Conformational impact on deformation of DNA TATA-box

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Abstract

The theoretical study of deformability of special sequence of DNA double helix TATA-box is presentated. The paper elaborates on the mechanisms of abnormal deformation of DNA TATA-box double helix that cannot be explained using the standard mechanical model of polymer molecules (WLC) and needs more detailed modeling. Analyzing of DNA TATA-box deformation it is shown the molecule can undergo significant deformations due to its property of the structural polymorphism, that is, possibility of the double helix fragment to exist in more then one conformations. In addition to elastic components (bending, twisting), the presented model includes the following deformation features: possibility of conformation rearrangement of the shapes of the sugar rings, effects of a specific nucleotide sequence and anisotropy, the coupling between components. Presented model allows describe abnormal deformation based on physical special fitures of double helix inner structure.

1 Introduction

The key properties of DNA functioning are contained in the structure of specific nucleotide sequences. Regulatory gene fragments have specific sequence pairs. One of these fragments is TATA-box, has a constant part of TATA and plays a major role in the transfer of genetic information, determining the beginning of reading the information recorded in the gene. TATA-box-binding with a certain part of the regulatory protein complex (TATA-binding protein, TBP) initiates the formation of a complex that signals the place of the beginning of reading genetic information and is responsible for the accuracy of protein 1 synthesis [1].

Figure 1 shows a schematic representation of the mechanism for reading genetic information, which begins with the recognition and deformation of the DNA TATA box. The structure of the TATA box associated with TBP was solved with high accuracy more than 20 years ago for the first time [2,3].

In the TATA box, significant deformations were observed without destruction of the double helix. The total deformation of the central part was approximately $90^\circ$ bend in the direction of major groove of the double helix and a $90^\circ$ unwinding. So there is a direct interaction of
Figure 1: Schematic representation of the mechanism for reading genetic information. Deformation of the TATA box upon binding to TBP leads to the formation of a DNA-protein complex, the formation of which determines the beginning of information reading from DNA during protein synthesis.

the regulatory protein with the informational part of the double helix, the base pairs of the fragment.

At the same time, the alternating purine-purimidine sequence poly (AT) does not show specific bendability in the free state. The main feature of the fragment is bistability of the conformation of the sugar ring found experimentally [4,5] even without binding to other molecules.

In the case of deformation of the TATA box bound with TBP, the property of conformational bistability is most clearly manifested due to certain boundary conditions. The formation of the complex of the TATA-box with TBP is characterized by intercalation of parts of the TBP molecule at the ends of the DNA fragment, while different forms of the sugar ring are observed in pairs adjacent to the intercalator.

According to the WLC model, which is usually used to describe DNA deformation, the deformation energy of the TATA box is greater than the energy of its melting and should have destroyed the double helix. Based on the fact that the TATA box retains the structure of the double helix in the complex with TBP, remembering that the formation of this complex determines the base pair from which transcription begins, it can be assumed that the TATA box must have specific physical characteristics that provide significant localized deformation with a recognition accuracy of up to 1 bp. [6].

In order to clarify the physical nature of high bendability of DND TATA-box, short fragments of the double helix of different sequences were investigated; however, it was not confirmed very special elastic stiffness of any sequences [7]. The difference in the values of the stiffness constant for different sequences is no more than 10%. The softening of such a value is not enough to provide bend like TATA-box undergoes. Greater flexibility of the double helix and, accordingly, a decrease in stiffness can be provided by local destruction of the double helix under stress [8]. Experimental data on the formation of cycles with a length of 158 bp. did not show the localization of deformation on the TATA sequence [9].

At the same time, the process of deformation of the TATA box upon interaction with TBP is described as sequential intercalation with subsequent approximating of the double helix bend to the shape of the saddle protein [10]. The physical mechanism of the formation of significant deformation localized in the sequence of the TATA-box DNA remains unclear.
Figure 2: The values of the dominant parameters of the central fragment TATA boxing. a) Twist of each base pair step in deformed TATA-box; b) Roll of each base pair step in deformed TATA-box; c) Sugar ring pucker of each nucleotide in deformed TATA-box. The arrows show the dominant deviations in the center of the TATA-side for the dominant parameters.

From our point of view, a significant TATA-specific change in the double helix conformation can occur in this fragment, which leads to an effective change in rigidity. Thus, due to its physical properties, a special DNA sequence exhibits a physical level of information, which is recognized by TBP in a sequence capable of achieving the deformation necessary and improbable for other fragments so that the process of starting the reading of genetic information begins [6]. Nevertheless, despite almost 30 years ago this conclusion, the completed physical interpretation has not been formulated.

We analyzed the changes in the structure of the double helix of the TATA box of DNA with certain boundary conditions, which are realized in a complex with the TBP protein, the structural parts of which are embedded between base pairs at the ends of the fragment. The most characteristic changes in the structure of the double helix are emphasized as dominant parameters: torsion, bending and change in the shape of the sugar ring. It was found that significant deformations correlate with sugar ring form change. It should be noted that such interrelation has remained unattended so far has not been specially studied.

However, NMR studies showed that the limitation of the mobility of sugar by replacing it with an inflexible analogue is reflected in the DNA flexibility [11]. Molecular modeling confirmed the correlation of structural parameters with a gradual change in one or both forms of sugar [12].

