Figure 14 shows that in the first case (curve (1)) the initial total energy of the DNA kink is not large enough to overcome the energy barrier. Therefore, when reaching the first boundary, the kink is reflected from the boundary and begins to move to the left end of the gene. After reaching the left end, the kink is reflected from the left end, which is possible only if the rest kink energy in the left neighboring region to the left is greater than the total energy of the kink. Just this scenario is shown in Fig. 14. After a few zig-zag motions, the kink eventually stops in the first block.

In the second case (curve (2)), the kink can overcome the right boundary of the first block and enter the second block (CDS). However, the kink does not reach the end of the second block and stops inside this block.

In the third case (curve (3), the kink passes the entire second block (CDS), continues moving in the third block and stops before reaching the right end of the gene.

Table 13 Details of the structure of the IFNA17 gene sequence

Block	Coordinates	$N_{j,A}$	$N_{j,T}$	$N_{j,G}$	$N_{j,C}$	N_j
1	1..49	15	12	7	15	49
2 (CDS)	50..619	157	145	130	138	570
3	620.980	110	146	44	61	361

Solution of the McLaughlin-Scott equation for the pBR322 plasmid by the method of blocks

Yakushevich and Krasnobaeva (2019) used the method of blocks to solve the McLaughlin-Scott equation for the pBR322 plasmid (Fig. 15a). This plasmid is widely used in gene research, and its components are applied to create new instrumental plasmids (Watson 1988). The sequence of the pBR322 plasmid consists of 4361 bases (Cloning vector pBR322, complete sequence, n.d.) (Appendix 6).

A linear version of the scheme (Fig. 15a), obtained by cutting circular DNA at the point S, is shown in Fig. 15b. It is known that the main chain of the plasmid contains two

Table 14 Coefficients of the McLaughlin-Scott equation and kink rest energy calculated for each of the IFNA17 gene blocks (Yakushevich and Krasnobaeva 2017)

Block	Coefficients of the McLaughlin-Scott equation			Kink rest energy	
	$\widetilde{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K'}$ (10^{-18} N·m)	$\widetilde{V}$ (10^{-20} J)	$\widetilde{\alpha}$ (10^{-34} J s)	$\widetilde{E_0}$ (10^{-20} J)
1	5.95	1.91	2.08	3.45	159.56
2 (CDS)	6.20	1.95	2.16	3.52	169.61
3	5.98	1.90	1.95	3.44	171.03

coding regions CDS-1 and CDS-2 with coordinates (86 ... 1276) and (1915 ... 2106), respectively, and the complementary chain contains one coding region CDS-3 with coordinates (3293 ... 4153).

Yakushevich and Krasnobaeva (2019) divided the sequence of the pBR322 plasmid into five blocks: two coding regions CDS-1 and CDS-2, as well as three intermediate regions with coordinates (1..85), (1277..1914) and (2107 .. 4361). For convenience, they were renumbered as shown in Fig. 16. The block structure of the sequence is shown in Table 15.

.

The coefficients of the McLaughlin-Scott equation and the kink rest energy are presented in Table 16.

When constructing the energy profile of the plasmid, the authors took into account the ring form of the plasmid. The result of the construction is presented in Fig. 17. The vertical axis shows the values of the kink rest energy. The horizontal axis shows the coordinates of the nitrogenous bases in the units of base pairs (bp), 1 bp = 3.4×10^{-10} m.

The energy profile contains two barriers that correspond to the coding regions CDS-1 and CDS-2. Because the kink behavior in many respects is similar to the behavior of a quasiparticle, the authors suggest that the behavior of the pBR322 kink is determined by whether the kink can overcome the barriers or not, and the latter depends on the initial kink velocity.

To construct 3D trajectories of kinks in the pBR322 plasmid, the authors used two coupled ordinary differential equations for each block (one equation for the kink velocity and the other for the kink coordinate):

$$\frac{d\widetilde{z}_k^{(i)}(t)}{dt} = \widetilde{v}_k^{(i)}(t), \tag{52}$$

$$\frac{d\widetilde{v}_k^{(i)}(t)}{dt} = -\frac{\widetilde{\beta}^{(i)}}{\widetilde{I}^{(i)}}\widetilde{v}_k^{(i)}(t)\left[1-\left(\frac{\widetilde{v}_k^{(i)}(t)}{\widetilde{C}^{(i)}}\right)^2\right], \quad i = 1, 2...5. \tag{53}$$

The solutions of the equations are presented in the form of trajectories in the space {v, z, t} (Fig. 18).

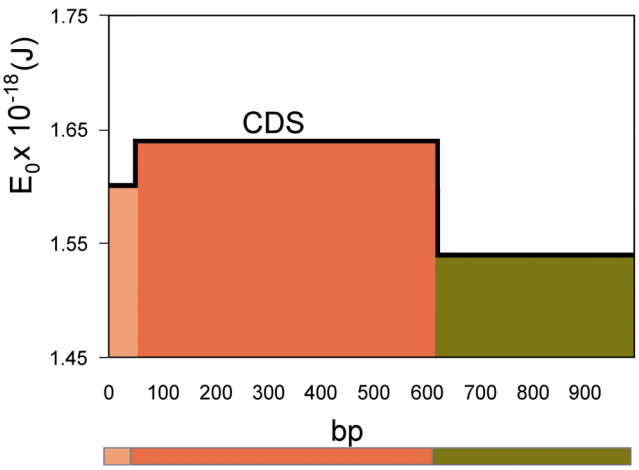

Fig. 13 Energy profile of the IFNA17 gene

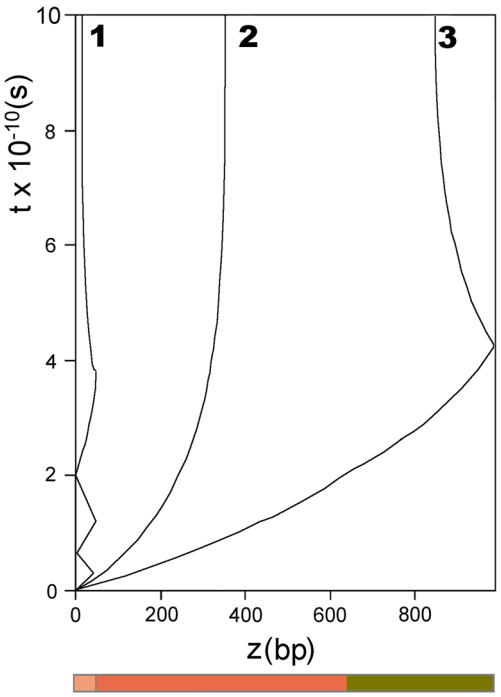

Fig. 14 Kink trajectories in the IFNA17 gene. Calculations were made for three values of the initial velocity: (1) v_{01} = 500 m/s, (2) v_{01} = 800 m/s and (3) v_{01} = 1500 m/s

