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## От однородного к неоднородному электронному аналогу ДНК

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В данной работе с помощью методов математического моделирования решается задача о построении электронного аналога неоднородной ДНК. Такие электронные аналоги, наряду с другими физическими моделями живых систем, широко используются в качестве инструмента для изучения динамических и функциональных свойств этих систем. Решение задачи строится на основе алгоритма, разработанного ранее для однородной (синтетической) ДНК и модифицированного таким образом, чтобы его можно было использовать для случая неоднородной (природной) ДНК. Этот алгоритм включает следующие шаги: выбор модели, имитирующей внутреннюю подвижность ДНК; построение преобразования, позволяющего перейти от модели ДНК к ее электронному аналогу; поиск условий, обеспечивающих аналогию уравнений ДНК и уравнений электронного аналога; расчет параметров эквивалентной электрической цепи. Для описания неоднородной ДНК была выбрана модель, представляющая собой систему дискретных нелинейных дифференциальных уравнений, имитирующих угловые отклонения азотистых оснований, и соответствующий этим уравнениям гамильтониан. Значения коэффициентов в модельных уравнениях полностью определяются динамическими параметрами молекулы ДНК, включая моменты инерции азотистых оснований, жесткость сахара-фосфатной цепи, константы, характеризующие взаимодействия между комплементарными основаниями внутри пар. В качестве основы для построения электронной модели была использована неоднородная линия Джозефсона, эквивалентная схема которой содержит четыре типа ячеек: А-, Т-, G- и С-ячейки. Каждая ячейка, в свою очередь, состоит из трех элементов: емкости, индуктивности и джозефсоновского контакта. Важно, чтобы А-, Т-, G- и С-ячейки джозефсоновской линии располагались в определенном порядке, который аналогичен порядку расположения азотистых оснований (А, Т, G и С) в последовательности ДНК. Переход от ДНК к электронному аналогу осуществлялся с помощью А-преобразования, что позволило рассчитать значения емкости, индуктивности и джозефсоновского контакта в А-ячейках. Значения параметров для Т-, G- и С-ячеек эквивалентной электрической цепи были получены из условий, накладываемых на коэффициенты модельных уравнений и обеспечивающих аналогию между ДНК и электронной моделью.

Ключевые слова: моделирование динамики ДНК, уравнение синус-Гордона, линия Джозефсона, неоднородный электронный аналог

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## From homogeneous to inhomogeneous electronic analogue of DNA

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In this work, the problem of constructing an electronic analogue of heterogeneous DNA is solved with the help of the methods of mathematical modeling. Electronic analogs of that type, along with other physical models of living systems, are widely used as a tool for studying the dynamic and functional properties of these systems. The solution to the problem is based on an algorithm previously developed for homogeneous (synthetic) DNA and modified in such a way that it can be used for the case of inhomogeneous (native) DNA. The algorithm includes the following steps: selection of a model that simulates the internal mobility of DNA; construction of a transformation that allows you to move from the DNA model to its electronic analogue; search for conditions that provide an analogy of DNA equations and electronic analogue equations; calculation of the parameters of the equivalent electrical circuit. To describe inhomogeneous DNA, the model was chosen that is a system of discrete nonlinear differential equations simulating the angular deviations of nitrogenous bases, and Hamiltonian corresponding to these equations. The values of the coefficients in the model equations are completely determined by the dynamic parameters of the DNA molecule, including the moments of inertia of nitrous bases, the rigidity of the sugar-phosphate chain, and the constants characterizing the interactions between complementary bases in pairs. The inhomogeneous Josephson line was used as a basis for constructing an electronic model, the equivalent circuit of which contains four types of cells: A-, T-, G-, and C-cells. Each cell, in turn, consists of three elements: capacitance, inductance, and Josephson junction. It is important that the A-, T-, G- and C-cells of the Josephson line are arranged in a specific order, which is similar to the order of the nitrogenous bases (A, T, G and C) in the DNA sequence. The transition from DNA to an electronic analog was carried out with the help of the A-transformation which made it possible to calculate the values of the capacitance, inductance, and Josephson junction in the A-cells. The parameter values for the T-, G-, and C-cells of the equivalent electrical circuit were obtained from the conditions imposed on the coefficients of the model equations and providing an analogy between DNA and the electronic model.