In order to build relevant deformation model of the TATA box, it is necessary to take into account the conformational degree of freedom reflecting the mobility of the sugar ring in DNA and its correlation with another deformation parameters. In this work, a model of deformation that takes into account the conformational mobility and its correlation with bending was constructed, an abnormally large localized deformation of DNA was obtained associated with conformational rearrangement of the form.

Obtained deformation does not require the destruction of the double helix, hydrogen bonds and stacking, as is characteristic of the deformed TATA-box of DNA upon interaction with TBP. It has been shown that the deformation is advantageous when the bending stiffness of the fragment decreases by about 10%, which is probably realized due to the neutralization of the charges of the fragment through interaction with the protein complex [13] and under specific boundary conditions of the conformational component, which arise due to the penetration of protein loops intercalated at the ends of the TATA box.
2 Modeling of deformation induced with sugar ring form changing of the TATA-box of DNA

2.1 Structural changes in the TATA-box of DNA in a complex with TBP

In order to describe the physical level of information set in the specific deformability of a DNA fragment, we analyze the structure of the TATA-box of DNA in a complex with TBP. The regulatory fragment TATA-box consists of 8 base pairs and undergoes significant structural changes during recognition and protein binding. The interaction of the TATA box with TBP is accompanied by inserting (intercalation) of the structural elements of protein (phenyl-alanine loops) between 1st and 2d, as well as 7th and 8th base pairs of the DNA fragment. Intercalation leads to a change in the structural parameters of the DNA base pair step adjacent to the intercalator.

Moreover, the same changes are cooperatively taking place in neighbor base pairs inside the TATA-box. The greatest changes occur in the following parameters of the double helix structure (dominant parameters of TATA-box deformation): the slope between adjacent pairs, roll increases, the twist angle decreases, and the sugar shape of 5′- nucleotides of base pairs, which are contacting with the intercalator changes. The amplitude of these changes dramatically exceeds the amplitudes of thermal fluctuations in the selected parameters. On the figure 2 one can see significant deviations in the dominant parameters from the values of the double helix forms characteristic for A and B. Loops schematically depict intercalators, and for neighbor bp steps, changes in the twist and roll parameters and the sugar ring of the fragment nucleotides are noticeable; however, in the middle of the fragment, the maximum deviation from the values in the A and B forms is observed.

Simultaneously observing the value of the pseudorotation angle for each nucleotide of the double helix, one can see changes in each strand of the double helix within the central fragment from close to $C2′$ – endo to close to $C3′$ – endo in the 5′ – 3′ direction in both strands. The figures show the values of the parameters presented in the work [1]. For other sequences of the TATA box, the type of deformation is the same, but the quantitative values may differ for different sequences. [2,3,6,14].

As a result, the TATA box manifests itself as a sequence that contains a certain conformational mobility, which manifests itself under fixed boundary conditions and induces deformation of the fragment. Deformation associated with a change in conformation of sugar ring pucker is called intrinsically induced deformation [15]. Obviously, the special mobility of the structure of the double helix of the TATA box cannot be described within the framework of a linear harmonic approach in modeling. Significant changes indicate a nonlinear deformation mechanism. At the same time, nonlinearity is contained in the bimodality of the shape of the sugar ring potential function of the TA-sequence; therefore, the inclusion of a conformational component describing sugar changes may explain the formation of a static bell-like deformation of the TATA box.
2.2 Dominant components of the deformation model TATA-boxing DNA

DNA double helix is polymorphic macromolecule and which exhibits a number of structures that arise during its functioning under external action equal to forces of piconewton order [10]. In particular, TA DNA sequences are known to exhibit the coexistence of both C'2- endo and C'3′- endo forms of sugar as fixed by NMR [1] and Raman [2]. Analysis of various DNA sequences also confirms the bimodality of TA DNA sequences in a number of parameters of the double helix structure. Deviations from the canonical forms were also observed in the molecular dynamics of the TATA box [18].

Thus, the AT-rich TATA box is a conformationally bistable complex in which the shape of sugar rings in the chains of the double helix is different and the dominant change can be a simultaneous change in the shape of sugars in both chains. Moreover, intercalated TBP loops at the ends of the TATA box fix different sugar conformations at the ends of the fragment. Study of the effect of modifying intercalators using molecular dynamics showed that the modification affects the amount of bending at the intercalation site, but not in the central part of the fragment [19].

Thus, the deformation of the central part of the TATA box is determined rather not by elastic deformation at the ends, but by changes in the conformations of sugars in the nucleotides adjacent to the intercalators. The conformational potential of the pseudorotation angle of the sugar ring of the DNA nucleotide has two minima of different depths, which determines the double-well shape of the potential energy of the TATA box pair. The minima of the conformational energy of the pair correspond to states of pairs at the ends of the fragment, fixed by intercalators.

For a theoretical description of DNA deformation under conditions when conformational changes in the double helix occur, let us consider DNA as a chain of links with external and internal degrees of freedom. The external degrees of freedom describe the deformation of a molecule as a homogeneous chain and are modeled by an elastic rod with 3 degrees of freedom: bend and twist - bending and torsional displacements of neighboring links, stretching - change the distance between adjacent links.

