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MECHANICAL ANALOG OF THE DNA BASE PAIR OSCILLATIONS

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Abstract: In this work we study rotational oscillations of two coupled DNA bases that form a base pair: adenine-thymine (AT) or guanine-cytosine (GG). We show that the problem can be reduced to the mechanical problem of two coupled unequal nonlinear pendulums oscillating in the horizontal plane. We obtain the Lagrange equations and estimate the values of the coefficients of the equations. We consider in details the case of small amplitudes of angular displacements and find the general solution of corresponding Lagrange equations.

1. Introduction

It is widely accepted now that the structure of the DNA molecule is not static, but dynamic. Among other internal motions rotational oscillations of the DNA bases around the sugar-phosphate chains are of special interest because they make an important contribution to the process of the opening of the DNA base pairs that in turn plays a crucial role in the process of DNA-protein recognition. Therefore, analysis of the DNA bases oscillations helps to understand better the dynamical mechanisms of biological activity of the DNA molecule.

In this work we study rotational oscillations of two coupled bases forming one of two possible DNA base pairs: adenine-thymine (AT) or guanine-cytosine (GG). The approach is based on the analogy between the rotational oscillations of the DNA bases (Fig.1a) and oscillations of nonlinear pendulums (Fig. 1b) which are well known and studied in mathematics and physics (see, for example [1, 2]).

The analogy has been noticed and used in the work of Englander and coauthors [3], and then the idea was widely spread among the investigators dealing with the internal DNA dynamics [4-7]. According to Englander's approach, oscillations of bases in one of two DNA chains can be imitated by the mechanical model consisting of horizontal chain of pendulums. Interaction between the DNA chains is approximately modeled by a constant field, which is an analog of the gravitational field in the mechanical modeling. Equation that governs oscillations of the pendulums has the form of the

sine-Gordon equation. However, an application of the Englander's model to DNA is not sufficiently correct, because the model does not take into account: (i) oscillations of bases in the second chain and (ii) interactions between the chains. Although the mentioned oscillations have been taken into account in the references [8-10], but the bases in both DNA chains have been suggested to be identical. This limitation has been removed in the work [11], where an empirical formula has been used to describe interaction between bases in pairs. One of the ways to improve the formula consists in constructing a more accurate mechanical analog a pair of DNA bases: AT or GC.

In this work we are aimed proposing the mechanical analog to overcome the deficiencies of the previous models. We apply this mechanical model to consider in details rotational oscillations of an DNA fragment consisting of only one base pair: adenine-thymine (AT) or guanine-cytosine (GG). Our paper consists of the following parts. In section 2 we describe the mechanical analog proposed, derive the function of Lagrange and corresponding equations of motion, and we estimate coefficients of the equations. In the next section we consider in details the case of small amplitudes. In the final section we discuss the results obtained.

2. Mechanical analog of the DNA base pair and equations of Lagrange.

In order to have a possibility to include into consideration the second DNA chain and to avoid the influence of gravitation field, a mechanical analog of DNA in the form of a vertical stack of horizontal planes with one pair of coupled pendulums on each of the planes is constructed. The pendulums interact with one another through a set of vertical and horizontal springs. In what follows we consider a fragment of the mechanical model consisting of only one base pair.

The function of Lagrange reads,

$$L = T - V = \frac{I_1}{2} \left(\frac{d\varphi_1}{dt} \right)^2 + \frac{I_2}{2} \left(\frac{d\varphi_2}{dt} \right)^2 - \frac{1}{2} K_{12} (l - a^*)^2,$$

where φ_1 and φ_2 are the angles of inclination of the 1-st and 2-nd pendulums; I_1 and I_2 are the moments of inertia of the 1-st and 2-nd pendulums; K_{12} and l are the rigidity and the length of the spring connecting the pendulums; a^* is the length of the spring in its relax state being less than the distance a (Fig. 3c) between masses of pendulums in the equilibrium state ($\varphi_2 = \varphi_1 = 0$). So, $l > a > a^*$. After taking into account approximation $a^* \ll l$, damping and general external force, corresponding equations of Lagrange take then the form:

