DNA as a Nonlinear Dynamical System

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SUMMARY: DNA is considered as a nonlinear dynamical system where internal motions of large amplitudes are possible. A short description of the history, results and perspectives of mathematical modeling one of the internal motions named local unwinding of the double helix, are discussed. A new mathematical model of the process of local unwinding, which consists of four nonlinear differential equations, is presented.

Introduction

In contradistinction to usual polymers the molecule of deoxyribonucleic acid (DNA) consists of two polymer chains (Fig. 1). The chains weakly interact with one another through hydrogen

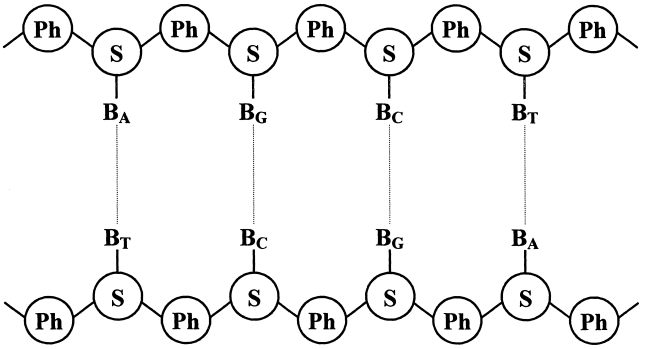

Fig.1. Two polynucleotide chains of DNA. **Ph** is a phosphate group, **S** is a sugar, $\mathbf{B_A}$, $\mathbf{B_T}$, $\mathbf{B_G}$ and $\mathbf{B_C}$ are bases (adenine, thymine, guanine and cytosine). Interactions between polynucleotide chains are shown by dotted lines.

bonds, and they are wound around each other to form the double helix (Fig. 2a). This structure discovered by Watson and Crick [1-2], is not, however, static. On the contrary, the molecule of DNA is a substantially dynamical system where many types of internal motions are possible [3-4]. Some of the motions have large amplitudes, and to model them mathematically investigators are to use the methods of nonlinear mathematics. Local unwinding of the double helix (Fig. 2b) belongs to this group of motions, and we consider mathematical modeling the motion in details. Some authors name this motion "the formation of open state". And an

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ability of DNA to form open states is often named by biologists as an ability of the DNA structure "to breath".

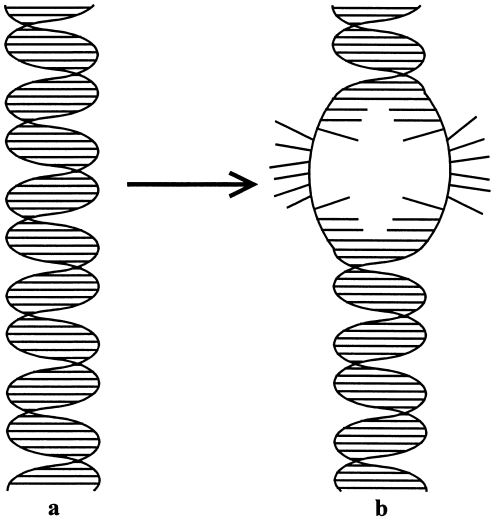

Fig. 2. Local unwinding of the double helix. Schematic picture of a fragment of the double helix without open state (a) and a fragment of DNA with one open state (b).

Why this internal motion attracts attention of investigators? The answer is: because of the important role which it plays in the DNA functioning. Indeed, it is widely accepted that the process of DNA-protein recognition includes the formation of open state to have a possibility to "recognize" the sequence of bases. Local unwinding is also an important element of the process of binding RNA-polymerase with promoter regions at the beginning of the process of transcription. Formation of open states is known as important part of process of DNA melting.

How this internal motion can be activated? We should say that there are several suggestions. Some investigators suggest that local unwinding of the double helix can be formed due to fluctuations which can occur in DNA at room temperature. Some other investigators suppose that open states can appear due to collisions of DNA with "hot" molecules of the solution. It seems also that local unwinding of DNA can be activated by external fields. At least, local unwinding can be activated by the binding of a protein molecule with a DNA site.