Displacement of structural elements within links described by an internal or conformational degree of freedom. Each link is a pair of nucleotides in which the change in the conformation of the sugar ring occurs along a certain conformational trajectory of the mutual arrangement of atoms (pseudorotation angle) and has two minima of potential energy (Fig 3,4). Thus, the conformational energy of a monomer unit is a double-well potential function for which the height of the barrier, the distance between the minima, and the difference in their depth determine the shape of structural changes in DNA on a given fragment. The conformational degree of freedom describes relative change in the positions of the centers of masses of structural elements of monomer link which is base pair. Figure 3 schematically shows the structure element of monomer link which consists of pair of nucleotides (base, five-membered sugar ring, backbone of phosphate group); position of nucleosides relative to the main axis of the double helix depicted by 'x' on the dyadic axis in the plane of the pair for the B and A conformations of the link. The change in conformations in both nucleosides from the position corresponding to the A-form to the position corresponding to the B-form and vice versa is described by the displacement of a pair of nucleosides within the unit and also leads to a shift in the center of mass of the nucleosides.

The movement of the link as a whole can also occur without changing the relative position of
Figure 3: Modelling of structural elements of a monomer unit and their arrangement in pairs relative to the dyad axis.

Figure 4: Modelling the potential function of a link characterizing the mutual arrangement of nucleotides in a pair. A - is the state corresponding to $C3' - endo$ sugar ring form, B - is the state corresponding to $C2' - endo$ sugar ring form, BA - is the state which is characterized with $C3' - endo$ form of sugar ring for 5’ and $C2' - endo$ sugar ring form for 3’ nucleotides of monomer link, AB - is the state which is characterized with $C3' - endo$ form of sugar ring for 3’ and $C2' - endo$ sugar ring form for 5’ nucleotides of monomer link.

structural elements inside the link and is determined by the displacement of the center of the link mass with mass $M = 2m_0 + m_1 + m_2$ and the relative position of the link masses are described by external components. The relative mass displacement inside the link is described by the mass $\mu = m_1 m_2 / (m_1 + m_2)$ and correspond changes in the internal conformational component. This approach was developed and formed as the Volkov-Kosevich model for describing the vibrations of the structural elements of DNA [20] and is successfully used to describe small vibrations of DNA in various media and complexes, as well as to describe structural transitions in DNA double helix [21].

According to this approach, each nucleotide is modeled by a physical pendulum, which can be located in several stable positions corresponding to different conformations of the sugar ring. In DNA, the change occurs along a certain conformational trajectory, the energy of which has two minima corresponding to two forms of the double helix A and B and is expressed in a change in the position of nucleosides centers of the mass in the plane of the double helix. For the B-form of DNA, the pair is close to the main axis, and for the A-form it is shifted outward from the axis, which is clearly seen on X-ray structural images, where the cavity in the middle is visible in the A-form, while in the B-form the axis passes through the center of the pairs. Therefore, B-A changes in the structure are expressed by the joint displacement of the masses of nucleosides from the center to the periphery as a whole.

In the case of the TATA box, the shape of the sugar in the nucleotides of a monomer unit pair is different. Therefore, the changes in the sugar rings correspond to the rotation of a pair of nucleosides, which untwisting ensures the arrangement of the pairs along the axis and the realization of bending while maintaining the stacking. The potential function will be double-well for simultaneous BA transition in one chain and AB in another and differ from the BA
transition in both chains by the position and depth of the wells.

A change in conformation inside a link leads to changes in the external degrees of freedom and is called internally-induced deformation. Potential field of DNA deformation forces, consisting of contributions from elastic deformation, internal conformational rearrangement, the relationship of these components and the action of external forces.

The potential energy of the field is determined by the following types of components: \( U_{el}(R) \) - energy of elastic deformation (torsion, tension, bending), described by 3-component deformation \( R \), \( U_{conf}(r) \) - energy of internal conformational change, is described by the component of the internal conformational rearrangement of the relative displacement structural elements within the link, \( r \); \( U_{\chi}(R, r) \) - potential energy, reflecting the relationship between the components, \( A(f, R) \) - the work of an external force applied to one of the elastic components.

\[
E = U_{el}(R) + U_{conf}(r) + U_{\chi}(R, r) - A(f, R).
\] (1)

The general view of the deformation energy of the double helix of DNA, taking into account the internal rearrangements of the structure (1), can be used to describe any deformations that are accompanied by a change in the shape of the sugar ring of nucleotides. However, we will focus on the possibility of using this model to describe the deformation at conformationally bistable fragment as TATA-box is.