$$I_1 \left(\frac{d^2\varphi_1}{dt^2} \right)^2 - \frac{1}{2} K_{12} [A_1 \sin \varphi_1 - B \sin(\varphi_1 + \varphi_2)] = -\beta \frac{d\varphi_1}{dt} + F, \quad (1)$$

$$I_2 \left(\frac{d^2\varphi_2}{dt^2} \right)^2 - \frac{1}{2} K_{12} [A_2 \sin \varphi_2 - B \sin(\varphi_1 + \varphi_2)] = -\beta \frac{d\varphi_2}{dt} + F, \quad (2)$$

where $A_1 = 2r_1(r_1 + r_2 + a)$, $A_2 = 2r_2(r_1 + r_2 + a)$, $B = 2r_1r_2$, and r_1, r_2 are the lengths of the first and of the second pendulums, respectively. In this case the system potential energy possesses the following form,

$$U(\varphi_1, \varphi_2) = \frac{1}{2} K_{12} [A_1(1 - \cos \varphi_1) + A_2(1 - \cos \varphi_2) - B(1 - \cos(\varphi_1 + \varphi_2)) + a^2]$$

3. Estimations of the coefficients values of equations (1) – (2) for AT and GC base pair.

Equations (1) – (2) contain coefficients characterizing both physical and geometrical properties of DNA. The values of first group of the coefficients have been estimated earlier in [12] (see Table 1.). Another (geometrical) group of coefficients (A_1, A_2, B , and a) estimated by us is presented in Table 2. The values of the coefficients β and F that are also presented in Table 2, are taken from reference [13].

i-th base	I_i [10^{-47} kg·m ²]	r_i [10^{-10} m]	i-th base	I_i [10^{-47} kg·m ²]	r_i [10^{-10} m]
A	7607,03	5,8	G	8217,44	5,7
T	4862,28	4,8	C	4106,93	4,7

Table 1. Values of the parameters

Base pair	A_1 [10^{-20} m ²]	A_2 [10^{-20} m ²]	B [10^{-20} m ²]	β [10^{-34} Js]	F [10^{-22} J]	a [10^{-10} m]
AT	208,8	172,8	55,68	4.25	3.12	7,4
GC	205,2	169,2	53,58	4.25	3.12	7,6

Table 2. Values of the coefficients.

The value of the coefficient K_{12} can be estimated with the help of condition of breaking the hydrogen bonds connecting bases in pairs and forming an open state. To find the condition, we suggest that the breaking of hydrogen occurs when the generalized force applied to one of the bases reaches its maximum value.

The generalized force (momentum) applied to the first base oscillator is equal to

$$M(\varphi_1, \varphi_2) = -\frac{1}{2} K_{12} [A_2 \sin \varphi_2 - B \sin(\varphi_1 + \varphi_2)]$$

Observe that the function $M(\varphi_1; \varphi_2)$ reaches in the $(-\pi, \pi) \times (-\pi, \pi]$ space maximum at the point $(-\pi/2, \pi)$. The value of potential energy at the maximum point is equal to

$U(\frac{-\pi}{2}, \pi) = \frac{1}{2} K_{12} \sqrt{A_1 + 2A_2 - B + 1}$, and hence the condition of breaking is governed by the following formula

$$\frac{1}{2} K_{12} \sqrt{A_1 + 2A_2 - B + 1} = \varepsilon_{12}, \quad (3)$$

where ε_{12} is the energy of interaction between bases in pairs (for the case of AT base pair $\varepsilon_{12} = \varepsilon_{AT} = 10$ kcal/mol = $0,695 \times 10^{-20}$ J; and for the case of GC base pair we have $\varepsilon_{12} = \varepsilon_{GC} = 15$ kcal/mol = $1,043 \times 10^{-20}$ J) [10]. Results of estimations of the coefficient K_{12} made with the help of formula (3) yields the value $2,51 \times 10^{-3}$ (N/ m) for AT base pair and $3,80 \times 10^{-3}$ (N/ m) for GC base pair.