Keywords: modeling DNA dynamics, sine-Gordon equation, Josephson line, non-uniform electronic analogue

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## 1. Introduction

Modeling is known as one of the most important tools for studying living systems. A striking example is the model of the DNA double helix proposed by Watson and Crick [Watson, Crick, 1953], which led to a breakthrough in understanding the mechanisms of functioning of this molecule. Further studies have shown, however, that it is important to create not only static, but also dynamic DNA models that reflect the internal mobility of the molecule. These models can be of various types: mechanical, electronic, optical. The main requirement for them is the ability to reproduce a variety of dynamic regimes which are observed or that could be observed in a DNA molecule, including one of the most interesting regimes — formation of the DNA open states, also named bubbles [Englander et al., 1980; Shigaev et al., 2013; Dzhimak et al., 2018]. These bubbles, are small (10–15 base pairs) regions inside of which the hydrogen bonds between complementary nitrous bases are broken [Hwa et al., 2003; van Erp et al., 2006; Tchernachenko et al., 2003; Grinevich et al., 2015; Sicard et al., 2015]. It is known that the bubbles are formed, for example, at the initial stage of transcription upon binding of RNA polymerase to promoter DNA regions [Robb et al., 2013; Pal et al., 2005]. The movement of the transcription bubbles (Fig. 1) along the double helix is considered as an important part of the transcription process, which affects velocity and efficiency of the process [Severin, 2016; Yakushevich et al., 2018].

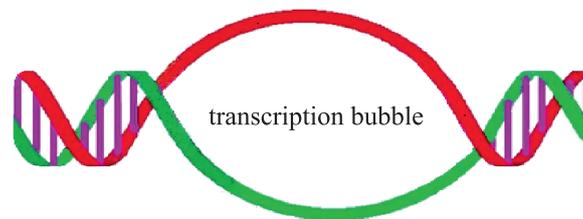


Fig. 1. Schematic representation of a transcription bubble

The first mathematical model, reproducing the movement of the DNA open states, has been proposed by Englander and coauthors [Englander et al., 1980]. It was based on the mechanical model of Scott [Scott, 1969], which is a chain of identical pendulums suspended on a horizontal thread at the same distance from each other and connected by springs [DNA Solitons..., 2007; The model of Scott, 2014]. Englander and coauthors suggested that pendulums imitate nitrogenous bases, the horizontal thread imitates the sugar-phosphate chain, and the gravitational field imitates the field induced by the second DNA strand. In essence, they proposed a simple mechanical analogue of homogeneous DNA, which allows reproducing the movement of transcriptional bubbles. Later the mechanical analogue was extended to the inhomogeneous case [Yakushevich, 2017]. The parameters of the analogue have been calculated for both homogeneous (poly (A)) and inhomogeneous (the fragment of the T7D bacteriophage) sequences.

The DNA mechanical analogue has a number of advantages, the main of which are the simplicity of reproducing the model and the ability to visualize a variety of dynamic regimes, including those whose mathematical study by other methods is difficult. However, the mechanical DNA model has one significant drawback: the model becomes extremely cumbersome in the case of long DNA sequences (of the order of 1000 or more base pairs). This drawback is absent in the electronic DNA models.

It has been recently shown [Yakushevich, 2017] that the uniform Josephson line [Scott, 1969; Lomdahl, 1985; Ustinov, 1998] with the equivalent circuit consisting of periodically repeating identical capacitances  $C$ , inductances  $L$  and Josephson contacts  $J$  (Fig. 2), can be considered as an example of the electronic analogue of homogeneous DNA. As for inhomogeneous DNA, the problem of the electronic analogue construction is still unsolved.

The aim of this paper is to solve this problem. We begin with the description of the mathematical model of the internal mobility of homogeneous DNA and method of constructing electronic analogue of homogeneous (synthetic) DNA. Then we generalize the approach to apply it to inhomogeneous case. We propose to use the non-uniform Josephson line as an electronic analogue of inhomogeneous DNA.

The equivalent circuit of the line should contain four types of the circuit cells: A-, T-, G-, and C-cells, each of which consists of three elements: capacitance  $C_i$ , inductance  $L_i$  and Josephson junction  $J_i$  ( $i = A, T, G, \text{ and } C$ ). It is assumed that the circuit cells are arranged in a specific order which is similar to the order of nitrous bases: adenines (A), thymines (T), guanines (G), and cytosines (C), in the DNA sequence.