How this motion could be described mathematically? The first nonlinear model of the internal DNA dynamics was proposed by Englander and co-authors in 1980 [5)] . They suggested that

the rotations of bases around sugar-phosphate chains made the main contribution to the local unwinding of the double helix, and proposed to use the dynamical equations describing the rotations as a mathematical model. The improved variant of the equations proposed later by Yomosa [6] and Takeno, Homma [7], has the form

$$I_1 (d^2\Theta_1/dt^2) - K_1R^2_0 a^2 (\partial^2\Theta_1/\partial z^2) + kR_0^2 [2 \sin\Theta_1 - \sin(\Theta_1 - \Theta_2)] = 0;$$
$$I_2 (d^2\Theta_2/dt^2) - K_2R^2_0 a^2 (\partial^2\Theta_2/\partial z^2) + kR_0^2 [2 \sin\Theta_2 - \sin(\Theta_2 - \Theta_1)] = 0; \quad (1)$$

where Θ_1 and Θ_2 are the angles of rotations of bases around the sugar-phosphate chains; I_1 and I_2 are the moments of inertia of bases; K_1 and K_2 are the coefficients of rigidity of the chains; k is the coefficient of rigidity of the hydrogen bonds; R_0 is the radius of DNA; a is the distance between bases along the chains. Later Barbi and co-authors [8] showed that equations describing rotations of nucleotides around the main DNA axis during the process of local unwinding have the same mathematical form but some other parameters. Kink (and antikink) solutions of equations (1) were interpreted as those describing local distortions of the DNA structure having the form of open states [9-11]. The solutions were applied to explain experimental data on hydrogen-tritium exchange [5], neutron scattering [12-13], effects of dissipation and external fields [14], functioning [15-16].

There is, however, another approach to the modeling of the dynamics of open states. It is based on the assumption that transverse motions of nucleotides (instead of the rotation motions of bases) make the main contribution to formation of open states. The approach was developed by Peyrard and co-authors [17-18] who showed an important role of transverse motions in the process of DNA denaturation. The model of Peyrard and coauthors consists of two coupled equations

$$m (d^2u/dt^2) - K [a^2 \partial^2u/\partial z^2] + \partial V/\partial u = 0;$$
$$m (d^2v/dt^2) - K [a^2 \partial^2v/\partial z^2] + \partial V/\partial v = 0; \quad (2)$$

describing the transverse motions in DNA. Here u and v are transverse displacements of nucleotides; m is a common mass of nucleotides; K is the coupling constant along each strand; a is the distance between neighboring base pairs; V is the Morse potential

$$V = D\{\exp[-A(u - v)] - 1\}^2 \quad (3)$$

representing the two or three hydrogen bonds which connect the two bases in a pair

A more accurate description of local unwinding of the double helix should include both types of internal motions: rotational motions of the bases around the sugar-phosphate chains and transverse motions along the hydrogen bonds. So, we can expect that corresponding mathematical model will consist of four coupled nonlinear equations: two for rotational motions and two for transverse ones. Below we discuss how these equations can be obtained.

Mathematical model of the local unwinding of DNA

To construct the model hamiltonian it is convenient to begin with discreet case and then to pass to continuos one. The discreet version of the model hamiltonian can be constructed as a combination of two more simple and well known hamiltonians: the hamiltonian describing torsion motions

$$H_{tors.} = \Sigma_n\{mR_0^2(\Theta_{n,1}^2 + \Theta_{n,2}^2)/2\}+\Sigma_n\{KR_0^2(\Theta_{n,1} - \Theta_{n-1,1})^2/2 + KR_0^2(\Theta_{n,2} - \Theta_{n-1,2})^2/2 + + kR_0^2[2(1 - \cos\Theta_{n,1}) + 2((1 - \cos\Theta_{n,2}) - (1-\cos(\Theta_{n,1} - \Theta_{n,2}))]\} \quad (4)$$

and the hamiltonian describing transverse motions

$$H_{transv.} = \Sigma_n\{[m(du_n/dt)^2 + m(dv_n/dt)^2]/2\}+ \Sigma_n K[(u_n - u_{n-1})^2/2 + (v_n - v_{n-1})^2/2] + + \Sigma_n V(u_n - v_n) \quad (5)$$