4. Small amplitude oscillations.

In the case, when angular displacements $\varphi_1(t)$ and $\varphi_2(t)$ are small, the Lagrange equations (1) - (2) can be linearized and they take the form

$$I_1 \frac{d^2 \varphi_1}{dt^2} + \frac{1}{2} K_{12} [A_1 \varphi_1 - B(\varphi_1 + \varphi_2)] = -\beta \frac{d\varphi_1}{dt} + F, \quad (4)$$

$$I_2 \frac{d^2 \varphi_2}{dt^2} + \frac{1}{2} K_{12} [A_2 \varphi_2 - B(\varphi_1 + \varphi_2)] = -\beta \frac{d\varphi_2}{dt} + F, \quad (5)$$

4.1. Case I ($\beta=0$ and $F=0$).

Standard theory of oscillations [14] is used to find that the general solutions of linear ODE's (4), (5), and the read

$$\varphi_1(t) = \frac{A_{(-)}}{\sqrt{I_1}} \cos(\omega_{(-)}t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_1}} \cos(\omega_{(+)}t - \alpha_{(+)}),$$

$$\varphi_2(t) = \frac{A_{(-)}}{\sqrt{I_2}} \left[\frac{\omega_{(-)}^2 - a_1}{c} \right] \cos(\omega_{(-)}t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_2}} \left[\frac{\omega_{(+)}^2 - a_2}{c} \right] \cos(\omega_{(+)}t - \alpha_{(+)}).$$

Amplitudes $A_{(-)}$, $A_{(+)}$ and phases $\alpha_{(-)}$, $\alpha_{(+)}$ are constants to be determined by initial conditions; fundamental frequencies $\omega_{(-)}$, $\omega_{(+)}$ have the following form

$$\omega_{(\pm)} = \sqrt{\frac{(a_1 + a_2)}{2} \pm \sqrt{\frac{1}{4}(a_1 + a_2)^2 + c^2}},$$

where $a_1 = \frac{1}{2} K_{12} \frac{(A_1 - B)}{I_1}$, $a_2 = \frac{1}{2} K_{12} \frac{(A_2 - B)}{I_2}$, $c = -\frac{1}{2} K_{12} \frac{B}{\sqrt{I_1 I_2}}$. The estimated values of the

frequencies obtained for AT and GC cases are presented in Table 3.

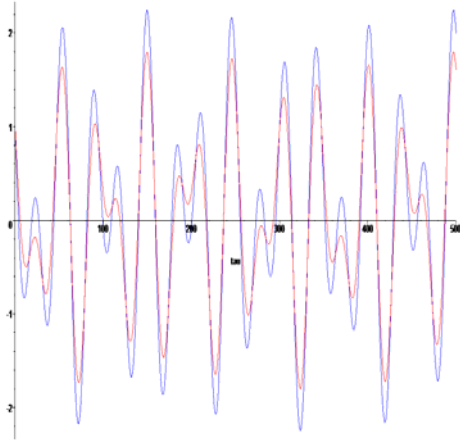
Base pair	$\omega_{(-)} [10^{12} (s^{-1})]$	$\omega_{(+)} [10^{12} (s^{-1})]$
AT	0,1264	0,1988
GC	0,1566	0,2532

Table 3. Estimated values of the frequencies.

The graphs of the solutions are shown in Fig. 1. for the initial conditions: $\varphi_1(0) = 1$;

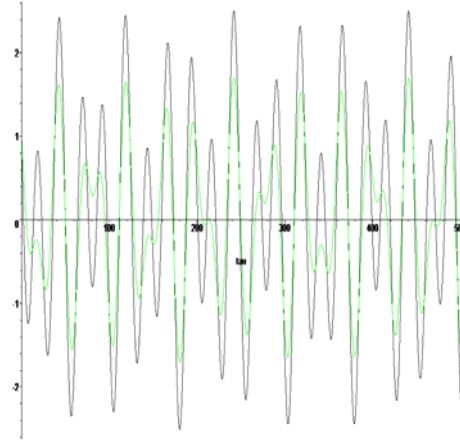
$$\varphi_2(0) = \frac{\sqrt{I_1}}{\sqrt{I_2}} \left[\frac{\omega_{(-)}^2 - a_1}{c} \right], \quad \frac{d}{dt} \varphi_1(0) = -\omega_{(+)} \frac{\sqrt{I_2}}{\sqrt{I_1}}, \quad \frac{d}{dt} \varphi_2(0) = -\omega_{(+)} \left[\frac{\omega_{(-)}^2 - a_2}{c} \right].$$