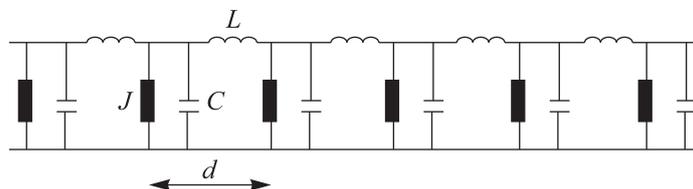


Fig. 2. Equivalent circuit of the uniform Josephson line.  $d$  is the cell size

## 2. A-transformation as a method of modeling an electronic analogue of homogeneous DNA

### 2a. Mathematical model of the internal mobility of homogeneous DNA

Let us start with the homogeneous DNA molecule the sequence of which consists of identical bases — adenines. The internal mobility of the molecule, including the formation of open states and their motion along the double helix, can be described in the following way [Englander et al., 1980]:

$$I_A \frac{d^2 \phi_n(t)}{dt^2} - KR_A^2 b^2 \frac{(\phi_{n+1}(t) - 2\phi_n(t) + \phi_{n-1}(t))}{b^2} + V_A \sin \phi_n(t) = 0. \quad (1)$$

Hamiltonian relating with Eq. (1) has the form:

$$H^{\text{DNA}} = \sum_n \left[ \frac{I_A}{2} \left( \frac{d\phi_n(t)}{dt} \right)^2 - \frac{KR_A^2 b^2}{2} \frac{(\phi_n(t) - \phi_{n-1}(t))^2}{b^2} + V_A (1 - \cos \phi_n(t)) \right]. \quad (2)$$

Here  $\phi_n(t)$  is the angular deviation of the  $n$ -th nitrogenous base located at time  $t$  in the vicinity of the point  $z_n$ ,  $b$  is the distance between nearest AT pairs,  $n = 1, 2, \dots, N$ . Although the DNA molecule has a wide variety of internal movements, however, it is believed that it is the angular deviations of the bases that make the main contribution to the formation of open states [Yakushevich, 2004].  $I_A = M_A R_A^2$  is the moment of inertia of adenine,  $M_A$  is the mass of adenine,  $R_A$  is the distance from the center of mass of the adenine to the sugar-phosphate chain,  $K$  is the stiffness coefficient (tensile) of the sugar-phosphate chain,  $V_A$  is a constant characterizing the interaction between complementary bases within the pair AT. For simplicity, it is assumed that the number  $N$  is large and the boundary effects can be neglected.

In the continuum approximation, Eq. (1) transforms to the sine-Gordon equation [Griffiths, Schiesser, 2012]:

$$I_A \frac{\partial^2 \phi(z,t)}{\partial t^2} - Kb^2 R_A^2 \frac{\partial^2 \phi(z,t)}{\partial z^2} + V_A \sin \phi(z,t) = 0, \quad (3)$$

and the Hamiltonian (2) transforms to:

$$H_{cont}^A = \int \left[ \frac{I_A}{2} \left( \frac{\partial \phi(z,t)}{\partial t} \right)^2 - Kb^2 R_A^2 \left( \frac{\partial \phi(z,t)}{\partial z} \right)^2 + V_A (1 - \cos \phi(z,t)) \right] \frac{dz}{b}. \quad (4)$$

One-soliton solution of Eq. (3) — kink:

$$\phi^A(z, t) = 4 \arctan \left( \exp \left( \frac{\gamma_A}{d_A} (z - v_A t - z_{0A}) \right) \right), \quad (5)$$

was used by Englander and co-authors as a mathematical model of the DNA open state [Englander et al., 1980]. Here  $v_A$  is the velocity of open state in the *poly* (A),  $d_A = \sqrt{Kb^2 R_A^2 / V_A}$  is the size of the open state,  $C_{0A} = \sqrt{Kb^2 R_A^2 / I_A}$  is the sound velocity in the *poly* (A),  $\gamma_A = \sqrt{1 - (v_A / C_{0A})^2}$ ,  $z_{0A}$  is an arbitrary constant.