### 3 Formation of localized DNA strain

Let us consider the formation of a bend at the region of changing of the double helix conformation. For the theoretical description of such deformations, a two-component model of internally induced deformation can be used, which describes the conformational transition between two states and the associated bending. The strain energy density associated with the conformational change in monomer units can be written as:

\[
\varepsilon(u, r) = \frac{C_u u^2}{2} + \frac{C_r r^2}{2} - \gamma_{ur} u F(r) + \Phi_e(r),
\] (2)

where \( u \) is the change in one component of the elastic rod, \( r \) is conformational change along the chain. \( \Phi(r) \) - double well conformational function, \( \gamma_{ur} F(r) \) - constant and potential of the conformation interrelation with double helix bending. The energy minimum condition determines the shape of the conformation-induced deformation:

\[
\frac{\partial \varepsilon(u, r)}{\partial u} = C_u u - \gamma_{ur} F(r) = 0;
\] (3)

\[
\frac{\partial \varepsilon(u, r)}{\partial r} = \frac{d\Phi_e(r)}{dr} - 2\gamma_{ur} \frac{F(r)}{dr} u = 0.
\] (4)

In the case of a local conformational transition, the change in the elastic component associated with the conformational component is also localized and proportional to the potential of the relationship between the change in the conformational state and elastic deformation \( F(r) \):

\[
u = \frac{\gamma_{ur} F(r)}{C_u}.
\] (5)

This solution depends on the shape of the conformational potential. For a bistable conformational potential, such that the depth of the wells is the same, the shape of the solutions has
the form of a kink in the conformational component and a bell-shaped deformation in bending. Kink for the conformational component corresponds to the fact that the conformational states are different at the ends of the fragment, and the bell-shaped shape of the bending component corresponds to the maximum bending in the center. For the conformational potential with different well depths, the shape of the solutions has the form of a bell for both the conformational and bending components, such a deformation describes the transition of the deformed fragment into A form, type B-A-B transition. In this way the conformational potential of the TATA box must have the same well depth.

Another restriction on the conformation-induced bending of the TATA box is the restriction on the rigidity of the deformed fragment. It turned out that the internal induced deformation may be more advantageous than uniform deformation of the same magnitude without conformational rearrangement. The advantage of the conformation-induced mechanism is realized in the range of rigidity of the elastic component

\[ \frac{\gamma^2_{ur}}{\epsilon} < C_u < 3\frac{\gamma^2_{ur}}{2\epsilon}. \]  

(6)

According to our previous estimates [22], this condition requires almost half the stiffness of the deformation of the elastic component. Despite the possibility of internal induced deformation, within the framework of the proposed model, the reasons for such a strong softening remained unclear, since the flexural rigidity of the TATA box sequence does not differ too much from the flexural rigidity of the DNA sequence as a whole. In the following subsections, we will consider the mechanism for the formation of bistability of the conformational potential, as well as softening of rigidity.

### 3.1 Formation of conformational bistability in the TATA box under the influence of force

The mechanism of formation of bistability of conformational states due to the mobility of the sugar ring was considered in detail for the threshold DNA lengthening [21]. In the case of a TATA box, the external action applied to the ends of the TATA box is protein loops that intercalate between 1–2 and 7–8 units, offer unwinding of the fragment and anchoring the sugar shape at the ends.

According to [23] p.387 during intercalation, structural changes spread to neighboring pairs to those adjacent to the intercalator, unwinding along at least three pairs before and after intercalation. The external forceful action of the iterators mainly leads to unwinding, and makes the conformational potential bistable, caused by a change in the forms of sugars (from C3-endo to C2-endo at one level of severity and from C2-endo to C3-endo at another severity level). When positioned at a certain distance between the intercalators, sugar conformation changes using similar functions, the double helix causes a bend.

A necessary condition for the transition is the possibility of transition from one form to another under certain boundary conditions, which are used by intercalators at the ends of the fragment. Let us formulate 3 conditions for the bending induced by the conformational transition:

1) bistability of a fragment: bimodality of sugar conformation in alternating sequences

2) the formation of an unstable conformational state under normal conditions with the help of external influence. In the case of the TATA box, the transition between the sugar forms in the strands caused by intercalators
3) The location of intercalators, as fixers of states, on distances that are multiples of the length of the cooperativity of structural changes. The cooperativity in DNA is 3-4 pairs, so the fragment length is 6-8 bp.

Taking into account torsion and bending, it can be expected that the unwinding of the fragment under the action of intercalators also leads to induced bending. Accounting for an external force can change double-well conformational potential to bistable with identical wells.

As energy (1) of elastic deformation $R$, we consider two coupled elastic components, torsion and bending, $u, v$, respectively. Suppose that the force is applied to the torsional component, and the torsion is associated with the internal component, the deformation energy density is:

$$\varepsilon(u, v, r) = \frac{C_v v^2}{2} \frac{C_u u^2}{2} \gamma_{uv} vu - \gamma_{vr} vF(r) - \frac{\Phi(r)}{2} - fv,$$

where $C_u, C_v, C_r$, are the bending, torsional and conformational stiffness parameters, respectively; $\gamma_{uv}, \gamma_{vr}$ - parameters of the relationship of torsion with bending and torsion with the conformational component. The minus sign in front of the syllable of the relationship of torsion and conformation reflects a decrease in energy deformation due to internal mobility. We choose with the sign the syllable twisting and stretching in the potential generation of deformation, since an interconnection occurs, which is observed only at large deformations and does not manifest itself in free DNA.

