Morse potential in DNA molecule – An experiment proposal

SLOBODAN ZDRAVKOVIĆ[1,*] and MILJKO V SATARIĆ[2]

[1]*Institut za nuklearne nauke Vinča, Poštanski fah 522, 11001 Beograd, Serbia*

[2]*Fakultet tehničkih nauka, Univerzitet u Novom Sadu, 21000 Novi Sad, Serbia*

**Corresponding author (Phone, +381-11-2392658; Email, szdjidji@vinca.rs; szdjidji@yandex.ru)*

We rely on the helicoidal Peyrard-Bishop model for DNA dynamics. Interaction between nucleotides at a same site belonging to different strands is modelled by a Morse potential energy. This potential depends on two parameters that are different for AT and CG pairs, which is a possible source for inhomogeneity. It was shown recently (Zdravković and Satarić 2011) that certain values of these parameters bring about a negligible influence of inhomogeneity on the solitonic dynamics. We propose an experiment that should be carried out in order to determine the values of both of these parameters.

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1. Introduction

It is well known that a DNA molecule consists of two compatible chains. Chemical bonds between neighbouring nucleotides belonging to the same strands are strong covalent bonds, while nucleotides at a certain site n, belonging to the different strands, are connected through weak hydrogen interaction. According to the helicoidal Peyrard-Bishop (HPB) model for DNA dynamics, the DNA chain is treated as a perfectly homogenous periodic structure and only transversal motions of nucleotides are taken into consideration (Dauxois 1991). The model assumes small oscillations around the bottom of the potential well. It is very common to describe this weak interaction by Morse potential energy (Dauxois 1991; Yakushevich 1998). Its expression is

$$V_{\mathrm{M}} = D(1 - e^{-ax})^2 \tag{1}$$

where the coordinate x describes the stretching of the nucleotide pair while the parameters D and a are the depth and the inverse width of the Morse potential. This function is shown in figure 1 for $a = 1.2\mathring{\mathrm{A}}^{-1}$ and D=0.07eV (Zdravković and Satarić 2009a). As the nucleotides oscillate around the bottom of the Morse potential well, the potential energy has values from zero to V and x belongs to the interval $[x_{\mathrm{A}},x_{\mathrm{B}}]$, as shown in figure 1.

DNA can be seen as a series of particles and springs and a displacement of a certain particle affects the neighbouring springs and nucleotides and, consequently, propagates along the molecule. According to the HPB model, such propagation is a modulated solitonic wave (Dauxois 1991; Zdravković and Satarić 2008b; Tabi *et al.* 2009). A key problem in DNA functioning is an impact of inhomogeneous effects on DNA dynamics. This can be viewed as the influence on the solitonic wave. It was mentioned above that the DNA chain is considered as a perfectly homogenous periodic structure. Hence, the only source for inhomogeneity represents the fact that there exist two different kinds of the nucleotide pairs. Namely, it is well known that adenine (A) and thymine (T) are connected by a double bond while guanine (G) and cytosine (C) are connected by a triple bond. Let us suppose that the AT and GC interactions are described by (a,D) and (a',D') parameters, respectively. Then, we can safely assume

$$D' = \frac{3}{2}D. \tag{2}$$

Of course, the experiments that will be described later are intended to check this relationship, as well as the relationship between a and a'.

Therefore, the question is if the wave characteristics like amplitude, speed, etc., are changed significantly

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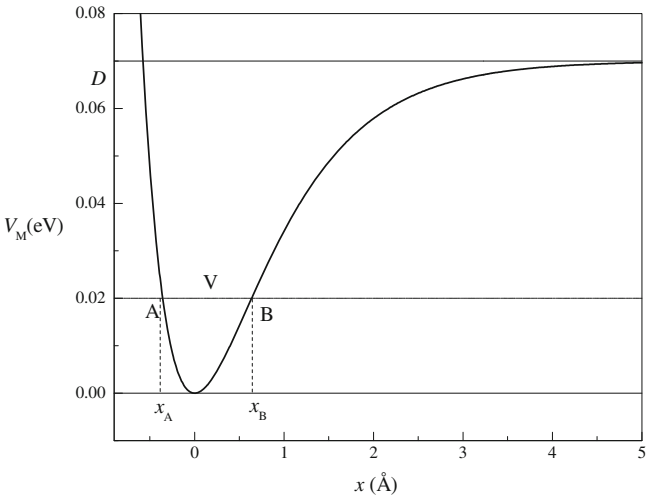