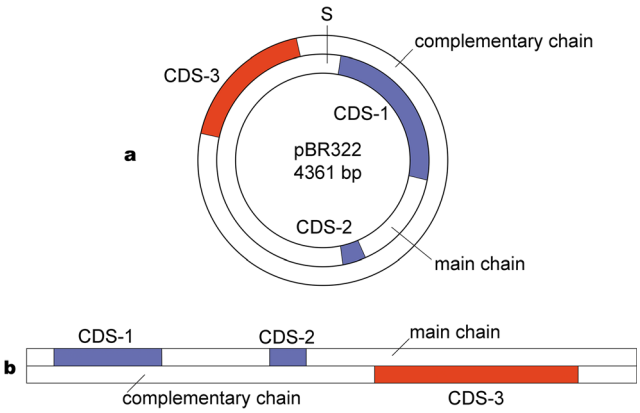

Fig. 15 Plasmid pBR32 (**a**) and its linear version (**b**). S is a cut point. The main and complementary chains are shown. Coding regions CDS-1 and CDS-2 are in the main polynucleotide chain, and CDS-3 is located in the complementary chain

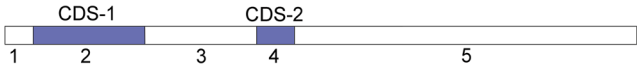

Fig. 16 The numbering of blocks in the main chain of the pBR322 plasmid

Table 15 Details of the blocks structure in the pBR322 sequence (Yakushevich and Krasnobaeva 2019)

Block	Coordinates	N^{A}	N^{T}	N_{G}	N^{C}	N
1	1..85	597	584	573	586	2340
2 (CDS-1)	86..1276	190	268	353	380	1191
3	1277..1914	142	145	160	191	638
4 (CDS-2)	1915..2106	54	37	48	53	192
5	2107..4361	597	584	573	586	2340

Discussion and perspectives

We have reviewed the use of the McLaughlin-Scott equation and related methods as potential tools for studying the dynamics of DNA open states which were considered here as nonlinear conformation excitations—kinks. We described how this equation has been used in the case of homogeneous DNA. The results on the dependence of the velocity and coordinate of the kink on time and the trajectory of the kink obtained in the absence and in the presence of external fields of various types were described. Four sets of DNA parameters were used to demonstrate the results: one set for the *poly* (A) sequence, one for the *poly* (T) sequence and two for the *poly* (G) and *poly* (C) sequences. This allowed us to compare the results obtained for each of the four cases.

In the second part of the review, it was shown how the McLaughlin-Scott equation could be applied to inhomogeneous DNA. Two approaches were described in detail. The first was based on the quasi-homogeneous approximation. The second was a combination of two methods: the quasi-homogeneous approximation and the block method. We illustrated how these approaches were used to study the dynamics of DNA open states in the IFNA17, ADRB2, NOS1 and IL-5 genes, in the A1, A2 and A3 promoter sequences of the

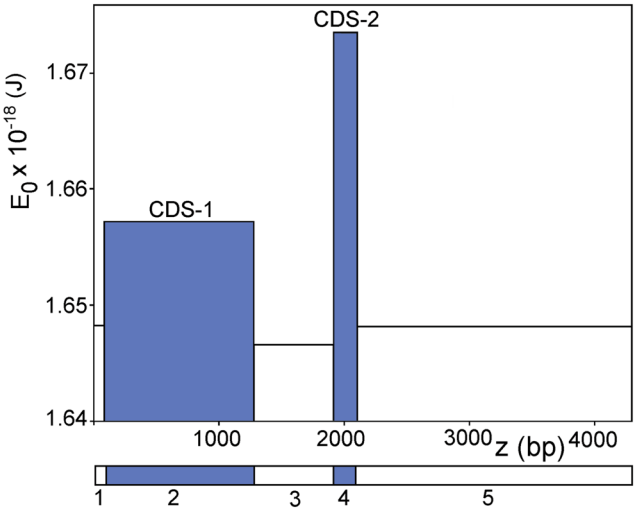

Fig. 17 Energy profile of the pBR322 plasmid

Table 16 Coefficients of the McLaughlin-Scott equation and the rest energy of kinks calculated for each of the pBR322 plasmid blocks (Yakushevich and Krasnobaeva 2019)

Block	Coefficients of the McLaughlin-Scott equation				Kink rest energy
	$\widetilde{I}$ (10^{-44} kg·m^2)	$\overrightarrow{K'}$ (10^{-18} N·m)	$\widetilde{V}$ (10^{-20} J)	$\widetilde{\alpha}$ (10^{-34} J s)	$\widetilde{E_0}$ (10^{-20} J)
1	6.19	1.94	2.18	3.51	1.65
2 (CDS-1)	6.05	1.90	2.26	3.44	1.66
3	6.09	1.92	2.21	3.47	1.65
4 (CDS-2)	6.26	1.96	2.23	3.55	1.67
5	6.19	1.94	2.18	3.51	1.65

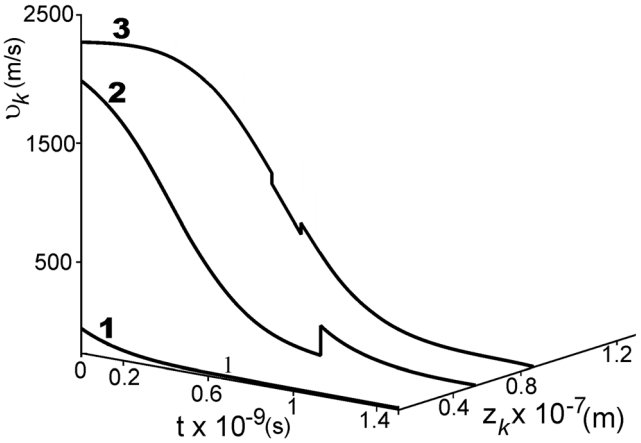

Fig. 18 3D trajectories of the kinks in the pBR322 plasmid. The curves 1, 2 and 3 correspond to initial kink velocities 150 m/s, 1650 m/s and 1879 m/s, respectively

bacteriophage T7 genome, as well as in the pTTQ18 and pBR322 plasmids (Fig. 19).