Table 1. Parameters of *poly* (A) [Yakushevich, Krasnobaeva, 2016]

$I_A \times 10^{-44}$ (kg·m <sup>2</sup> )	$M_A \times 10^{-25}$ (kg)	$R_A \times 10^{-10}$ (m)	$K$ (J/m <sup>2</sup> )	$b \times 10^{-10}$ (m)	$V_A \times 10^{-20}$ (J)
7.61	2.26	5.8	6.75	3.4	2.09

Substitution of (5) into (4) gives the formula:

$$E_A = 8\sqrt{KR_A^2 V_A}, \quad (6)$$

that determines the minimum energy of the open state formed in the sequence *poly* (A). With the help of the values of the parameters collected in Table 1, and the formulas presented above we estimate the values of the size of the open state and its minimum energy:  $d_A = 35.44 \times 10^{-10}$  m,  $E_A = 1.743 \times 10^{-18}$  J.

## 2b. Uniform Josephson line

Let us begin with the uniform Josephson line that has been applied in [Yakushevich, 2017] as an electronic analogue of homogeneous DNA. Equation for the phase difference of the wave functions of the superconductors forming the Josephson junctions in the line has the form [Scott, 1969]:

$$C_A \left( \frac{\Phi_0}{2\pi} \right) \frac{\partial^2 \phi(z, t)}{\partial t^2} - \frac{d^2}{L_A} \left( \frac{\Phi_0}{2\pi} \right) \frac{\partial^2 \phi(z, t)}{\partial z^2} + J_{0A} \sin \phi(z, t) = 0, \quad (7)$$

where  $\phi(z, t)$  is the phase difference of the wave functions of the superconductors forming the Josephson junction,  $C_A$  is the capacitance,  $L_A$  is the inductance,  $d$  is the cell size,  $\Phi_0$  is the magnetic flux quantum,  $J_{0A}$  is the critical value of the current flowing through the Josephson junction.

Hamiltonian corresponding to Eq. (7) can be written as [Yakushevich, 2017]:

$$H_{cont}^{El} = \int \left[ \frac{1}{2} C_A \left( \frac{\Phi_0}{2\pi} \right)^2 \left( \frac{\partial \phi(z, t)}{\partial t} \right)^2 - \frac{1}{2} \frac{d^2}{L_A} \left( \frac{\Phi_0}{2\pi} \right)^2 \left( \frac{\partial \phi(z, t)}{\partial z} \right)^2 + J_{0A} \left( \frac{\Phi_0}{2\pi} \right) (1 - \cos \phi(z, t)) \right] \frac{dz}{d}. \quad (8)$$

The discrete version of the model (7)–(8) takes then the following form:

$$C_A \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 \phi_n}{dt^2} - \frac{d^2}{L_A} \left( \frac{\Phi_0}{2\pi} \right) \frac{(\phi_{n-1} - 2\phi_n + \phi_{n+1})}{d^2} + J_{0A} \sin \phi_n = 0, \quad (9)$$

$$H_A^{El} = \sum_n \left[ \frac{1}{2} C_A \left( \frac{\Phi_0}{2\pi} \right)^2 \left( \frac{d\phi_n}{dt} \right)^2 - \frac{1}{2} \frac{d^2}{L_A} \left( \frac{\Phi_0}{2\pi} \right)^2 \frac{(\phi_n - \phi_{n-1})^2}{d^2} + J_{0A} \left( \frac{\Phi_0}{2\pi} \right) (1 - \cos \phi_n) \right], \quad n = 1, 2, \dots, N. \quad (10)$$

### 2c. A-transformation

To transform the DNA Eq. (1) to the equation for the Josephson line (9), and the Hamiltonian (2) to the Hamiltonian (10), let us introduce new variables  $\xi_n$  and  $\tau$ :

$$\xi_n = \alpha_A z_n, \quad \tau = \beta_A t, \quad (11)$$

where  $\alpha_A$  and  $\beta_A$  are the coefficients of the transformation. Variable  $\xi_n$  can be written also as:  $\xi_n = \alpha_A z_n = \alpha_A n b = n d$ , where  $d = \alpha_A b$ .

In the new variables, equation (1) takes the form:

$$I_A \beta_A^2 \frac{d^2 \phi_n}{d\tau^2} - K R_A^2 d^2 \frac{(\phi_{n+1} - 2\phi_n + \phi_{n-1})}{d^2} + V_A \sin \phi_n = 0, \quad (12)$$

where  $d = \alpha_A b$ . Further, transformation (11) will be called an A-transformation.