However, it should be noted that the relationship between the elastic components can be either positive or negative, depending on the deformation path [24]. $F(r)$ and the conformational double-well conformational potential, $\Phi(r)$, have a similar shape for the state equilibrium with conformational change equal to 0, $\Phi(r_0) = F(r_0) = 0$. The maximum of different functions corresponds to the same conformational change value, $r = r_1$. Another metastable state can be different and can be transformed into a bistable state by using the [21] force. The new state of equilibrium, $r_f$, is determined by strength. The state in which the minimum energy is realized for all degrees of freedom is found by equating to 0 the derivatives with respect to all components of the system:

$$\frac{\partial \varepsilon(u, v, r)}{\partial v} = C_v v^2 \gamma_{uv} u - \gamma_{vr} F(r) - fh = 0;$$

(8)

$$\frac{\partial \varepsilon(u, v, r)}{\partial u} = C_u u \gamma_{uv} v = 0;$$

(9)

$$\frac{\partial \varepsilon(u, v, r)}{\partial r} = \frac{d\Phi(r)}{dr} - 2\gamma_{vr} \frac{F(r)}{dr} v = 0.$$

(10)

By expressing bending strain (4) and substituting it into expression (3), the expression for expression in the equation for conformational change (5) obtains the equation of a new conformational state.

$$\frac{d\Phi(r)}{dr} - \frac{\gamma_{vr}^2}{C_v} \frac{F^2(r)}{dr} - 2f \frac{\gamma_{vr}}{C_v} \frac{F(r)}{dr} = 0,$$

(11)

where $\tilde{C}_v = C_v - \gamma_{uv}^2/C_u$ is effectively softened torsional stiffness due to the torsion-bending constraint.

Equation (6) in the absence of an external force satisfies the condition $\Phi(r) = \epsilon_0 F^2(r)$, therefore, substituting this expression in (6) we get the expression:

$$\left[ (\frac{\gamma_{vr}^2}{C_v} F(r) - fh \frac{\gamma_{vr}}{C_v} \frac{F(r)}{dr} ) F(r) \right] = 0;$$

(12)
The state of the extremum \( r_{0f} \) determined by the force \( f \) can be found by equating to 0 the first factor in (7)

\[
F(r_{0f}) = \frac{\gamma_{vr} f}{C_{v} \varepsilon_0 - \gamma_{vr}^2} = \frac{\gamma_{vr} f}{C_v}.
\]

(13)

And integrating (5) over the conformational component, the energy macromolecules under the action of sily can be transformed into a bistable form:

\[
\varepsilon(r) = \frac{1}{2} \left( \varepsilon_0 - \frac{\gamma_{vr}^2}{C_v} \right) F^2(r) - f h \frac{\gamma_{vr}}{C_v} F(r) + C_r,
\]

(14)

where \( C_r = \frac{\gamma_{vr}^2}{2 C_v} F(r_f) \) satisfies the conditions \( \varepsilon(r_f) = 0 \) and makes it possible to rewrite the conformational energy into a bistable form. Equation (3) can be used to express the twist deformation, which consists of two parts: caused by the applied force, \( v_f \) and associated with the transformation of the conformational potential into a bistable state \( v_r \):

\[
v = v_f + v_r
\]

(15)

\[
v_f = \frac{f h}{C_v}, \quad v_r = \frac{\gamma_{vr} F(r)}{C_v}
\]

(16)

\[
\tilde{F} = F(r - F r_{0f})
\]

(17)

In the case of the TATA box, the role of force is played by the intercalation of protein loops, which makes the conformational potential bistable; moreover, the conformations of the ends of the TATA box correspond to different states of new potential

\[
\Phi_v(r) = \frac{1}{2} \varepsilon(F(r) - F(r_{0f}))^2,
\]

(18)

where the lowering of the barrier is described by the expression:

\[
\varepsilon = \left( \varepsilon_0 - \frac{\gamma_{vr}^2}{C_v} \right).
\]

(19)

Thus, for a sequence with certain stiffness parameters, there is a force at which conformational bistability of the double helix structure occurs. This means that, with a high probability, two conformational states are realized and the place of the boundary can be realized in the deformed structure of the DNA chain as a whole, expressed in deformation and elastic parameters of torsion and bending.

### 3.2 Effective softening of bending stiffness in conformation-induced deformation by twist-bend coupling

Since the bending of the TATA-box of DNA occurs in the unwound fragment, and unwinding itself under the action of intercalators probably leads to bending, in this work we included an additional elastic component, torsion \( v \), and its relationship with bending. Since the size of the structural elements is small in comparison with the chain of the \( h \ll L \) macromolecule, in order to obtain analytical expressions describing the conformational changes and the associated
deformation of two elastic components, we write down the three-component deformation model in the continuum approximation.

\[
E = \frac{1}{2} \int_{-\infty}^{\infty} \frac{dz}{h} \left[ C_u u'^2 + C_v v'^2 + gr'^2 + \Phi(r) + 2\gamma_{ur} u' F(r) + 2\gamma_{uv} u' v' \right],
\]

where \( r_{n+1} - r_n = r' \) - conformational change, \( u_{n+1} - u_n = u' \), \( v_{n+1} - v_n = v' \) elastic deformations bending and torsion. The Euler-Lagrange equation takes the following form:

\[
C_u u'' + \gamma_{uv} v'' + \gamma_{ru} \frac{\partial F(r)}{\partial r} r' = 0; \tag{21}
\]

\[
C_v v'' + \gamma_{uv} u'' = 0; \tag{22}
\]

\[
gr'' - \frac{1}{2} \frac{\partial \Phi(r)}{\partial r} - \gamma_{ur} \frac{\partial F(r)}{\partial r} u' = 0. \tag{23}
\]