We should note, however, that in all works described above, the authors use the DNA dynamic models that take into account the mobility of nitrogenous bases in only one of the two polynucleotide DNA chains. In this case, the second chain is modeled only as an average field.

Another limitation is associated with the choice of angular displacements of nitrogenous bases as dominants. It is assumed that they make the main contribution to the DNA open states formation. However, there are other approaches where the transverse displacements of the bases are chosen as dominants. The well-known Peyrard-Bishop model (Peyrard and Bishop 1989; Dauxois et al. 1993) takes into account just such motions.

Certain restrictions are also imposed by the use of the block method in which the dynamic characteristics of native DNA sequences are replaced by approximate ones, obtained by dividing the real sequence into several blocks and averaging the dynamic parameters within each block.

The question of the correctness of applying the results obtained for open states to the study of the dynamics of the transcriptional bubble still remains open, since the latter is a part of a more complex and multicomponent system (Shimamoto 2013; Shimamoto and Imashimizu 2021) and its dynamics is largely limited by biochemical processes involved into the transcription process.

Despite all these limitations, the approach based on the McLaughlin-Scott equation can be regarded as promising because of its reliability, simplicity and convenience, especially when modeling the behavior of the open states of DNA, and when predicting their behavior under the action of various external fields. We believe that the McLaughlin-Scott approach can be useful for further studies of the relationship between the dynamic and functional properties of DNA and opens up new possibilities for the application of analytical methods of theoretical physics and nonlinear mathematics investigations of both DNA and other biological molecules.

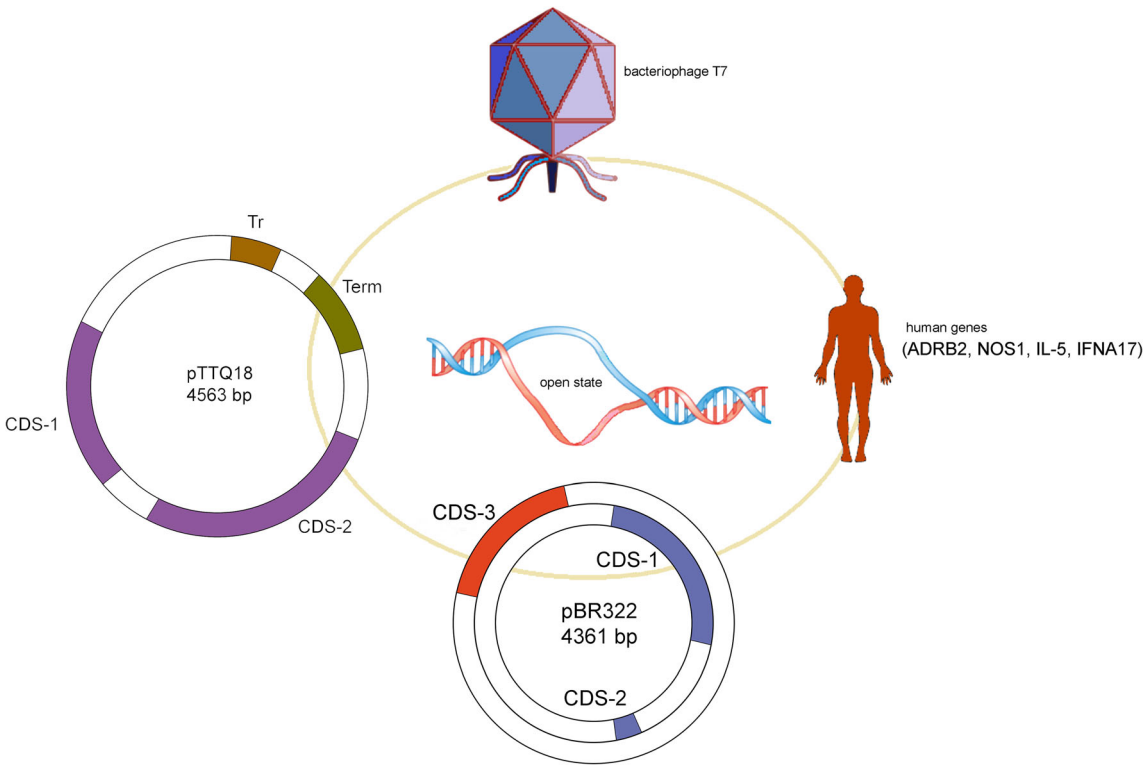

Fig. 19 The diagram presents the living systems considered in the review. They are arranged in a circle around the DNA open state

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12551-021-00801-0.

