Long DNA molecule as a pseudoscalar liquid crystal

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We show that a long DNA molecule can form a novel condensed phase of matter, the pseudoscalar liquid crystal, that consists of aperiodically ordered DNA fragments in right-handed $B$ and left-handed $Z$ forms. We discuss the possibility of transformation of $B$-DNA into $Z$-DNA and vice versa via first-order phase transitions as well as transformations from the phase with zero total chirality into pure $B$- or $Z$-DNA samples through second-order phase transitions. The presented minimalistic phenomenological model describes the pseudoscalar liquid crystal phase of DNA and the phase transition phenomena. We point out to a possibility that a pseudoscalar liquid nano-crystal can be assembled via DNA-programming.

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DNA is a biopolymer that provides with the basic mechanisms of biological information processing. Schrödinger was the first who recognized that a gene or the whole chromosome thread is an aperiodic crystal [1]. It consists of two types of base pairs (AT and CG nucleotide pairs) which are placed in a random order along the molecular chain. Meanwhile natural DNA exists as a double helix bound state [2]. Each base in one strand is connected to a base in the other strand by hydrogen bond link. Successive bonds are slightly angled to each other leading to the famous double-helix form of DNA. Depending on its environment and mechanical strain, the DNA double helix may have several different helical forms, of which the most common are right-handed $A$- and $B$-DNA [3], and the most peculiar is the left-handed $Z$-DNA [4]. Several different helical conformations of DNA may even coexist as domains of the same long molecule [5] as well as transform into each other.

Previously it was pointed out [6] that different condensed matter phases may be formed inside long polymers, including a liquid crystal phase. In the present paper we will concentrate on the formation of a novel liquid crystal phase within a long DNA molecule. The main idea here is that the pieces of the molecule may have different helicity (being in $B$ or $Z$ forms). This situation is similar to the case of the pseudoscalar liquid crystal that was hypothetically introduced by Zel’ dovich back in 1974 [7]. The peculiarity of such a phase is that a local right-handed helix may transform into a left-handed one and vice versa meanwhile interacting with other helical parts of the molecule. Change of the temperature leads to an ordering that happens via a spontaneously broken chiral symmetry phase transition. The ordered phase thus represents the pseudoscalar liquid crystal [7]. The order parameter for liquid crystals is the orientation of its molecules and for a pseudoscalar liquid crystal the order parameter is the chirality [8]. In our case it is the local difference between the number of oppositely-handed helices. A substantial difference from the other liquid crystals [8] consisting of chiral molecules is that the helices in pseudoscalar crystals can change their chirality under external conditions.

Consider a DNA molecule as a sequence of pieces containing right- and left-handed helices, being in one of the two $B$ or $Z$ forms with opposite chiralities. The pieces interact with each other that may lead, as we show below, to phase transitions bringing the molecule, e.g., to a pure left-handed $Z$-DNA. The proposed mechanism can explain how one of the structures, say the $Z$-form, emerges during intracellular processes. For the quantitative purposes we will employ a combination of Ising-type nearest-neighbor interactions and random interactions of distant along the chain parts which may come close. The long-range interactions may occur due to random bending of the DNA molecule caused, e.g., by looping proteins [10].

We now present the following simple phenomenological model for description of pseudoscalar liquid crystal phase of DNA. This is a statistical mechanical model defined on a one-dimensional lattice with each site corresponding to a rung of the ladder. A spin variable $\chi_i$ is associated with each site $i$, where we choose $\chi_i = -1$ to correspond to the energetically more favorable right-handed helical rotation (that means the particular base pair belongs to the $B$-form segment of the molecule) and $\chi_i = +1$ for the base pair in the left-handed $Z$-form. Notice that one-dimensional Ising models with chiral variables were applied to study random copolymers and bent-core liquid crystals in [11]. Their study can be easily extended to account for long-range interactions, e.g., via loop formation in the case of copolymers.