From equation (20) \( v'' = -\gamma_{uv} u''/C_v \), which, substituting into Eq. (19) and integrating over \( z \), we obtain an equation for the deformation shape of the elastic component, which is suborb to the expression for deformation in two-component model, but with effectively lower rigidity due to the interconnection of the urp components

\[
u' = -\gamma_{ur} F(r)/(C_u - \gamma_{uv}^2/C_v). \tag{24}
\]

When there is no deformation of the molecular chain at the edges of the deformed fragment, this corresponds to a minimum of the conformational potential and the following boundary conditions \( r \to \pm 1 \), \( r' \to 0 \), \( u' \to 0 \), \( v' \to 0 \), \( z \to \infty \). For \( F(r) = 1 - r^2 \), where \(-1 \leq r/r_{0f} \leq 1\) static solution of equations (19-21) has the form of a three-component soliton:

\[
r(z) = \pm th(\sqrt{Q}z/h); \tag{25}
\]

\[
u(z) = 1/2 \gamma_{uv}(C_u - \gamma_{uv}^2/C_v) \sqrt{Q} th(\sqrt{Q}z/h); \tag{26}
\]

\[
u(z) = \frac{\gamma_{ur}\gamma_{uv}}{(C_u - \gamma_{uv}^2/C_v) \sqrt{Q}} th(\sqrt{Q}z/h), \tag{27}
\]

where \( Q = (\epsilon - \gamma_{ru}^2/(C_u - \gamma_{uv}^2/C_v))/g \). The form of static deformation is described by a bell-shaped soliton:

\[
\rho_u(z) = hu' = -\frac{\gamma_{ur}}{(C_u - \gamma_{uv}^2/C_v) \sqrt{Q}} ch^{-2}(\sqrt{Q}z/h). \tag{28}
\]
Table 1: Range of stiffness in percent for which conformation-induced deformation is advantageous. The maximum value of \( C_u/C_{u_0} \), which intrinsic induced bending has advantage for. The minimum value of \( C_u/C_{u_0} \), for which the barrier between conformational states disappears. Where \( C_u \) is the bending stiffness of the deformed fragment, \( C_{u_0} \) is the average bending stiffness.

|                      | Max value \( C_u/C_{u_0} \) | Min value \( C_u/C_{u_0} \) |
|----------------------|-----------------------------|-----------------------------|
| I bend + conformation| 0.54                        | 0.36                        |
| II bend + twist + conformation | 0.79                        | 0.61                        |
| II + anisotropy      | 0.95                        | 0.73                        |

Table 2: Parameters of the intrinsic-induced deformation for two value of the conformational potential barrier

| \( L, bp \) | \( \text{bend},^o \) | \( \text{twist},^o(\text{II,III}) \) | \( \frac{C}{C_p}(\text{I}) \) | \( \frac{C}{C_p}(\text{II}) \) | \( \frac{C}{C_p}(\text{III}) \) | \( \frac{E_{el}}{L-1} \) | \( \frac{E_{ind}}{L-1} \) |
|-------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| \( \varepsilon = 2.5 \) | 4               | 27              | 16              | 0.6             | 0.85            | 1               | 0.66            | 0.47            |
|             | 6               | 52              | 30              | 0.48            | 0.73            | 0.878           | 0.76            | 0.18            |
|             | 8               | 78              | 44              | 0.45            | 0.7             | 0.845           | 0.77            | 0.1             |
| \( \varepsilon = 3 \) | 4               | 34              | 19              | 0.19            | 0.72            | 0.87            | 0.83            | 0.49            |
|             | 6               | 66              | 37              | 0.39            | 0.64            | 0.77            | 0.9             | 0.17            |
|             | 8               | 91              | 52              | 0.372           | 0.622           | 0.75            | 0.9             | 0.09            |

\[
\rho_v(z) = h\nu' = \frac{\gamma_{uv}\gamma_{uv}}{(C_u - \gamma_{uv}^2/C_v)^2} \sqrt{Q} \frac{z}{h}. \tag{29}
\]

According to equation (26), the most deformed part is the central part of the stressed fragment, corresponding to the maximum deviation from the conformational minima.

The soliton width is determined from the slope of the tangent at the center of the conformational transition as \( L = 2/r'(0) = 2h/\sqrt{Q} \):

\[
L = \sqrt{\frac{g}{\epsilon - \gamma_{uv}^2/(C_u - \gamma_{uv}^2/C_v)}}, \tag{30}
\]

Due to the dependence of formulas (22-25) on \( \sqrt{Q} \), \( Q > 0 \) and \( \epsilon - \gamma_{uv}^2/(C_u - \gamma_{uv}^2/C_v) > 0 \). And we have the first condition for the parameters of the model. Substituting solution (23-25) into the energy equation (18) and integrating over the width of the soliton (27), we obtain the deformation energy \( E_{ind} \sim (\epsilon - \gamma_{uv}^2/(C_u - \gamma_{uv}^2/C_v)) \) that accompanied by a change in the conformation of monomeric units. Elastic part of the self-induced bending energy \( E_{el} \sim \frac{1}{2} \gamma_{uv}^2/(C_u - \gamma_{uv}^2/C_v) \)

4 Evaluations and discussions

To determine the conditions for the implementation of the proposed deformation scenario, let us estimate the model parameters. To determine the preference condition for localized deformation
accompanied by conformational rearrangement, \((E_{\text{ind}} < E_{\text{el}})\). This is the second condition for the parameters of the model.