As a first step let us generalize the model hamiltonian (5) by rewriting it in a vector form

$$H_{general.} = \Sigma_n[m(d\mathbf{U}_{n,1}/dt)^2 + m(d\mathbf{U}_{n,2}/dt)^2]/2 +\Sigma_n K[|\mathbf{U}_{n,1} - \mathbf{U}_{n-1,1}|^2/2 + + |\mathbf{U}_{n,2} - \mathbf{U}_{n-1,2}|^2/2] + \Sigma_n V(|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|) \quad (6)$$

where $\mathbf{U}_{n,i}(t)$ is the displacement vector of the n-th base of the i-th chain and V is the potential

$$\mathbf{U}_{n,1} = \{u_n; 0; 0\}; \mathbf{U}_{n,2} = \{v_n; 0; 0\}); V(|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|) = D\{\exp[-a|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|] - 1\}^2 \quad (7)$$

As a second step let us generalize hamiltonian (4) by rewriting it in a vector form

$$H = \Sigma_n[m(d\mathbf{U}_{n,1}/dt)^2 + m(d\mathbf{U}_{n,2}/dt)^2]/2 + \Sigma_n K[|\mathbf{U}_{n,1} - \mathbf{U}_{n-1,1}|^2/2 + |\mathbf{U}_{n,2} - \mathbf{U}_{n-1,2}|^2/2] + + \Sigma_n k|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|^2/2 \quad (8)$$

Here $\mathbf{U}_{n,i}$ (t) is the displacement vector of the n-th base of the i-th chain

$$\mathbf{U}_{n,1} = \{ R_0 (1 - \cos\Theta_{n,1}); -R_0 \sin\Theta_{n,1}; 0\}$$
$$\mathbf{U}_{n,2} = \{-R_0 (1 - \cos\Theta_{n,2}); \ R_0 \sin\Theta_{n,2}; 0\} \qquad (9)$$

Note that hamiltonian (8) contains the term

$$\Sigma_n k |\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|^2 /2 \qquad (10)$$

which can be considered as a first term in the expansion of the potential $V(|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|)$. Indeed, if we take the potential function in the form

$$V(|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|) = D\{\exp[-a |\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|] - 1\}^2 \qquad (11)$$

and expand (11)

$$V(|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|) = D\{a |\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|\}^2 + ... = 2Da^2|\mathbf{U}_{n,1} - \mathbf{U}_{n,2}|^2 /2 + ..., \qquad (12)$$

we obtain that (10) is the first term of expansion (12), and that in this case $k = 2Da^2$.

From the analysis of the hamiltonians written above we can make an important conclusion: vector hamiltonian (6) (or its more simple variant (8)) is valid for modeling both types of internal motions: transverse motions (when torsional motions are absent) and torsional motions (when transverse motions are absent). In other words the vector hamiltonian is invariant, and only vectors $U_{n,i}$ are changing when we are passing from one type of internal motions to the other.

A remarkable consequence of the result is that it gives us a possibility to construct the so-called combined model which takes into account both the transverse and the torsional motions. Indeed, let us assume that combined model has the form (6) (or (8)) with vectors $\mathbf{U}_{n,i}$

$$\mathbf{U}_{n,1} = \{R_0 (1 - \cos\Theta_{n,1}) + u_{n,1} \cos\Theta_{n,1} \ ; - R_0 \sin\Theta_{n,1} + u_{n,1} \sin\Theta_{n,1}; 0\}$$
$$\mathbf{U}_{n,2} = \{- R_0 (1 - \cos\Theta_{n,2}) + u_{n,2} \cos\Theta_{n,2} \ ; \ R_0 \sin\Theta_{n,2} + u_{n,2} \sin\Theta_{n,2}; 0\} \qquad (13)$$

which include both transverse and torsional displacements. Here $u_{n,1} = u_n$; $u_{n,2} = v_n$.