AT



a

GC



b

Fig. 1. Solutions for AT (a) and GC (b) base pairs. A base oscillations are shown by red line, T – by blue line, G – by green line and T – by black line ($\beta=0$ and $F=0$, $\tau = 10^{-24}t$).

4.2. Case II ($\beta \neq 0$ and $F=0$).

In the studied case we get

$$\varphi_1(t) = \frac{A_{(-)}}{\sqrt{I_1}} \exp(-\delta_1 t) \cos(w_{(-)} t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_1}} \exp(-\delta_1 t) \cos(w_{(+)} t - \alpha_{(+)}) ,$$

$$\varphi_2(t) = \frac{A_{(-)}}{\sqrt{I_2}} \exp(-\delta_2 t) \left[\frac{w_{(-)}^2 - \bar{a}_1}{c} \right] \cos(w_{(-)} t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_2}} \exp(-\delta_2 t) \left[\frac{w_{(+)}^2 - \bar{a}_2}{c} \right] \cos(w_{(+)} t - \alpha_{(+)}) ,$$

where: $\delta_1 = \frac{\beta}{2I_1}$, $\delta_2 = \frac{\beta}{2I_2}$, $\bar{a}_1 = a_1 - \delta_1^2$, $\bar{a}_2 = a_2 - \delta_2^2$. Fundamental frequencies $w_{(-)}$, $w_{(+)}$ are

$$\omega_{(\pm)} = \sqrt{\frac{(a_1 + a_2) - (\delta_1^2 + \delta_2^2)}{2} \pm \sqrt{\frac{1}{4}[(a_1 - a_2)^2 + (\delta_1^2 - \delta_2^2)] + c^2}}$$

Estimated values of the frequencies are shown in Table 4.

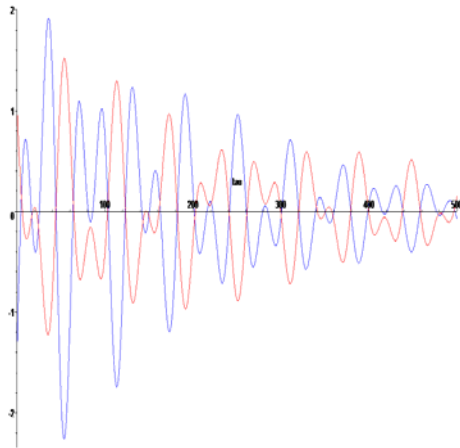
Base pair	$w_{(-)}$	$w_{(+)}$
AT	0,1124	0,2066
GC	0,0600	0,2916

Table 4. Estimated values of the frequencies.

The graphs of the solutions are shown in Fig.4, where we used the same initial conditions as in the previous case.

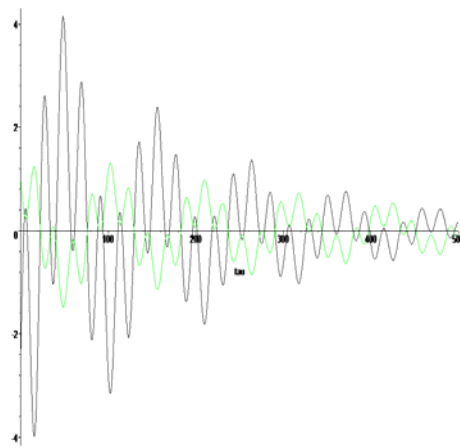
As follows from Fig 2, the angle amplitudes decreases more slowly in the case of AT base pair than the case of GC base pair. This means that the life time of excitations activated in the fragments of the DNA chains consisting of AT base pairs is larger than that in the chains consisting of GC base pairs.