Then Eq. (12) can be rewritten as follows:

$$\left. \begin{aligned} & \frac{M_A R_A^2 \beta_A^2}{C_A \left(\frac{\Phi_0}{2\pi}\right)^2} \left\{ C_A \left(\frac{\Phi_0}{2\pi}\right)^2 \frac{d^2 \phi_n}{d\tau^2} - \left[ \frac{K R_A^2}{M_A R_A^2 \beta_A^2} C_A L_A \right] \frac{d^2 \left(\frac{\Phi_0}{2\pi}\right)^2 (\phi_{n-1} - 2\phi_n + \phi_{n+1})}{d^2} + \right. \\ & \left. C_A \left(\frac{\Phi_0}{2\pi}\right)^2 \left\{ + \left[ \frac{V_A}{M_A R_A^2 \beta_A^2} \frac{C_A}{J_{0A}} \left(\frac{\Phi_0}{2\pi}\right) \right] J_{0A} \left(\frac{\Phi_0}{2\pi}\right) \sin \phi_n \right\} \right\} = 0. \end{aligned} \quad (13)$$

As a next step, let us require all expressions enclosed in square brackets to be equal to one:

$$\left[ \frac{V_A}{M_A R_A^2 \beta_A^2} \frac{C_A}{J_{0A}} \left(\frac{\Phi_0}{2\pi}\right) \right] = 1, \quad \left[ \frac{K R_A^2}{M_A R_A^2 \beta_A^2} C_A L_A \right] = 1. \quad (14)$$

As a result, Eq. (1) transforms up to a constant coefficient into Eq. (9):

$$A \left\{ C_A \left(\frac{\Phi_0}{2\pi}\right)^2 \frac{d^2 \phi_n}{d\tau^2} - \frac{d^2 \left(\frac{\Phi_0}{2\pi}\right)^2 (\phi_{n-1} - 2\phi_n + \phi_{n+1})}{d^2} + J_{0A} \left(\frac{\Phi_0}{2\pi}\right) \sin \phi_n \right\} = 0, \quad (15)$$

where  $A = \frac{M_A R_A^2 \beta_A^2}{C_A \left(\frac{\Phi_0}{2\pi}\right)^2}$ . At the same time, Hamiltonian (2) transforms into Hamiltonian (10) up to the

same constant:

$$H_A^{\text{DNA}} = A \sum_n \left[ C_A \left(\frac{\Phi_0}{2\pi}\right)^2 \frac{d^2 \phi_n}{d\tau^2} - \frac{d^2 \left(\frac{\Phi_0}{2\pi}\right)^2 (\phi_{n-1} - 2\phi_n + \phi_{n+1})}{d^2} + J_{0A} \left(\frac{\Phi_0}{2\pi}\right) (1 - \cos \phi_n) \right]. \quad (16)$$

From formulas (14) we find:

$$\beta_A = \sqrt{C_A L_A \frac{K}{M_A}}, \quad (17)$$

$$J_{0A} = \frac{V_A}{K R_A^2} \frac{\left(\frac{\Phi_0}{2\pi}\right)}{L_A}. \quad (18)$$

If we take:  $L_A = 10 \mu\text{H}$  (or  $10^{-5} \text{ J/A}^2$ ),  $C_A = 0.1 \text{ nF}$  (or  $10^{-10} \text{ A}^2 \text{ s}^2/\text{J}$ ) and  $\Phi_0 \cong 2.68 F W b$  (or  $2.068 \times 10^{-15} \text{ J/A}$ ), then according to formula (18) the Josephson current becomes equal

to  $J_{0A} \cong 2.99nA$  (or  $2.99 \times 10^{-12}$  A), and the transformation coefficient calculated by formula (16) becomes equal to  $\beta_A = 1.728 \times 10^5$ . If we take the size of the circuit cell  $d = 8 \mu\text{m}$  ( $8 \times 10^{-6}$  m), then the second transformation coefficient becomes equal to  $\alpha_A = \frac{d}{b} = 2.353 \times 10^4$ .