References

Ablowitz MJ, Segur H (1980) Solitons and inverse spectral transform. SIAM, Philadelphia

Alderton WK, Cooper CE, Knowles RG (2001) Nitric oxide synthases: structure, function and inhibition. Biochem J 357:593–615. https://doi.org/10.1042/0264-6021:3570593

Alexandrov BS, Gelev V, Bishop AR et al (2010a) DNA breathing dynamics in the presence of a terahertz field. Phys Lett 374:1214–1217. https://doi.org/10.1016/j.physleta.2009.12.077

Alexandrov BS, Gelev V, Yoo SW et al (2010b) DNA dynamics play a role as a basal transcription factor in the positioning and regulation of gene transcription initiation. Nucleic Acids Res 38:1790–1795. https://doi.org/10.1093/nar/gkp1084

Amann E, Brosius J, Ptashne M (1983) Vectors bearing a hybrid trp-lac promoter useful for regulated expression of cloned genes in Escherichia coli. Gene 25:167–178. https://doi.org/10.1016/0378-1119(83)90222-6

Bailey LJ, Doherty AJ (2017) Mitochondrial DNA replication: a PrimPol perspective. Biochem Soc Trans 45:513–529. https://doi.org/10.1042/BST20160162

Barbi M, Cocco S, Peyrard M et al (1999) A twist opening model for DNA. J Biol Phys 24:97–114. https://doi.org/10.1023/A:1005139326775

Barbi M, Lepri S, Peyrard M, Theodorakopolous N (2003) Thermal denaturation of a helicoidal DNA model. Phys Rev E 68:061909. https://doi.org/10.1103/PhysRevE.68.061909

Bengtsson K, Orho-Melander M, Melander O et al (2001) Beta (2)-adrenergic receptor gene variation and hypertension in subjects with type 2 diabetes. Hypertension 37:1303–1308. https://doi.org/10.1161/01.hyp.37.5.1303

Bergues-Pupo AE, Bergues JM, Falo F (2013) Modeling the interaction of DNA with alternating fields. Phys Rev E Stat Nonlinear Soft Matter Phys 87:022703. https://doi.org/10.1103/PhysRevE.87.022703

Bishop AI, Nieminen TA, Heckenberg NR et al (2003) Optical application and measurement of torque on microparticles of isotropic nonabsorbing material. Phys Rev A 68:033802. https://doi.org/10.1103/PhysRevA.68.033802

Bleichert F, Botchan MR, Berger JM (2017) Mechanisms for initiating cellular DNA replication. Science 355:215–222. https://doi.org/10.1126/science.aah6317

Bochieri P, Loinger A (1970) A conjecture concerning the classical theory of blackbody radiation. Lett. Nuovo Cimento 4:310–312

Braun OM, Kivshar YS (1998) Nonlinear dynamics of the Frenkel-Kontorova model. Phys Rep 306:1–108

Braun OM, Kivshar YS (2004) The Frenkel-Kontorova model. Springer Verlag, New York

Bychkov VA, Ryazantseva NV, Novitsky VV (2011) Analysis of the combined effect of polymorphisms interferon genes OAS1, OAS3, PKR, IFNA17 and IFNG in susceptibility to chronic viral hepatitis C. Bull Siber Med 10:19–23. https://doi.org/10.20538/1682-0363-2011-3-19-23

Bykov VG (2014) Sine-Gordon equation and its application to tectonic stress transfer. J Seismol 18:497–510. https://doi.org/10.1007/s10950-014-9422-7

Cadoni M, De Leo R, Demelio S (2011) Soliton propagation in homogeneous and inhomogeneous models for DNA torsion dynamics. J Nonlinear Math Phys 18:287–319. https://doi.org/10.1142/S1402925111001544

Cadoni M, De Leo R, Demelio S, Gaeta G (2009) Twist solitons in complex macromolecules: from DNA to polyethylene. Int J Nonlin Mech 43:1094–1107. https://doi.org/10.1016/j.ijnonlinmec.2008.03.010

Cadoni M, De Leo R, Gaeta G (2007) Composite model for DNA torsion dynamics. Phys Rev E 75:021919. https://doi.org/10.1103/PhysRevE.75.021919

Caudrey PJ, Eilbeck JC, Gibbon JD (1975) The sine-Gordon equation as a model classical field theory. Nuov Cim B 25:497–512. https://doi.org/10.1007/BF02724733

Chamberlin MJ (1974) The selectivity of transcription. Annu Rev Biochem 43:721–775

Chevizovich D, Michieletto D, Mvogo A, Zakiryanov F, Zdravković S (2020) A review on nonlinear DNA physics. R Soc Open Sci 7:200774. https://doi.org/10.1098/rsos.200774

Clark D, Pazdernik N (2015) Biotechnology, 2nd edn. Academic Cell, Amsterdam

Cloning vector pBR322, complete sequence. http://www.ncbi.nlm.nih.gov/nuccore/J01749.1

Contopoulos-Ioannidis DG, Manoli EN, Ioannidis JP (2005) Meta-analysis of the association of beta2-adrenergic receptor polymorphisms with asthma phenotypes. J Allergy Clin Immunol 115:963–972. https://doi.org/10.1016/j.jaci.2004.12.1119

Crick FHC, Watson JD (1954) The complementary structure of deoxyribonucleic acid. Proc Royal Soc A 223:80–96. https://doi.org/10.1098/rspa.1954.0101

Cuenda S, Sanchez A (2004a) Disorder and fluctuations in nonlinear excitations in DNA. Fluctuat Noise Lett 4:L491–L504. https://doi.org/10.1142/S0219477504002099

Cuenda S, Sanchez A (2004b) Nonlinear excitations in DNA: aperiodic models versus actual genome sequences. Phys Rev E 70:051903. https://doi.org/10.1103/physreve.70.051903

Dallongeville J, Helbecque N, Cottel D et al (2003) The gly16-arg16 and gln27-glu27 polymorphisms of beta-2-adrenergic receptor are associated with metabolic syndrome in men. J Clin Endocrinol Metabol 88:4862–4866. https://doi.org/10.1210/jc.2003-030173

Dauxois T, Peyrard M, Bishop AR (1993) Dynamics and thermodynamics of a nonlinear model for DNA denaturation. Phys Rev E 47:684. https://doi.org/10.1103/PhysRevE.47.684

Derks G, Gaeta G (2011) A minimal model of DNA dynamics in interaction with RNA-polymerase. Physica D: Nonlinear Phenom 240:1805–1817. https://doi.org/10.1017/S0956792511000301

Dominguez-Adame F, Sanchez A, Kivshar YS (1995) Soliton pinning by long-range order in aperiodic systems. Phys Rev E 52:2183. https://doi.org/10.1103/PhysRevE.52.R2183