Inserting (13) into (8) we obtain the hamiltonian for combined model

$$H = (m/2)\,\Sigma_n \{[\,(du_{n,1}/dt)^2 + (R_0 - u_{n,1})^2\,(d\Theta_{n,1}/dt)^2] +$$
$$+ [(du_{n,2}/dt)^2 + (R_0 + u_{n,2})^2\,(d\Theta_{n,2}/dt)^2]\} +$$
$$+ (K/2)\,\Sigma_n \{[\,2R^2_0\,[1 - \cos(\Theta_{n,1} - \Theta_{n-1,1})] + u^2_{n,1} + u^2_{n-1,1} - 2\,u_{n,1}\,u_{n-1,1}\cos(\Theta_{n,1} - \Theta_{n-1,1}) -$$
$$-2\,R_0\,u_{n,1}\,[1 - \cos(\Theta_{n,1} - \Theta_{n-1,1})] - 2\,R_0\,u_{n-1,1}\,[1 - \cos(\Theta_{n,1} - \Theta_{n-1,1})]]$$
$$+ [2R^2_0\,[1 - \cos(\Theta_{n,2} - \Theta_{n-1,2})] + u^2_{n,2} + u^2_{n-1,2} - 2\,u_{n,2}\,u_{n-1,2}\cos(\Theta_{n,2} - \Theta_{n-1,2}) +$$
$$+ 2\,R_0\,u_{n,2}\,[1 - \cos(\Theta_{n,2} - \Theta_{n-1,2})] + 2\,R_0\,u_{n-1,2}\,[1 - \cos(\Theta_{n,2} - \Theta_{n-1,2})]]\} +$$
$$+ (k/2)\,\Sigma_n \{[\,2R_0^2\{(1 - 2\cos\Theta_{n,1}) + (1 - 2\cos\Theta_{n,2}) + [1 + \cos(\Theta_{n,1} - \Theta_{n,2})]\}\} +$$
$$- 2R_0\,u_{n,1}\,(1 - 2\cos\Theta_{n,1}) + 2R_0\,u_{n,2}\,(1 - 2\cos\Theta_{n,2}) +$$
$$+ u_{n,1}{}^2 + u^2_{n,2} - 2\,u_{n,1}\,u_{n,2}\cos(\Theta_{n,1} - \Theta_{n,2}) +$$
$$- 2R_0\,u_{n,1}\cos(\Theta_{n,1} - \Theta_{n,2}) + 2R_0\,u_{n,2}\cos(\Theta_{n,1} - \Theta_{n,2})]\} \qquad (14)$$

To simplify calculations, we used here formula (8) instead of (6). It is convenient also to introduce new variables

$$f_{n,1} = u_{n,1}/R_0;\quad f_{n,2} = -u_{n,2}/R_0;\quad \Psi_{n,1} = \Theta_{n,1};\quad \Psi_{n,2} = -\Theta_{n,2} \qquad (15)$$

Then the final form for the model hamiltonian is

$$H = H(f) + H(\Psi) + H(\text{interact.}) \qquad (16)$$

where

$$H(f) = (m\,R^2_0/2)\,\Sigma_n\,(df_{n,1}/dt)^2 + (m\,R^2_0/2)\,\Sigma_n\,(df_{n,2}/dt)^2 + (K\,R^2_0/2)\,\Sigma_n\,(f_{n,1} - f_{n-1,1})^2 +$$
$$+ (K\,R^2_0/2)\,\Sigma_n\,(f_{n,2} - f_{n-1,2})^2 + (k\,R^2_0/2)\,\Sigma_n\,(f_{n,1} + f_{n,2})^2 \qquad (17)$$

$$H(\Psi) = (m\,R^2_0/2)\,\Sigma_n\,(d\Psi_{n,1}/dt)^2 + (m\,R^2_0/2)\,\Sigma_n\,(d\Psi_{n,2}/dt)^2 +$$
$$+ (KR^2_0)\,\Sigma_n\,[1 - \cos(\Psi_{n,1} - \Psi_{n-1,1})] + + (KR^2_0)\,\Sigma_n\,[1 - \cos(\Psi_{n,2} - \Psi_{n-1,2})] +$$
$$+ (kR_0^2)\,\Sigma_n\,\{2\,(1 - \cos\Psi_{n,1}) + 2\,(1 - \cos\Psi_{n,2}) - [1 - \cos(\Psi_{n,1} + \Psi_{n,2})]\} \qquad (18)$$

$$H(\text{interact.}) = (m\,R^2_0/2)\,\Sigma_n\,(-2\,f_{n,1} + f^2_{n,1})\,(d\Psi_{n,1}/dt)^2 +$$
$$+ (m\,R^2_0/2)\,\Sigma_n\,(-2f_{n,2} + f_{n,2}{}^2)(d\Psi_{n,2}/dt)^2 +$$
$$+ (K\,R^2_0)\,\Sigma_n\,[1 - \cos(\Psi_{n,1} - \Psi_{n-1,1})]\,[f_{n,1}\,f_{n-1,1} - f_{n-1,1} - f_{n,1}] +$$
$$+ (K\,R^2_0)\,\Sigma_n\,[1 - \cos(\Psi_{n,2} - \Psi_{n-1,2})]\,[f_{n,2}\,f_{n-1,2} - f_{n,2} - f_{n-1,2}] -$$