### 3. Modeling an electronic analogue of inhomogeneous DNA

#### 3a. Generalization of the method of A-transformation

Consider the inhomogeneous DNA molecule the sequence of which contains four types of non-identical bases: adenines, thymines, guanines and cytosines. The internal mobility of the molecule including the open states dynamics can be described in the following way [Grinevich et al., 2015]:

$$I_n \frac{d^2 \phi_n}{dt^2} - KR_n d^2 \frac{(R_{n+1} \phi_{n+1} - 2R_n \phi_n + R_{n-1} \phi_{n-1})}{d^2} + V_n \sin \phi_n = 0. \quad (19)$$

Applying the A-transformation (11) to Eq. (19), we obtain:

$$I_n \beta_A^2 \frac{d^2 \phi_n}{d\tau^2} - KR_n d^2 \frac{(R_{n+1} \phi_{n+1} - 2R_n \phi_n + R_{n-1} \phi_{n-1})}{d^2} + V_n \sin \phi_n = 0. \quad (20)$$

After several simple equivalent transformations, Eq. (20) takes the following form:

$$\frac{I_n \beta_A^2}{C_n \left( \frac{\Phi_0}{2\pi} \right)} \left\{ \begin{aligned} & C_n \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 \phi_n}{d\tau^2} - \left[ C_n \frac{KR_n R_{n+1} L_n}{I_n \beta_A^2} \right] L_n \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 (\phi_{n+1})}{d^2} - \\ & - \left[ C_n \frac{KR_n R_n L_n}{I_n \beta_A^2} \right] L_n \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 (-2\phi_n)}{d^2} - \left[ C_n \frac{KR_n R_{n-1} L_n}{I_n \beta_A^2} \right] L_n \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 (\phi_{n-1})}{d^2} + \\ & + \left[ C_n \left( \frac{\Phi_0}{2\pi} \right) \frac{V_n}{I_n \beta_A^2} \frac{1}{J_{0n}} \right] J_{0n} \sin \phi_n \end{aligned} \right\} = 0. \quad (21)$$

Let us require all the expressions in square brackets in Eq. (21) to be equal to one:

$$\left[ C_n \frac{KR_n R_n L_n}{I_n \beta_A^2} \right] = 1, \quad \left[ C_n \left( \frac{\Phi_0}{2\pi} \right) \frac{V_n}{I_n \beta_A^2} \frac{1}{J_{0n}} \right] = 1. \quad (22)$$

Then Eq. (21) and the corresponding Hamiltonian take the following form:

$$\frac{I_n \beta_A^2}{C_n \left( \frac{\Phi_0}{2\pi} \right)} \left\{ C_n \left( \frac{\Phi_0}{2\pi} \right) \frac{d^2 \phi_n}{d\tau^2} - \frac{d^2 (\phi_n)}{L_n \left( \frac{\Phi_0}{2\pi} \right) R_n} \frac{1}{d^2} [R_{n+1} \phi_{n+1} - 2R_n \phi_n + R_{n-1} \phi_{n-1}] + J_{0n} \sin \phi_n \right\} = 0. \quad (23)$$

$$H_{inhom}^{El} = \frac{I_n \beta_A^2}{C_n \left( \frac{\Phi_0}{2\pi} \right)^2} \left[ \sum_n \left\{ \frac{1}{2} C_n \left( \frac{\Phi_0}{2\pi} \right)^2 \left( \frac{d\phi_n}{d\tau} \right)^2 - \frac{1}{2} \frac{d^2 (\phi_n)}{R_n \left( \frac{\Phi_0}{2\pi} \right)^2} \frac{(R_n \phi_n - R_{n-1} \phi_{n-1})^2}{d^2} + \right. \right. \\ \left. \left. + J_{0n} \left( \frac{\Phi_0}{2\pi} \right) (1 - \cos \phi_n) \right\} \right]. \quad (24)$$

From (22) we find:

$$\beta_A^2 = L_n C_n \frac{K}{M_n}, \quad J_{0n} = \left( \frac{\Phi_0}{2\pi} \right) \frac{1}{L_n} \frac{V_n}{KR_n^2}. \quad (25)$$

The requirement of invariance of the coefficient in front of curly brackets in (24), with respect to the number  $n$  gives an additional condition:

$$\frac{I_n \beta_A^2}{C_n \left(\frac{\Phi_0}{2\pi}\right)^2} = \frac{I_{n-1} \beta_A^2}{C_{n-1} \left(\frac{\Phi_0}{2\pi}\right)^2}. \quad (26)$$