It is reasonable to assume that the neighbor base pairs will try to get into the same form and thus we will take the nearest-neighbor interactions to be ferromagnetic. Besides the nearest-neighbor interactions we will take into account random interactions between base pairs which are distant along the chain but come close in space. We assume an arbitrary folding of the DNA molecule so that any two base pairs may get connected, e.g., via the looping proteins [10]. The proposed model has the following Hamiltonian

$$H = -g \sum_{i=1}^{N-1} \chi_i \chi_{i+1} - \gamma \sum_{i<j}^{N} J_{ij} \chi_i \chi_j - h \sum_{i=1}^{N} \chi_i + \alpha \sum_{i<j}^{N} J_{ij}$$

where $g > 0$ is the coupling parameter of nearest-neighbor interactions responsible for the torsional stiffness of the polymer; $J_{ij}$ are the link variables, taking values 0 and 1 when the $i$ and $j$ nodes are uncoupled or coupled, e.g.,
by looping proteins, correspondingly; \( \gamma > 0 \) is the energy of interaction between two distant base pairs coupled via appeared link; \( h \) is the half of the energy difference between the states with opposite helicity; \( \alpha \) is the energy of formation of a link connecting \( i \) and \( j \) sites. We introduce and will use another parameter \( c \) defined via \( c/(N-c) = e^{-\alpha\beta} \), where \( \beta \) is the inverse temperature. The ratio can be roughly treated as the probability of a link formation (see [12] for more rigorous formulations and details of a related model that describes a network of fluctuating links). We will assume sparse connectivity \( c/N \ll 1 \) as we suppose that the number of uncoupled distant base pairs that tend to get coupled is much less than the number of base pairs \( N \).

The proposed model can be reduced to an effective mean-field Hamiltonian with the link variables being eliminated. Indeed, we proceed with calculation of the partition function \( Z = \text{Tr}_X \text{Tr}_J \exp \left[ -\beta H \right] \), where \( \text{Tr}_X \equiv \prod_{i=1}^N \sum_{\chi_i = \pm 1} \) and \( \text{Tr}_J \equiv \prod_{ij} \sum_{\chi_{ij} = 0,1} \) are traces over the corresponding variables. Taking the trace \( \text{Tr}_J \) we obtain the following expression for the partition function

\[
Z = \text{Tr}_X e^{\beta \left[ g \sum_{i=1}^{N-1} \chi_i \chi_{i+1} + h \sum_{i=1}^N \chi_i \right]}
\]

\[
\times \prod_{ij} \left( 1 + e^{-\beta \alpha + \beta \gamma \chi_{ij}} \right)
\]

Recalling the definition of \( c \) and that \( c \ll N \), we get for the last product factor \( \exp \left[ c \sum_{ij} \beta \gamma \chi_{ij} \right] \). Noting then the identity \( (r = \pm 1) e^{\beta \gamma \tau} = b_0 + b_1 \tau, b_r = \tanh^r(\beta \gamma) \cosh(\beta \gamma) \) \( (r = 0,1) \) we can now rewrite the partition function as

\[
Z = e^{\frac{1}{2}c(N-1) \cosh \beta \gamma} \text{Tr}_X e^{\beta \left[ g \sum_{i=1}^{N-1} \chi_i \chi_{i+1} + h \sum_{i=1}^N \chi_i \right]}
\]

\[
\times \exp \left[ \frac{c}{N} \sinh \beta \gamma \sum_{ij} \chi_i \chi_j \right]
\]

Thus we have arrived at the partition function with the following effective Hamiltonian

\[
H = -g \sum_{i=1}^{N-1} \chi_i \chi_{i+1} - \gamma' \sum_{i<j} \chi_i \chi_j - h \sum_{i=1}^N \chi_i
\]

where the coupling parameter is \( \gamma' = \frac{c}{N} \sinh \beta \gamma \). The first term is responsible for interactions between nearest-neighbor base pairs. It assures that neighbor pairs tend to get the same value of chirality. The second term in the Hamiltonian describes the effective mean-field interaction between base pairs. The last term is the half of the energy difference between the right- and left-handed helices at the sites of the chain.

We now introduce the order parameter \( \mu = \frac{1}{N} \sum_{i=1}^N \chi_i \) which takes the values \( \mu = -1 \) and \( \mu = 1 \) for the pure samples of \( B \) and \( Z \) forms of DNA, respectively. To calculate the partition function for the above mean-field Hamiltonian we use the relationship \( \sum_{i<j} \chi_i \chi_j = \frac{1}{2} (\sum_{i=1}^N \chi_i)^2 - \frac{1}{2} N \), the Hubbard-Stratonovich transformation \( e^{\frac{1}{2} \mu (\sum_{i=1}^N \chi_i)^2} = \int_{-\infty}^{\infty} \frac{dz}{\sqrt{2\pi/a}} e^{-\frac{a \mu^2}{2} + a \mu \sum_{i=1}^N \chi_i} \) and the expression for the partition function of the one-dimensional (1D) Ising model \([13]\). Then the partition function takes the form \( Z \propto \int_{-\infty}^{\infty} d\mu e^{\beta N f(\mu)} \) with the effective free energy \( f(\mu) \) given by

\[
f(\mu) = \frac{1}{2} \mu^2 - \beta^{-1} \ln \cosh(\beta(h + \mu)) + \sqrt{\sinh^2 \beta(h + \mu) + e^{-4\beta g}}
\]

where we have defined \( b = c \sinh \beta \gamma \).