Drobotenko MI, Dzhimak SS, Svidlov AA et al (2018) A mathematical model for base pair opening in a DNA double helix. Biophysics 63:177–182. https://doi.org/10.1134/S0006350918020069

Dubois A, Francois C, Descamps V et al (2009) Enhanced anti-HCV activity of interferon alpha 17 subtype. Virol J 6:70. https://doi.org/10.1186/1743-422X-6-70

Dunn JJ, Studier FW, Gottesman M (1983) Complete nucleotide sequence of bacteriophage T7 DNA and the locations of T7 genetic elements. J Mol Biol 166:477–535. https://doi.org/10.1016/S0022-2836(83)80282-4

Dwiputra D, Hidayat W, Zen FP (2017) Nonlinear dynamics of DNA bubble induced by site specific DNA-protein interaction. J Phys Conf Ser 856:012005–012009. https://doi.org/10.1088/1742-6596/856/1/011001

Ekomasov EG (2009) Solitons of the modified sine-Gordon equation. Bashkir State University, Ufa http://matem.anrb.ru/bsuconf/2009/Ekomasov.pdf

Englander W, Kallenbach NR, Heeger AJ et al (1980) Nature of the open state in long polynucleotide double helices: possibility of soliton

excitations. Proc Natl Acad Sci U S A 77:7222–7226. https://doi.org/10.1073/pnas.77.12.7222

Fedyanin VK, Gochev I, Lisy V (1986) Nonlinear dynamics of bases in continual model of DNA double helices. Stud Biophys 116:59–64

Forth S, Sheinin MY, Inman J et al (2013) Torque measurement at the single-molecule level. Annu Rev Biophys 42:583–604. https://doi.org/10.1146/annurev-biophys-083012-130412

Frenkel YI, Kontorova T (1939) On the theory of plastic deformation and twinning. Izv Akad Nauk Ser Fiz 1:137–149

Gaeta G, Reiss C, Peyrard M, Dauxois T (1994) Simple models of nonlinear DNA dynamics. La Rivista Nuovo Cimento 17:1–48. https://doi.org/10.1007/BF02724511

Gaeta G, Venier L (2008a) Solitary waves in twistopening models of DNA dynamics. Phys Rev E 78:011901. https://doi.org/10.1103/PhysRevE.78.011901

Gaeta G, Venier L (2008b) Solitary waves in helicoidal models of DNA dynamics. J Nonlinear Math Phys 15:186–204. https://doi.org/10.2991/jnmp.2008.15.2.6

Gaeta G (1990) On a model of DNA torsion dynamics. Phys Lett A 143:227–232. https://doi.org/10.1016/0375-9601(90)90744-9

Gaeta G (1994) A realistic version of the Y model for DNA dynamics and selection of soliton speed. Phys Lett A 190:301–308. https://doi.org/10.1016/0375-9601(94)90759-5

Gaeta G (2007) Solitons in Yakushevich-like models of DNA dynamics with improved intrapair potential. J Nonlinear Math Phys 14:57–81. https://doi.org/10.2991/jnmp.2007.14.1.6

Gaeta G (2006) Solitons in the Yakushevich model of DNA beyond the contact approximation. Phys Rev E 74:021921. https://doi.org/10.1103/PhysRevE.74.021921

Genome of bacteriophage T7. https://www.ncbi.nlm.nih.gov/nuccore/V01146

Gerus AI, Vikulin AV (2016) Rotational model of a block geoenvironment: mathematical aspects and numerical results. In: Materials of the regional scientific conference "Volcanism and related processes" dedicated to the Volcanologist's Day, March 30 - April 1, 2015. IViS FEB RAS, Petropavlovsk-Kamchatsky, pp 116–121

Grasemann H, Yandava CN, Drazen JM (1999) Neuronal NO synthase (NOS1) is a major candidate gene for asthma. Clin Exp Allergy 29:39–41

Grinevich AA, Ryasik AA, Yakushevich LV (2015a) Modeling the DNA bubbles dynamics. J Biomol Struct Dyn 33:84. https://doi.org/10.1080/07391102.2015.1032763

Grinevich AA, Ryasik AA, Yakushevich LV (2015b) Trajectories of DNA bubbles. Chaos, Solitons Fractals 75:62–75. https://doi.org/10.1016/j.chaos.2015.02.009

Grinevich AA, Ryasik AA, Yakushevich LV (2013) The dynamics of polynucleotide chain consisting of two different homogeneous sequences, divided by interface. Comput Res Model 5:241–253. https://doi.org/10.20537/2076-7633-2013-5-2-241-253

Grinevich AA, Yakushevich LV (2018) The influence of the DNA torque on the dynamics of transcription bubbles in plasmid PTTQ18. J Theor Biol 453:68–77. https://doi.org/10.1016/j.jtbi.2018.04.036

Gulevich DR, Kusmartsev FV (2006) Perturbation theory for localized solutions of sine-Gordon equation: decay of a breather and pinning by microresistorю. Phys Rev B 74:214303. https://doi.org/10.1103/PhysRevB.74.214303

Gumerov AM, Ekomasov EG, Murtazin RR et al (2015) Transformation of sine-Gordon solitons in models with variable coefficients and damping. Comput Math Math Phys 55:628–637. https://doi.org/10.7868/S0044466915040031

Harada Y, Ohara O, Takatsuki A et al (2001) Direct observation of DNA rotation during transcription by Escherichia coli RNA polymerase. Nature 409:113. https://doi.org/10.1038/35051126

He Y, Yan C, Fang J et al (2016) Near-atomic resolution visualization of human transcription promoter opening. Nature 533:359–365. https://doi.org/10.1038/nature17970

Hien DL, Nhan NT, Ngo VT et al (2007) Simple combined model for nonlinear excitations in DNA. Phys Rev E 76:021921. https://doi.org/10.1103/PhysRevE.76.021921

Homma S, Takeno S (1984) A coupled base-rotator model for structure and dynamics of DNA. Prog Theor Phys 72:679–693. https://doi.org/10.1143/PTP.72.679

Homo sapiens adrenoceptor beta 2 (ADRB2) https://www.ncbi.nlm.nih.gov/nuccore/NG_016421.1