Figure 1. Morse potential energy as a function of the nucleotide pair stretching for $a = 1.2\text{Å}^{-1}$ and D=0.07eV.

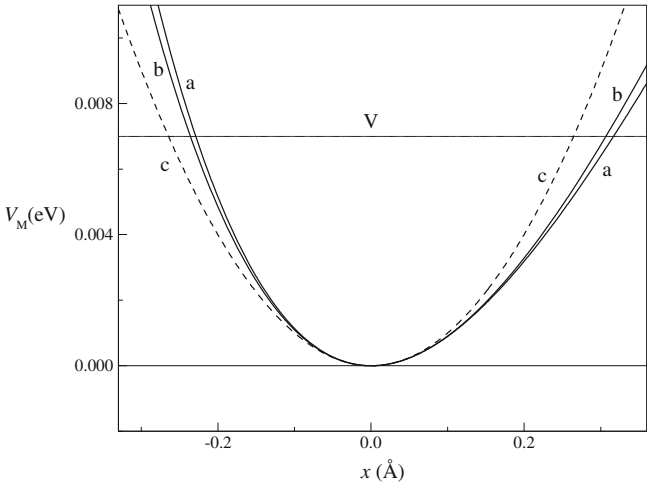

Figure 2. Morse potential energy as a function of the stretching x for different nucleotide pairs (a) D=0.07eV, $a = 1.2\text{Å}^{-1}$, (b) D'=1.5 · 0.07eV, $a' = 0.97\text{Å}^{-1}$, (c) Symmetric potential $0.1x^2$.

whenever the wave reaches a new type of the nucleotide pair. If DNA dynamics, i.e. the solitonic wave, were very sensitive to these inhomogeneities the wave would not exist or, at least, would be extremely unstable. This, practically, means that the impact of the different nucleotide bonds on the wave characteristics determine the stability of the DNA molecule.

It was argued recently that DNA is stable if the bottom of the Morse potential well in figure 1 is only slightly affected by this inhomogeneity (Zdravković and Satarić 2011). In other words, we were looking for a combination of the two relevant parameters, which brings about a constant shape of the bottom of the potential well. It was shown that the bottoms of the Morse potential wells for the different nucleotide pairs can be almost equal even though the values of the pairs of the parameters (a,D) and (a',D') are rather different. The assumption that the energy V is constant along DNA, i.e. V′=V was used to calculate the relationship between a and a', corresponding to the AT and CG pairs (Zdravković and Satarić 2011). This is demonstrated in figure 2. One can see that the lines (a) and (b), corresponding to the AT and GC pairs, are hardly distinguishable. Notice that the chosen value for V is a little bit bigger than half of the value $\frac{1}{2}k_BT$. The line (c) represents a symmetric potential $0.1x^2$. The curve (b), describing the stronger interaction, i.e. the CG pair, is closer to the symmetric one (c) than the curve (a), describing the weaker bond. Therefore, to plot figure 2, the values of the parameters a and D were estimated (Zdravković and Satarić 2006, 2009a). The value of the parameter a' was calculated according to the procedure explained in (Zdravković and Satarić 2011) while D' was calculated from equation (2). In what follows we suggest an experiment that should be carried out to check our predictions.