From (22) and (26) we find:

$$L_{n-1} = L_n \frac{R_n^2}{R_{n-1}^2}. \quad (27)$$

Then Eq. (23) and Hamiltonian (24) take the following form:

$$\frac{I_n \beta_A^2}{C_n \left(\frac{\Phi_0}{2\pi}\right)^2} \left\{ C_n \left(\frac{\Phi_0}{2\pi}\right) \frac{d^2 \phi_n}{d\tau^2} - \frac{d^2}{\sqrt{L_n}} \left(\frac{\Phi_0}{2\pi}\right) \left( \frac{1}{\sqrt{L_{n+1}}} \phi_{n+1} - 2 \frac{1}{\sqrt{L_n}} \phi_n + \frac{1}{\sqrt{L_{n+1}}} \phi_{n-1} \right) + J_{0n} \sin \phi_n \right\} = 0, \quad (28)$$

$$H_{in\text{hom}}^{El} = \frac{I_n \beta_A^2}{C_n \left(\frac{\Phi_0}{2\pi}\right)^2} \left[ \sum_n \left\{ \frac{1}{2} C_n \left(\frac{\Phi_0}{2\pi}\right)^2 \left(\frac{d\phi_n}{d\tau}\right)^2 - \frac{1}{2} d^2 \frac{1}{\sqrt{L_n}} \left(\frac{\Phi_0}{2\pi}\right)^2 \left( \frac{1}{\sqrt{L_n}} \phi_n - \frac{1}{\sqrt{L_{n-1}}} \phi_{n-1} \right)^2 + \left[ J_{0n} \left(\frac{\Phi_0}{2\pi}\right) (1 - \cos \phi_n) \right] \right\} \right]. \quad (29)$$

### 3b. Equivalent circuit for electronic model of inhomogeneous DNA

Let us apply the results obtained above to construct an electronic analogue of inhomogeneous DNA. In other words let us construct an equivalent circuit of the non-uniform Josephson line that contains four types of cells: A-, T-, G-, and C-cells, by analogy with the four types of bases (A, T, G, and C) in the DNA sequence. The location of the cells in the line should be the same as the location of the nitrogenous bases in the DNA sequence.

Without loss of generality, let us take the DNA sequence shown in Fig. 3, *a*. To construct the equivalent circuit, it is necessary to take the capacitance  $C_A$ , the inductance  $L_A$ , the Josephson contact with maximum current  $J_{0A}$ , and place them in the  $(n-1)$ -th circuit cell. Then we need to take the capacitance  $C_T$ , the inductance  $L_T$ , the Josephson contact with maximum current  $J_{0T}$ , and place them in the  $n$ -th cell. Continuing the circuit building in a similar way we obtain the desired equivalent circuit (Fig. 3, *b*). It remains only to calculate the values of the circuit parameters.

Three of the circuit parameters:  $C_A$ ,  $L_A$ , and  $J_{0A}$ , have been estimated already in the previous section. To calculate the other nine parameters, let us use formulas (25) and (27) and the data on the parameters of the inhomogeneous DNA gathered in Table 2.

Table 2. Parameters of inhomogeneous DNA [Yakushevich, 2017]

Type of the $n$ -th base in the DNA sequence	$I_n \times 10^{-44}$ (kg·m <sup>2</sup> )	$M_n \times 10^{-25}$ (kg)	$R_n \times 10^{-10}$ (m)	$K$ (J/m <sup>2</sup> )	$b \times 10^{-10}$ (m)	$V_n \times 10^{-20}$ (J)
A	7.61	2.26	5.8	6.75	3.4	2.09
T	4.86	2.11	4.8	6.75	3.4	1.43
G	8.22	2.53	5.7	6.75	3.4	3.12
C	4.11	1.86	4.7	6.75	3.4	2.12