Homo sapiens interferon alpha 17 (IFNA17). https://www.ncbi.nlm.nih.gov/nuccore/NM_021268.2

Homo sapiens interleukin 5 (IL5). https://www.ncbi.nlm.nih.gov/gene3567

Homo sapiens nitric oxide synthase 1 (NOS1) https://www.ncbi.nlm.nih.gov/nuccore/NM_001204218.1

Israel E, Drazen JM, Liggett SB et al (2000) The effect of polymorphisms of the beta(2)-adrenergic receptor on the response to regular use of albuterol in asthma. Am J Respir Crit Care Med 162:75–80. https://doi.org/10.1164/ajrccm.162.1.9907092

Ivancevic VG, Ivancevic TT (2013) Sine-Gordon solitons, kinks and breathers as physical models of nonlinear excitations in living cellular structures. J Geometr Symmetr Phys 31:1–56. https://doi.org/10.7546/jgsp-31-2013-1-56

Jeffrey A, Kakutani T (1972) Weak nonlinear dispersive waves: a discussion centered around the Korteveg-deVries equation. SIAM Rev 14:582–643

Karpen ME, deHaseth PL (2015) Base flipping in open complex formation at bacterial promoters. Biomolecules 5:668–678. https://doi.org/10.3390/biom5020668

Keener JP, McLaughlin DW (1977) Solitons under perturbations. Phys Rev A 16:777. https://doi.org/10.1103/PhysRevA.16.777

Kirkegaard K, Buc H, Spassky A, Wang JC (1983) Mapping of single-stranded regions in duplex DNA at the sequence level: single-strand-specific cytosine methylation in RNA polymerase-promoter complexes. Proc Natl Acad Sci U S A 80:2544–2548

Kivshar YS, Malomed BA (1989) Dynamics of solitons in nearly integrable systems. Rev Mod Phys 61:763–915. https://doi.org/10.1103/RevModPhys.61.763

Klaue D, Seidel R (2009) Torsional stiffness of single superparamagnetic microspheres in an external magnetic field. Phys Rev Lett 102:028302. https://doi.org/10.1103/PhysRevLett.102.028302

Krasnobaeva LA, Shapovalov AV (2008) Kink velocity in nonstationary external fields for the sine-Gordon model with allowance for dissipation effects. Russ Phys J 51:77–84. https://doi.org/10.1007/s11182-008-9020-7

Krasnobaeva LA, Shapovalov AV (2009) Kink motion by ac external force and dissipation. Comput Res Model 1:263–271. https://doi.org/10.20537/2076-7633-2009-1-3-263-271

Krasnobaeva LA, Volkov IA, Yakushevich LV (2012) Dynamics of kinks activated in the genes ADRB2, NOS1 and IL-5. Comput Res Model 4:391–399. https://doi.org/10.20537/2076-7633-2012-4-2-391-399

Krasnobaeva LA, Yakushevich LV (2015) Rotational dynamics of bases in the gene coding interferon alpha 17 (IFNA17). J Bioinforma Comput Biol 13:1540002. https://doi.org/10.1142/S0219720015400028

Krasnobaeva LA, Yakushevich LV (2020) The dynamic and statistical properties of DNA kinks. Biophysics 65:24–29. https://doi.org/10.1134/S0006350920010091

Krumhansl JA, Alexander DM (1983) Nonlinear dynamics and conformational excitations in biomolecular materials. In: Clementi E, Sarma RH (eds) Structure and dynamics: nucleic acids and proteins. Adenine Press, New York, pp 61–80

Krumhansl JA, Wysin GM, Alexander DM et al (1985) Further theoretical studies of nonlinear conformational motions in double-helix DNA. In: Clementi E, Corongiu G, Sarma MH, Sarma RH (eds) Structure and motion: membranes, nucleic acids and proteins. Adenine Press, New York, pp 407–415

Kulik IO (1967) Wave propagation in a Josephson tunnel junction in the presence of vortices and the electrodynamics of weak superconductivity. JETP 24:1307

Lammers JW, Barnes PJ, Chung KF (1992) Non-adrenergic, non-cholinergic airway inhibitory nerves. Eur Respir J 5:239–246

Lawn RM, Adelman J, Dul TJ et al (1983) DNA sequence of two closely linked human leukocyte interferon genes. Science 212:1159–1162. https://doi.org/10.1126/science.6165082

Lennholm E, Hornquist M (2003) Revisiting Salerno's sine-Gordon model of DNA: active regions and robustness. Physica D 177:233–241. https://doi.org/10.1016/S0167-2789(02)00769-8

Lipfert J, Kerssemakers JWJ, Jager T et al (2010) Magnetic torque tweezers: measuring torsional stiffness in DNA and RecA-DNA filaments. Nat Methods 7:977–980. https://doi.org/10.1038/nmeth.1520

Lui LF, Wang JC (1987) Supercoiling of the DNA template during transcription. Proc Natl Acad Sci U S A 84:7024–7027. https://doi.org/10.1073/pnas.84.20.7024

Ma J, Bai L, Wang MD (2013) Transcription under torsion. Science 340:1580–1583. https://doi.org/10.1126/science.1235441

Malomed BA (1988) Interaction of a soliton with an impurity in the sine-Gordon model of a commensurate charge-density-wave system. J Phys C Solid State Phys 21:5163–5181

Manoranjan JJ, Bishop VS, Rasmussen AR et al (2018) Allostery through protein-induced DNA bubbles. Sci Rep 5:9037–9043. https://doi.org/10.1038/srep09037

McLaughlin DW, Scott AC (1977) Fluxon interactions. Appl Phys Lett 30:545. https://doi.org/10.1063/1.89229

McLaughlin DW, Scott AC (1978a) Perturbation analysis of fluxon dynamics. Phys Rev A 18:1652. https://doi.org/10.1103/PhysRevA.18.1652

McLaughlin DW, Scott AC (1978b) A multisoliton perturbation theory. In: Lonngren K, Scott A (eds) Solitons in action. Academic Press, New York, pp 201–256