2. Experiment proposal

Micromanipulative experiments were carried out from 1992 (Smith *et al.* 1992). Hence, one single molecule can be mechanically manipulated (Bustamante *et al.* 1994; Lee *et al.* 1994; Boland and Ratner 1995; Smith *et al.* 1996; Bockelmann *et al.* 1997, 1998; Allemand *et al.* 1998; Strunz *et al.* 1999; Clausen-Schaumann *et al.* 2000; Williams *et al.* 2004; Lionnet *et al.* 2006; Galburt *et al.* 2009; Mosconi *et al.* 2009). Some relevant review papers include (Strick *et al.* 2003; Peyrard 2004; Moffitt *et al.* 2008). Results of some of these experiments were used to estimate the upper value of the parameter a (Zdravković and Satarić 2006). Also, some experiment proposals were suggested recently (Zdravković and Satarić 2008a, 2009b, 2010). In this article we propose how to experimentally determine the values of D and a. Of course, depending on the prepared DNA sample, one can determine the values of these parameters for both AT and GC pairs.

Let us start with figure 3. A nucleotide pair at a position n is stretched and the applied force, which should be measured, is F_1. Suppose that A is a force coming from 'springs' between the nucleotides belonging to the same strands. Let B be a force resulting from the interactions of the nucleotide

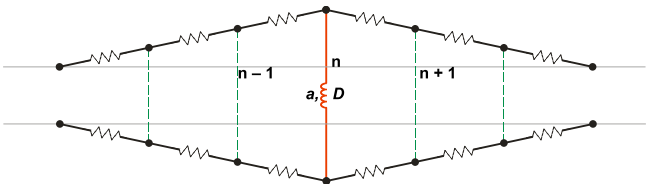

Figure 3. A stretched segment of a double-stranded DNA.

pairs at the positions $n\pm1$, $n\pm2$, etc. Then, the expression for the total force F_1 becomes

$$F_1 = A + B + 2aDe^{-ax}(1 - e^{-ax}). \quad (3)$$

The last term is the force coming from the interaction between nucleotides at the site n. Of course, this term is a first derivative of the function $V_M(x)$, given by equation 1.

The next step is deformation of the same DNA pattern except that there are two equal pairs, n and n', which are stretched. This is shown in figure 4. The measured force is

$$F_2 = A + B + 4aDe^{-ax}(1 - e^{-ax}). \quad (4)$$

Of course, the stretching x should be equal in both cases. From equations 3 and 4 we easily obtain a relationship between a and D, i.e.

$$F_2 - F_1 = 2aDe^{-ax}(1 - e^{-ax}). \quad (5)$$

The experiment should be repeated for $x' \neq x$, which brings about

$$F_2' - F_1' = 2aDe^{-ax'}\left(1 - e^{-ax'}\right). \quad (6)$$

Finally, we easily obtain a formula

$$\frac{F_2 - F_1}{F_2' - F_1'} = \frac{e^{-ax}(1 - e^{-ax})}{e^{-ax'}(1 - e^{-ax'})} \quad (7)$$

where only a is unknown. Therefore, the values of the parameters a and D can be calculated from equations 7 and 5 or 6.

According to figures 3 and 4 one might think that only one or two nucleotide pairs should be stretched. If so, this could be a very difficult task. However, this is not correct. The only important is that the numbers of the stretched pairs are not equal in these two figures. For example, if p_1 and p_2 nucleotide pairs are involved in figures 3 and 4, then equations 3 and 4 become

$$F_i = A + B + 2p_iaDe^{-ax}(1 - e^{-ax}), \quad i = 1, 2. \quad (8)$$

Finally, we want to point out that figures 3 and 4 might not correspond to the real experiments. According to them, one might conclude that both strands should be stretched at the same time. One possible more realistic experimental setup could be as follows. The linearly stretched DNA chain

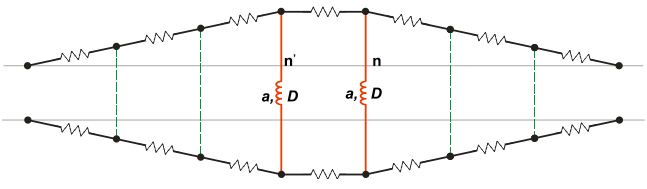

Figure 4. A stretched segment of a double-stranded DNA with two equal pairs in the middle.

is attached to a flat surface of silicon. The thin cantilever of atomic force microscope (AFM) should pull up a segment of one strand while the other remains stick to the surface. The covalent bonds between silicon atoms of substrate and carbon atoms of DNA are strong while the Morse forces between nucleotides are weaker. This enables the measurement of the force between the strands. In order to control the number of displaced nucleotides by AFM cantilever, the fluorescence labelling method could be applied by using small molecules of dye attached to the same strand around the contact position.