The interrelation of the \(u; v\) components leads to an effective softening of the \(u\)-component; therefore, the condition for the advantage of the internal conformational bending mechanism over uniform elastic bending changes to \(\gamma_{uv}^2/\epsilon + \gamma_{uv}^2/C_v < C_u < 3\gamma_{uv}^2/2\epsilon + \gamma_{uv}^2/C_v\).

In addition, taking into account the effect of anisotropy in the bending of the spiral structure leads to an effective decrease in the rigidity \(C_u \rightarrow kC_u, k < 1\). And the stiffness range that provides the advantage of the internally induced bending mechanism expands: \((\gamma_{ur}^2/\epsilon + \gamma_{uv}^2/C_v)/k < C_u < (3\gamma_{ur}^2/2\epsilon + \gamma_{uv}^2/C_v)/k\). According to our estimate, for the TATA-box sequence, \(k = 0.83\). This value matches the range anisotropy effect described in [25].

Thus, the relationship between the elastic components and the anisotropy of the helical structure opens up opportunities for the emerging conformational transformations in elastic components. To estimate the range of advantages of the internal induced mechanism, we used the following values of the model parameters. Flexural stiffness \(C_u = 94 \text{ kcal/mol}\), torsional stiffness \(C_v = 75 \text{ kcal/mol}\), relationship between torsion and bending, \(\gamma_{uv} = 0.5\sqrt{C_uC_v} = 42 \text{ kcal/mol}\).

The parameters of conformational rigidity, the barrier between conformational states, and the relationship between conformation and bending were evaluated in a previous study [5]. They are respectively: \(g = 20 \text{ kcal/mol}, \epsilon = 3 \text{ kcal/mol}, \gamma_{ur} = 0.6\sqrt{\epsilon C_u} = 10 \text{ kcal/mol}\).

For the given parameter values, we calculate the range in which the conformation-induced mechanism has the advantage of Table 1. Model I includes bending and conformational change, model II adds the relationship of torsion and bending, model III also takes into account the bending anisotropy. The ratio of the fragment rigidity to the average bending rigidity of the DNA double helix \(C_u/C_{uo}\) shows the degree of deviation of the bending rigidity parameter of a DNA fragment for localization of conformation-induced deformation in it.

In a simple two-component model, the deformed fragment must undergo significant changes, up to local destruction. The assumption that the elastic components are interconnected leads to a more probable internal induced deformation. Finally, the inclusion of the influence of anisotropy makes it probable that internal induced deformation appears in a fragment with 5% softened rigidity.

More detailed results of applying the deformation models are presented in Table 2. The effect of reducing the barrier of the conformational potential under the action of the untwisting force of intercalators obtained in Section 3.1, formula 19 is also considered. In this case, the barrier is \(\epsilon = 2.5 \text{ kcal/mol}\). bending, unwinding, softening of the fragment \(C_u/C_{uo}\) for three types of models, as well as the energy per base pair at elastic uniform deformation with the same softening of the fragment stiffness and the average energy per pair at the conformationally induced localized bending of the DNA fragment.

All values are given for localized deformations on 4, 6, 8 base pairs. As can be seen from Table 2 for the third model, which takes into account both the internal component and its relationship with the external one and the relationship between internal components, the anisotropy of bending and the effect of a decrease in the barrier between conformational states during the formation of bistability under the action of the untwisting force intercalators, without softening the stiffness for 4 pairs and with about 12% reduced stiffness, localized bending can form according to the conformation-induced mechanism.

It is interesting to note that for a localized deformation with a length of 6 pairs, the bending magnitude is 52° and untwisting by 27° provided that the flexural stiffness decreases by 12.2%, which is realized due to the neutralization of charges by the protein complex. Thus, the general
conformation-induced deformation of the central fragment of the TATA box into $95^\circ$ untwisting and $85^\circ$ bending is realized.

In the paper the model of deformation of conformationally bistable DNA fragment was formulated. The model allows to describe consistent mechanism of deformation of the DNA TATA box during binding with protein complex. The maximum deformation in the center and its stability sufficient for proteins to recognize it is argued. The main elements of the model of intrinsic-induced DNA deformation are bistability of the conformational potential of the DNA fragment, the coupling of internal conformational changes with a change in parameters determining twist and bending deformation, the coupling between torsion and bending and effect of bending anisotropy of double helix DNA. These elements form the physical basis of the unique deformation of the TATA-box of DNA and make it possible to explain and predict the mechanisms of controlled DNA compaction.