Mordvinov VA, Furman DP (2009) Cytokines: biological properties and regulation of human interleukin-5 gene expression. Vestnik VOGiS (Inform Bull Vavilov Soc Genet Breed Sci) 13:53–67

Nelson P (1999) Transport of torsional stress in DNA. Proc Natl Acad Sci U S A 96:14342–14347. https://doi.org/10.1073/pnas.96.25.14342

Nitta J, Matsuda A, Kawakami T (1984) Propagation properties of fluxons in a well-damped Josephson transmission line. J Appl Phys 55:2758–2762 http://hdl.handle.net/10097/51948

Peyrard M (ed) (1995) Nonlinear excitations in biomolecules. Springer, Berlin

Peyrard M, Bishop AR (1989) Statistical mechanics of a nonlinear model for DNA denaturation. Phys Rev Lett 62:2755–2758. https://doi.org/10.1103/PhysRevLett.62.2755

Plasmid pTTQ18, complete sequence. https://www.addgene.org/69122/sequences

Porta AL, Wang MD (2004) Optical torque wrench: angular trapping, rotation, and torque detection of quartz microparticles. Phys Rev Lett 92:190801. https://doi.org/10.1103/PhysRevLett.92.190801

Quintero NR, Kevrekidis PG (2001) Nonequivalence of phonon modes in the sine-Gordon equation. Phys Rev E 64:056608. https://doi.org/10.1103/PhysRevE.64.056608

Rajaraman R (1982) Solitons and instantons: an introduction to solitons and instantons in quantum field theory. Amsterdam, Oxford, North-Holland

Reif A, Herterich S, Strobel A (2006) A neuronal nitric oxide synthase (NOS-I) haplotype associated with schizophrenia modifies prefrontal cortex function. Mol Psychiatry 11:286–300. https://doi.org/10.1038/sj.mp.4001779

Rubinstein J (1970) Sine-Gordon equation. J Math Phys 11:258–266

Ryasik A, Orlov M, Zykova E et al (2018) Bacterial promoter prediction: selection of dynamic and static physical properties of DNA for reliable sequence classification. J Bioinforma Comput Biol 16:1840003. https://doi.org/10.1142/S0219720018400036

Salerno M (1991) Discrete model for DNA-promoter dynamics. Phys Rev A 44:5292–5297. https://doi.org/10.1103/PhysRevA.44.5292

Salerno M (1992) Dynamical properties of DNA promoters. Phys Lett A 167:49–53. https://doi.org/10.1016/0375-9601(92)90624-U

Salerno M (1995) Nonlinear dynamics of plasmid pBR322 promoters. In: Peyrard M (ed) Nonlinear excitations in biomolecules. Springer, New York, pp 147–153

Salerno M, Kivshar Yu S (1994) DNA promoters and nonlinear dynamics. Phys Lett A 193:263–266. https://doi.org/10.1016/0375-9601(94)90594-0

Sasse-Dwight S, Gralla JD (1989) $KMnO_4$ as a probe for lac promoter DNA melting and mechanism in vivo. J Biol Chem 264:8074–8081. https://doi.org/10.1016/S0021-9258(18)83152-0

Saucier JM, Wang JC (1972) Angular alteration of the DNA helix by E. coli RNA polymerase. Nat New Biol 239:167–170. https://doi.org/10.1038/newbio239167a0

Scott AC (1969) A nonlinear Klein-Gordon equation. Am J Phys 37:52–61. https://doi.org/10.1119/1.1975404

Scott AC, Chu FYF, McLaughlin DW (1973) The soliton: a new concept in applied science. Proc IEEE 61:1443–1483. https://doi.org/10.1109/PROC.1973.9296

Scott-Rassel J (1844) Report on waves. Proc Roy Soc Edinburgh 319-320

Severin ES (2016) Biochemistry. GEOTAR–Media, Moscow

Shapovalov AV, Krasnobaeva LA (2009) Solitons of the sine-Gordon equation. TGU, Tomsk

Shi C, Shang F, Zhou M et al (2016) Triggered isothermal PCR by denaturation bubble-mediated strand exchange amplification. Chem Commun 52:11551–11554. https://doi.org/10.1039/C6CC05906F

Shikhovtseva ES, Nazarov VN (2016) Non-linear longitudinal compression effect on dynamics of the transcription bubble in DAN. Biophys Chem 214–215:47–53. https://doi.org/10.1016/j.bpc.2016.05.005

Shimamoto N (2013) Nanobiology of RNA polymerase: biological consequence of inhomogeneity in reactant. Chem Rev 113:8400–8422. https://doi.org/10.1021/cr400006b

Shimamoto N, Imashimizu M (2021) RNA polymerase and transcription mechanisms: the forefront of physicochemical studies of chemical reactions. Biomolecules 11:32. https://doi.org/10.3390/biom11010032

Shinkai T, Ohmori O, Hori H (2002) Allelic association of the neuronal nitric oxide synthase (NOS1) gene with schizophrenia. Mol Psychiatry 7:560–563. https://doi.org/10.1038/sj.mp.4001041

Sicard F, Destainville N, Manghi M (2015) DNA denaturation bubbles: free-energy landscape and nucleation/closure rates. J Chem Phys 142:903–910. https://doi.org/10.1063/1.4905668

Siebenlist U, Simpson RB, Gilbert W (1980) E. coli RNA polymerase interacts homologously with two different promoters. Cell 20:269–281. https://doi.org/10.1016/0092-8674(80)90613-3

Singh AR, Granek R (2017) Manipulation of double-stranded DNA melting by force. Phys Rev E 96:032417–032422. https://doi.org/10.1103/PhysRevE.96.032417

Stark J, Chan C, George AJ (2007) Oscillations in the immune system. Immunol Rev 216:213–231. https://doi.org/10.1111/j.1600-065X.2007.00501.x

Stark MJ (1987) Multicopy expression vectors carrying the lac repressor gene for regulated high-level expression of genes in Escherichia coli. Gene 51:255–267. https://doi.org/10.1016/0378-1119(87)90314-3

Swanson E (2011) Swanson modeling DNA response to terahertz radiation. Phys Rev E Stat Nonlinear Soft Matter Phys 83:040901. https://doi.org/10.1103/PhysRevE.83.040901