One of the biggest problems in micromanipulative experiments could be thermal vibrations. In what follows we suggest how to reduce their impact on the experiment proposed in this study.

Suppose that only one nucleotide is attached. As its motion is in one direction we can estimate its thermal amplitude x_T as

$$\frac{k_BT}{2} = D(1 - e^{-a x_T})^2. \quad (9)$$

For $a = 1.2\,\text{Å}^{-1}$ and $D = 0.07\,\text{eV}$, one obtains $x_T = 0.47$ Å, which is a very large value. The real stretching is $y_T = \frac{x_T}{\sqrt{2}} = 0.33$ Å, but this is still too large. However, if n nucleotides are attached, then

$$\frac{k_BT}{2} = nD(1 - e^{-a x_T})^2, \quad (10)$$

which, as an example, brings about $x_T = 0.1$ Å for $n \approx 14$. Of course, these calculations are bases on the assumption that the nucleotide pairs are independent. However, the calculations obviously show that the thermal influence can be reduced if more nucleotides are attached. Note that it is easier to attach a few nucleotides than a single one.

3. Conclusion

In this article we suggest a possible experimental scenario to determine the values of the two crucial parameters describing DNA dynamics. We believe that this could support or refute our predictions explained in Introduction. Namely, a certain combination of the pairs of the parameters (a,D) and (a',D') yields a constant shape of the bottom of the Morse potential well. This is very important for DNA stability (Zdravković and Satarić 2011) as was explained above.

The initial deformations x and x' in equations 5–7 are arbitrary. This point deserves a discussion. In Zdravković and Satarić (2010) we explained that the measured constant of the longitudinal spring k should be understood as an average value. This means that k depends on the initial deformation. In this case we do not know if such dependency exists for a and D. Therefore, the experiment should be carried out for different pairs of x and x'.

Of course, if a and D depend on x, then the question is what values should be used in future calculations. When the soliton moves through the DNA moleculem then x_A in figure 1 is its amplitude. Hence, the initial deformation should be equal to x_A. We explained how this value can be experimentally determined (Zdravković and Satarić 2010). The value x_A is nothing but the initial deformation which brings about the known solitonic speed (Hakim *et al.* 1984). Therefore, in such case, both x and x' should be close to x_A.

It is well known that a measuring uncertainty can be decreased if the measurement is repeated a few times and if a mean value is taken for the final result. For example, any pair (p_1,p_2) in equation 8 brings about equation 7. The measurement should be repeated n times giving the values $a_1, a_2, \ldots, a_n$. The final result would be the mean value, i.e. $a = (a_1 + \ldots + a_n)/n$.

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References

Allemand JF, Bensimon D, Lavery R and Croquette V 1998 Stretched and overwound DNA forms a Pauling-like structure with exposed bases. *Proc. Natl. Acad. Sci. USA* **95** 14152–14157

Bockelmann U, Essevaz-Roulet B and Heslot F 1997 Molecular Stick-Slip Motion Revealed by Opening DNA with Piconewton Forces. *Phys. Rev. Lett.* **79** 4489–4492

Bockelmann U, Essevaz-Roulet B and Heslot F 1998 DNA strand separation studied by single molecule force measurements**.** *Phys. Rev. E* **58** 2386–2394

Boland T and Ratner BD 1995 Direct measurement of hydrogen bonding in DNA nucleotide bases by atomic force microscopy. *Proc. Natl. Acad. Sci. USA* **92** 5297–5301