References

[1] J.L.Kim, S.K.Burley, 1.9 A resolution refined structure of TBP recognizing the minor groove of TATAAAAAG, Nat.Struct.Biol., 1(9), 638-653 (1994)

[2] Youngchang Kim, James. H. Geiger, Steven Hahn, Paul B. Sigler, Crystal structure of a yeast TBP/TATA-box complex Nature volume 365,512–520(1993)

[3] Joseph L. Kim, Dimitar B. Nikolov,Stephen K. Burley, Co-crystal structure of TBP recognizing the minor groove of a TATA element Nature, 365, 520–527 (1993)

[4] A. Klug, A. Jack, M. A. Viswamitra, Olga Kennard, Z. Shakked, T. A. Steitz, Mol. Biol., 131, 669-680 (1979)

[5] S.Brahms, S.K.Brahmachari, N.Angelier and J.G.Brahms,NAR, v.9 ,4879-4893 (1981)

[6] Klug A. Opening the gateway. Erratum in Nature, 365, 6447 (1993)

[7] Sequence dependence of DNA bending rigidity, Stephanie Geggier and Alexander Vologodskii PNAS August 31, 107 (35) 15421-15426, (2010)

[8] Strong bending of the DNA double helix Alexander Vologodskii and Maxim D. Frank-Kamenetskii, Nucleic Acids Research, Vol. 41, No. 14 6785–6792 (2013)

[9] Amzallag A., Vailliant C., Jacob M., Unser M., Bednar J., Kahn J.D., Dubochet J., Stasiak A., Maddocks J.H. 3D reconstruction and comparison of shapes of DNA minicircles observed by cryo-electron microscopy, Nucleic Acids Res., 34, 125(2006)

[10] D.B. Nikolov and S.K. Burley, RNA polymerase II transcription initiation: A structural view, PNAS January 7, 94 (1) 15-22 (1997)

[11] Zhengrong Wu,Melissa Maderia,§ Joseph J. Barchi, Jr.,§ Victor E. Marquez,§ and Ad Bax,Changes in DNA bending induced by restricting nucleotide ring pucker studied by weak alignment NMR spectroscopy Proc Natl Acad Sci U S A., 102(1), 24–28 (2005)

[12] E.N. Nesterova, V.P. Chuprina, B.I. Poltev, Possible A-conformations and intermediate between B- and A-forms conformations of DNA fragments with alternating purine-pyrimidine sequences, Molecular Biology (Russian),33,p.845-854 1999
[13] R. Lavery, A. Lebrun, J.-F. Allemand, D. Bensimon, and V. Croquette, J. Phys.: Condens. Matter 14, R383 (2002)

[14] Jou Z.S.(1), Chiu T.K., Leiberman P.M., Baikalov I, Berk A.J., Dickerson R.E., How proteins recognize the TATA box, J. Mol Biol. Aug 16, 261(2), 239-254 (1996)

[15] Donald M. Crothers, Tali E. Haran, and James G. Nadeau, Intrinsically Bent DNA, THE JOURNAL OF BIOLOGICAL CHEMISTRY, 265, 7093-7096 (1990)

[16] Ten years of tension: single-molecule DNA mechanics Carlos Bustamante, Zev Bryant, Steven B. Smith, NATURE, 421(23), 423-427 (2003)

[17] P.D. Dans, A. Perez, I. Faustino, R. Lavery, M. Orozco, Exploring polymorphisms in B-DNA helical conformations, Nucleic Acids Res, 40(21), 10668-10678 (2012)

[18] D. Flatters and R. Lavery Biophysical Journal, 75, 372-381 (1998)

[19] Achim Sandmann, Heinrich Sticht, Probing the role of intercalating protein sidechains for kink formation in DNA PLOS ONE, 12, (2018)

[20] Volkov SN, Kosevich AM, Wainreb GE. Theoretical studies in low-frequency vibrations of DNA macromolecules. Biopolym Cell, 5(6), 32-39 (1989)

[21] Sergey N. Volkov, Understanding the mechanism of DNA threshold elongation, Low Temperature Physics/Fizika Nizkikh Temperatur, 44(7), 893–904 (2018)

[22] P.P. Kanevska, S.N. Volkov, Intrinsically induced deformation of a DNA macromolecule, Ukr.J.Phys., 51, 1003-1009 (2006)

[23] W. Saenger, Principles of Nucleic Acid Structure, Springer-Verlag, New York. 1984.

[24] Jeff Gore, Zev Bryant, Marcelo Nollmann, Mai U. Le, Nicholas R. Cozzarelli, Carlos Bustamante, DNA overwinds when stretched, Nature 442, 836-839 (2006)

[25] A. Vologotskii, Biophysics of DNA Cambridge University Press, Cambridge, United Kingdom (2015)

[26] S.N. Volkov, Modeling B-A transformations of DNA double helix, J. Biol. Phys., 31, 323-337 (2005)

[27] Gali Guzikevich-Guerstain and Zippora Shakked, A novel form of the DNA double helix imposed on TATA-box by TATA-binding protein, Nature Structural Biology, 3(1), (1996)

[28] M.Y. Tolstorukov, R.L. Jernigan, V.B. Zhurkin, Protein – DNA hydrophobic recognition in the minor groove is facilitated by sugar switching, Journal of Molecular Biology, 337, 65-76 (2004)