AT



a

GC



b

Fig. 2. Solutions for AT (a) and GC (b) base pairs. A base oscillations are shown by red line, T – by blue line, G – by green line and T – by black line ($\beta \neq 0$ and $F=0$, $\tau = 10^{-24} t$).

4.3. Case III ($\beta \neq 0$ and $F \neq 0$).

In this case solutions of the equations consist of two parts. The first part is the general solution, the second one is a particular solution of the system (4) – (5). Assuming that constants f_{01} and f_{02} are particular solutions of the system, the solutions of equations (4) – (5) have the following form

$$\varphi_1(t) = \frac{A_{(-)}}{\sqrt{I_1}} \exp(-\delta_1 t) \cos(w_{(-)} t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_1}} \exp(-\delta_1 t) \cos(w_{(+)} t - \alpha_{(+)}) + f_{01},$$

$$\varphi_2(t) = \frac{A_{(-)}}{\sqrt{I_2}} \exp(-\delta_2 t) \left[\frac{w_{(-)}^2 - \bar{a}_1}{c} \right] \cos(w_{(-)} t - \alpha_{(-)}) + \frac{A_{(+)}}{\sqrt{I_2}} \exp(-\delta_2 t) \left[\frac{w_{(+)}^2 - \bar{a}_2}{c} \right] \cos(w_{(+)} t - \alpha_{(+)}) + f_{02},$$

$$\text{where: } f_{01} = \frac{2F_0 A_2}{K_{12}} [A_1 A_2 - B(A_1 + A_2)], \quad f_{02} = \frac{2F_0 A_1}{K_{12}} [A_1 A_2 - B(A_1 + A_2)].$$

The graphs of the solutions are very similar to those presented in the previous section. The only difference is associated with the adding constants f_{01} and f_{02} , which does not change essentially the results.

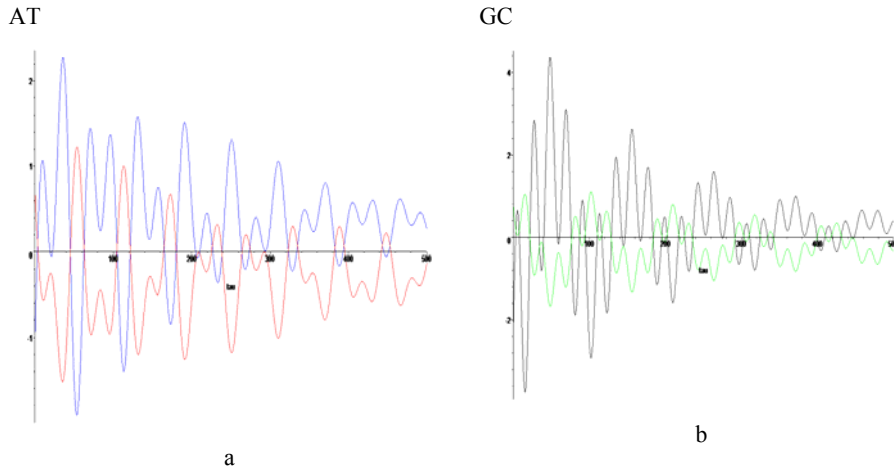


Figure 3. Solutions for AT (a) and GC (b) base pairs. A base oscillations are shown by red line, T – by blue line, G – by green line and T – by black line ($\beta \neq 0$ and $F \neq 0$, $\tau = 10^{-24} t$).

5. Conclusions

In this work we studied rotational oscillations of two coupled DNA bases that form a base pair: adenine-thymine (AT) or guanine-cytosine (GG). We showed that the problem can be reduced to the mechanical problem of two coupled unequal nonlinear pendulums oscillating in the horizontal plane. We obtained the Lagrange equations, found analytical solutions in the case of small amplitudes of angular displacements, and constructed the trajectories of the studied dynamical system in the configuration space.

At the same time the work we have done can be considered as a basis for consideration of many other problems associated with the DNA dynamics including, for example, the analysis of small amplitude oscillations under the action of periodical force and the studying of large amplitude oscillations of DNA bases.

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