Bustamante C, Marko JF, Siggia ED and Smith S 1994 Entropic elasticity of lambda-phage DNA. *Science* **265** 1599–1600

Clausen-Schaumann H, Rief M, Tolksdorf C and Gaub HE 2000 Mechanical Stability of Single DNA Molecules. *Biophys. J.* **78** 1997–2007

Dauxois T 1991 Dynamics of breather modes in a nonlinear "helicoidal" model of DNA. *Phys. Lett. A* **159** 390–395

Galburt EA, Grill SW and Bustamante C 2009 Single molecule transcription elongation. *Methods* **48** 323–332

Hakim MB, Lindsay SM and Powell J 1984 The speed of sound in DNA. *Biopolymers* **23** 1185–1192

Lee GU, Chrisey LA and Colton RJ 1994 Direct measurement of the forces between complementary strands of DNA. *Science* **266** 771–773

Lionnet T, Joubaud S, Lavery R, Bensimon D and Croquette V 2006 Wringing Out DNA. *Phys. Rev. Lett.* **96** 178102

Moffitt JR, Chemla YR, Smith SB and Bustamante C 2008 Recent Advances in Optical Tweezers. *Annu. Rev. Biochem*. **77** 205–228

Mosconi F, Allemand JF, Bensimon D and Croquette V 2009 Measurement of the Torque on a Single Stretched and Twisted DNA Using Magnetic Tweezers**.** *Phys. Rev. Lett.* **102** 078301

Peyrard M 2004 Nonlinear dynamics and statistical physics of DNA. *Nonlinearity* **17** R1

Smith SB, Finzi L and Bustamante C 1992 Direct mechanical measurements of the elasticity of single DNA molecules by using magnetic beads. *Science* **258** 1122–1126

Smith SB, Cui Y and Bustamante C 1996 Overstretching B-DNA: The Elastic Response of Individual Double-Stranded and Single-Stranded DNA Molecules. *Science* **271** 795–799

Strick TR, Dessinges MN, Charvin G, Dekker NH, Allemand JF, Bensimon D and Croquette V 2003 Stretching of macromolecules and proteins. *Rep. Prog. Phys.* **66** 1–45

Strunz T, Oroszlan K, Schäfer R and Güntherodt H-J 1999 Dynamic force spectroscopy of single DNA molecules. *Proc. Natl. Acad. Sci. USA* **96** 11277 -11282

Tabi CB, Mohamadou A and Kofané TC 2009 Modulated Wave Packets in DNA and Impact of Viscosity. *Chin. Phys. Lett.* **26** 068703

Williams MC, Pant K, Rouzina I and Karpel RL 2004 Single molecule force spectroscopy studies of DNA denaturation by T4 gene 32 protein. *Spectroscopy-Int. J.* **18** 203–211

Yakushevich LV 1998 *Nonlinear Physics of DNA*. In: Wiley Series in Nonlinear Science (Chichester, UK: John Wiley and Sons Ltd.)

Zdravković S and Satarić MV 2006 Single Molecule Unzippering Experiments on DNA and Peyrard-Bishop-Dauxois Model. *Phys. Rev. E* **73** 021905

Zdravković S and Satarić MV 2008a Solitonic speed in DNA. *Phys. Rev. E* **77** 031906

Zdravković S and Satarić MV 2008b Nonlinear Schrödinger equation and DNA dynamics. *Phys. Lett. A* **373** 126–132

Zdravković S and Satarić MV 2009a Parameter selection in a Peyrard-Bishop-Dauxois model for DNA dynamics. *Phys. Lett. A* **373** 2739–2745

Zdravković S and Satarić MV 2009b DNA dynamics - Experiment proposals. *Phys. Lett. A* **373** 4453–4459

Zdravković S and Satarić MV 2010 Stacking interaction in DNA molecule. *J. Comput. Theor. Nanosci.* **7** 2031–2035

Zdravković S and Satarić MV 2011 Transverse interaction in DNA molecule. *BioSystems* **105** 10–13

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