To further analyze equilibrium properties of the substance under consideration the extreme values of \( \mu \) are to be obtained via \( f'(\mu) = 0 \) that leads to the following state equation

\[
\mu = \frac{\sinh \beta(h + \mu)}{\sqrt{\sinh^2 \beta(h + \mu) + e^{-4\beta g}}}
\]

The dependence of the order parameter \( \mu \) on temperature \( T \) is presented in Fig. 1. For the zero-field case \( (h = 0) \) one would have a second-order phase transition. The molecule spontaneously transforms into a structure that has non-zero total chirality. It chooses between \( B \) and \( Z \) forms. The critical temperature of the phase transition is determined via \( \beta_c b = e^{2\beta_c g} = 1 \). If the field is non-zero then the system goes through the phase transition to get the form that is favored by the sign of the field. The field \( h \) depends on the external parameters that are determined by environmental conditions such as pH value, salt concentration, and other chemical as well as mechanical factors (e.g., locally applied forces and torques).

For a fixed constant temperature there can be a first-order phase transition for chirality versus the field as demonstrated in Fig. 2. The phase transition transforms the right-handed \( B \)-DNA into left-handed \( Z \)-DNA at the
The critical point \( h_c = 0 \) where the external parameter changes its sign. Z-DNA corresponds to a state of the molecule with the energy higher than the one in B form. Among the factors which induce \( B - Z \) transitions are \((K - X)_n - K\) peptide, polynuclear Pt-complexes, etc [14]. The inverse \( Z - B \) transition can be induced by KWGK peptide, daunomycin, and several other substances [14].

\( B - Z \) transitions have been extensively investigated that led to several models [14]. Recently molecular dynamics [13] and coarse-grained model [10] simulations were carried out to provide with more satisfactory explanation of the molecular mechanisms of the \( B - Z \) transitions. In contrast, we here focus on the phenomenology of the transitions that are described by the minimalistic model presented above. The main goal was to demonstrate the possibility of transformations under the influence of the external factors and temperature.

As we mentioned it was shown that different helical conformations of DNA may coexist as domains of the same long molecule [2]. Now consider a chromatin, that is the complex of DNA and proteins in which the generic material is packaged inside the cells with nuclei [3]. Let us assume that a DNA molecule in chromatin happens to consist of right- and left-handed parts placed in a random order along the chain. Besides, chromatin structure is dynamic [17] that is important because changes in its structure can be inherited independent of the DNA sequence itself, the so-called epigenetic inheritance. Our model is able, in principle, to mimick the case of DNA molecule with a dynamic structure as it provides with a plasticity mechanism via the fluctuating links (random bending of DNA molecule caused by looping proteins) that (dis)connect base pairs. Thus a question arises if a DNA molecule in a chromatin can naturally exist in the state of matter we consider here, the pseudoscalar liquid crystal. This is truly an astonishing possibility and further experimental and theoretical investigation of the molecular details would shed more light onto that.

In conclusion, we have shown that a long DNA molecule, that consists of aperiodically ordered right-handed \( B \) and left-handed \( Z \) fragments, can form a novel condensed phase of matter, the pseudoscalar liquid crystal. We presented a minimalistic phenomenological model that describes the pseudoscalar liquid crystal phase of DNA and related phase transition phenomena. Generally speaking, one can use the following 1D Hamiltonian for theoretical treatment of the pseudoscalar liquid crystal

\[
H = \frac{g}{2} \int dl \left( \frac{\partial \chi(l)}{\partial l} \right)^2 + \gamma \int dl dl' J(l, l') \chi(l) \chi(l') + \int dh(l) \chi(l)
\]

with the continuous along the chain variable \( \chi(l) \) and the interaction potential \( J(l, l') \). Here \( \chi(l) \) plays the role of the liquid crystal chiral variable defined as \( n \cdot \nabla \times n \) with \( n \) being the director for conventional liquid crystals [3], and \( h(l) \) being a heterogenous (random) external field.

Further experimental research is needed to identify if this condensed state of matter exists in nature. Yet another foreseeable way towards the new state of matter would be assembling pseudoscalar liquid nano-crystals via DNA-programming [10].

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examples of pseudoscalars are magnetic flux, spin helicity and the chirality which is considered in the present paper.

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