$$- (2k R^2_0) \Sigma_n (f_{n,1}) (1 - \cos\Psi_{n,1}) - (2k R^2_0)\Sigma_n (f_{n,2}) (1 - \cos\Psi_{n,2}) +$$
$$+ (k R^2_0) \Sigma_n (-f_{n,1} f_{n,2} + f_{n,1} + f_{n,2})[1 - \cos(\Psi_{n,1} + \Psi_{n,2})] \qquad (19)$$

Here H(f) is a part of the model hamiltonian which describes only transverse displacements; H(Ψ) is a part of the model hamiltonian which describes only torsional displacements; H(interact.) is a part of the model hamiltonian which describes interaction between these two types of motions.

In the continuous approximation the model hamiltonian takes the form

$$H = H(f) + H(\Psi) + H_{int.} =$$
$$= (\rho_m R^2_0/2) \int dz [(\partial f_1/\partial t)^2 + (\partial f_2/\partial t)^2] + (Y R^2_0/2) \int dz [(\partial f_1/\partial z)^2 + (\partial f_2/\partial z)^2] +$$
$$+ (y R^2_0/2) \int dz (f_1 + f_2)^2 + (\rho_m R^2_0/2) \int dz [(1- f_1)^2 (\partial\Psi_1/\partial t)^2 + (1- f_2)^2(\partial\Psi_2/\partial t)^2] +$$
$$+ (Y R^2_0/2) \int dz [(1- f_1)^2 (\partial\Psi_1/\partial z)^2 + (1- f_2)^2 (\partial\Psi_2/\partial z)^2] +$$
$$+ (y R_0^2) \int dz \{2 (1-f_1) (1 - \cos\Psi_1) +$$
$$+ 2 (1-f_2) (1 - \cos\Psi_2) + (-f_1 f_2 + f_1 + f_2 - 1) [1 - \cos(\Psi_1 + \Psi_2)]\} \qquad (20)$$

where m/a = ρ_m; Ka = Y; k/a = y. And the four dynamical equations which we expected to find take the form

$$\rho_m (d^2 f_1/dt^2) + \rho_m (1- f_1) (d\Psi_1/dt)^2 = Y \partial^2 f_1/\partial z^2 + Y (\partial\Psi_1/\partial z)^2 (1 - f_1) -$$
$$- y (f_1 + f_2) + 2y (1 - \cos\Psi_1) - y (1 - f_1) [1 - \cos(\Psi_1 + \Psi_2)] \qquad (21)$$

$$\rho_m (d^2 f_2/dt^2) + \rho_m (1- f_2) (d\Psi_2/dt)^2 = Y \partial^2 f_2/\partial z^2 + Y (\partial\Psi_2/\partial z)^2 (1 - f_2) -$$
$$- y (f_1 + f_2) + 2y (1 - \cos\Psi_2) - y (1 - f_2) [1 - \cos(\Psi_1 + \Psi_2)] \qquad (22)$$

$$\rho_m (1 - f_1) (d^2\Psi_1/dt^2) - 2\rho_m (df_1/dt) (d\Psi_1/dt) = Y (\partial^2\Psi_1/\partial z^2) (1- f_1) -$$
$$- 2Y (\partial\Psi_1/\partial z) [\partial f_1/\partial z] - 2y \sin\Psi_1 + y (1 - f_1) \sin(\Psi_1 + \Psi_2) \qquad (23)$$

$$\rho_m (1 - f_2) (d^2\Psi_2/dt^2) - 2\rho_m (df_2/dt) (d\Psi_2/dt) = Y (\partial^2\Psi_2/\partial z^2) (1- f_2) -$$
$$- 2Y (\partial\Psi_2/\partial z) [\partial f_2/\partial z] - 2y \sin\Psi_2 + y (1 - f_1) \sin(\Psi_1 + \Psi_2) \qquad (24)$$

Conclusion

A short history of mathematical modeling of local unwinding of the double helix, has been described. The method of constructing a new combined model has been presented and corresponding mathematical equations have been obtained..

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