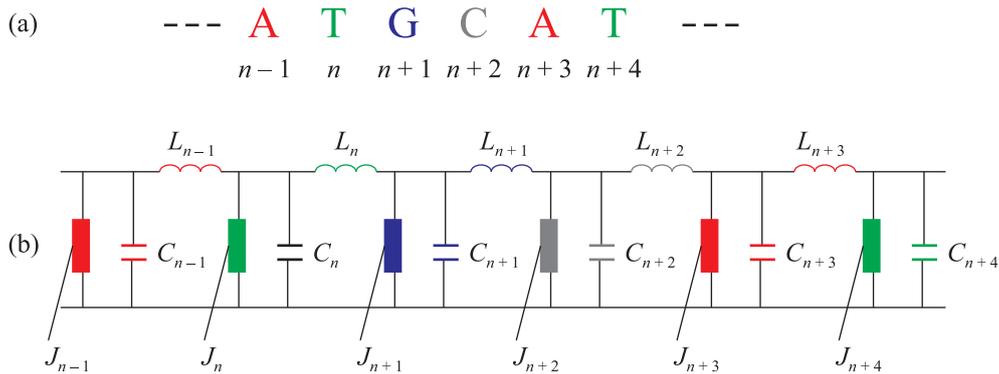


Fig. 3. DNA sequence (a) and corresponding equivalent circuit of the DNA electronic analogue (b)

As a result, we obtain analytical formulas for the other nine circuit parameters:

$$C_T = C_A \frac{I_A}{I_T}, \quad C_G = C_A \frac{I_A}{I_G}, \quad C_C = C_A \frac{I_A}{I_C}, \tag{30}$$

$$L_T = L_A \frac{R_A^2}{R_T^2}, \quad L_G = L_A \frac{R_A^2}{R_G^2}, \quad L_C = L_A \frac{R_A^2}{R_C^2}, \tag{31}$$

$$J_{0T} = \frac{C_T V_T I_A}{C_A V_A I_T} J_{0A}, \quad J_{0G} = \frac{C_G V_G I_A}{C_A V_A I_G} J_{0A}, \quad J_{0C} = \frac{C_C V_C I_A}{C_A V_A I_C} J_{0A} \tag{32}$$

and the estimated values of these parameters that are shown in Table 3.

Table 3. Parameters of the equivalent circuit

Type of the $n$ -th circuit cell	$C_n \times 10^{-10}$ ( $\text{A}^2 \text{c}^4 / \text{kg m}^2$ )	$L_n \times 10^{-5}$ ( $\text{kg m}^2 / \text{c}^2 \text{A}^2$ )	$J_{0n} \times 10^{-11}$ ( $\text{kg} \cdot \text{m}^2$ )	$\Phi_0 \times 10^{-15}$ ( $\text{kg m}^2 / \text{c}^2 \text{A}$ )	$d \times 10^{-6}$ (m)
A	1.000	1.000	0.299	2.068	8
T	1.564	1.460	0.500	2.068	8
G	0.926	1.035	0.382	2.068	8
C	1.852	1.523	1.040	2.068	8

### 4. Discussion

In this article, we generalized the proposed earlier approach to construct an electronic model of inhomogeneous DNA. The model was the non-uniform Josephson line with the equivalent circuit containing four types of cells: A-, T-, G-, and C-cells, which were arranged in a specific order which is similar to that of nitrous bases (A, T, G, and C) in the DNA sequence. We obtained the analytical formulas determining the relationship between the parameters of inhomogeneous DNA and the parameters of the electronic model, and estimated their values.

The advantage of the proposed electronic model is its simplicity, compactness and cheapness. The model can be used to investigate various dynamic regimes that can occur in DNA under various initial and boundary conditions. As a result of these investigations, new interesting solutions of the model nonlinear equations could be found.

It should be noted, however, some limitations of our approach. Most of them were due to the desire to simplify calculations. So, when describing mathematically the DNA internal mobility molecule we took into account only one type of the DNA internal motions — the angular oscillations of nitrous bases in one of two polynucleotide chains. The second chain was modeled only as an averaged field. Our mathematical description did not also include the interaction of angular vibrations of bases

with other degrees of freedom, and, in particular, with transverse and longitudinal motions of nucleotides. We did not take into account the helical nature of the DNA structure. At least, we did not include effects of dissipations although this was not difficult to do by inserting resistances into the cells of the equivalent circuit.

It is obvious that removing these restrictions will complicate the task of construction of the DNA electronic analogue. We believe, however, that the basic principles and approaches described above can be successfully applied in the cases of more complex and accurate mathematical descriptions of the DNA internal mobility.

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