Takeno S, Homma S (1983) Topological solitons and modulated structure of bases in DNA double helices. Prog Theor Phys 70:308–311. https://doi.org/10.1143/PTP.70.308

Watson JD, Crick FHC (1953) Molecular structure of nucleic acids: a structure for deoxyribose nucleic acid. Nature 171:737–738. https://doi.org/10.1038/171737a0

Watson N (1988) A new revision of the sequence of plasmid pBR322. Gene 70:399–403. https://doi.org/10.1016/0378-1119(88)90212-0

Yakushevich LV (1987) The effect of damping, external fields and inhomogeneity on the nonlinear dynamics of biopolymers. Stud Biophys 121:201–207

Yakushevich LV (1989) Nonlinear DNA dynamics: a new model. Phys Lett A 136:413–417. https://doi.org/10.1016/0375-9601(89)90425-8

Yakushevich LV (2004) Nonlinear physics of DNA. Wiley, Weinheim

Yakushevich LV, Balashova VN, Zakiryanov FK (2016) On the DNA kink motion under the action of constant torque. Math Biol Bioinform 11:81–90. https://doi.org/10.17537/2016.11.81

Yakushevich LV, Balashova VN, Zakiryanov FK (2018a) Is it possible to govern the movement of the transcription bubbles of DNA by constant and periodic external fields? Biometr Biostat Int J 7:218–224. https://doi.org/10.15406/bbij.2018.07.00212

Yakushevich LV, Balashova VN, Zakiryanov FK (2018b) Features of the DNA kink motion in the asynchronous switching on and off of the constant and periodic fields. Comput Res Model 10:545–558. https://doi.org/10.20537/2076-7633-2018-10-4-545-558

Yakushevich LV, Gapa S, Awrejcewicz J (2011) Rotational oscillations of bases in the DNA short fragments. In: Awrejcewicz J, Kazmierczak M, Olejnik P, Mrozowski J (eds) Dynamical systems—theory and applications. Left Grupa, Lodz, pp 269–274

Yakushevich LV, Grinevich AA, Ryasik AA (2014) Simulation of a kink movement in homogeneous and heterogeneous DNA sequences taking into account the dissipation. Russ J Numer Anal Math Model 29:197–204. https://doi.org/10.1515/rnam-2014-0015

Yakushevich LV, Kashapova GR, Zakiryanov FK (2012) Influence of periodic field with constant and slowly changing frequency on movement of DNA kink. Biophysics 57:14–18. https://doi.org/10.1134/S0006350912010186

Yakushevich LV, Kashapova GR, Zakiryanov FK (2013) Dynamics of soliton in the form of kink in the periodic field. Vestnik MSTU Stankin 3:103–107

Yakushevich LV, Krasnobaeva LA (2007) Influence of dissipation and external field on the dynamics of local conformational perturbations in DNA. Biophysics 52:179–184. https://doi.org/10.1134/S0006350907020066

Yakushevich LV, Krasnobaeva LA (2008a) A new approach to studies of nonlinear dynamics of kinks activated in inhomogeneous polynucleotide chains. Int J Nonl Mech 43:1074–1081. https://doi.org/10.1016/j.ijnonlinmec.2008.05.003

Yakushevich LV, Krasnobaeva LA (2008b) Peculiar features of kink dynamics in inhomogeneous DNA. Biophysics 53:21–25. https://doi.org/10.1134/S0006350908010041

Yakushevich LV, Krasnobaeva LA (2016) Forced oscillations of DNA bases. Biophysics 61:241–250. https://doi.org/10.1134/S000635091602024X

Yakushevich LV, Krasnobaeva LA (2017) Trajectories of the DNA kinks in the sequences containing CDS regions. Math Biol Bioinform 12:1–13. https://doi.org/10.17537/2017.12.1

Yakushevich LV, Krasnobaeva LA (2019) Plasmid pBR322 and nonlinear conformational distortions (kinks). Math Biol Bioinform 14:327–339. https://doi.org/10.17537/2019.14.327

Yakushevich LV, Krasnobaeva LA, Shapovalov AV et al (2005) One- and two-soliton solutions of the sine-Gordon equation as applied to DNA. Biophysics 50:450–455

Yakushevich LV, Ryasik AA (2012) Dynamical characteristics of DNA kinks and antikinks. Comput Res Model 4:209–217. https://doi.org/10.20537/2076-7633-2012-4-1-209-217

Yakushevich LV, Savin AV, Manevitch LI (2002) Nonlinear dynamics of topological solitons in DNA. Phys Rev E 66:016614. https://doi.org/10.1103/PhysRevE.66.016614

Yomosa S (1983) Soliton excitations in deoxyribonucleic acid (DNA) double helices. Phys Rev A 27:2120–2125. https://doi.org/10.1103/PhysRevA.27.2120

Yomosa S (1984) Solitary excitations in deoxyribonucleic acid (DNA) double helices. Phys Rev A 30:474–480. https://doi.org/10.1103/PhysRevA.30.474

Zakiryanov FK, Yakushevich LV (2013) Control of the dynamics of the kink of the modified sine-Gordon equation by the external exposure with varying parameters. Comput Res Model 5:821–834. https://doi.org/10.20537/2076-7633-2013-5-5-821-834

Zharnitsky V, Mitkov I, Gronbech-Jensen N (1998a) π kinks in strongly ac driven sine-Gordon systems. Phys Rev E 58:52–55. https://doi.org/10.1103/PhysRevE.58.R52

Zharnitsky V, Mitkov I, Levi M (1998b) Parametrically forced sine-Gordon equation and domain walls dynamics in ferromagnets. Phys Rev B 57:5033–5035. https://doi.org/10.1103/PhysRevB.57.5033

Zhou GF, Zhang CT (1991) A short review on the nonlinear motion in DNA. Phys Scr 43:347. https://doi.org/10.1088/0031-8949/43/3/025

Zuo Y, Steitz TA (2017) A structure-based kinetic model of transcription. Transcription 8:1–8. https://doi.org/10.1080/21541264.2016.1234821