

# Packing a Semi-Flexible Molecular Chain

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二重ラセン DNA は直径が 2nm, 持続長が 50nm 程度の剛直な高分子である。細胞内に存在して遺伝情報を蓄えている DNA は、全長が mm-cm のオーダーであるので、このような長い分子鎖は全体としては、半剛直 (semiflexible) な紐としての性質を持つ。私たちは、半剛直な紐状分子の折り畳み転移は、著しい不連続性を示し、ランダウ流の対称性による定義では、一次相転移であることを明らかにしてきている。今回の講演では、このような半剛直性の分子の紐の折り畳み転移の平衡論および、速度過程に依存した、折り畳み構造の多様性について論じたのち、真核細胞での DNA の折り畳み構造であるクロマチンの構造論についての私たちの最近の研究結果について報告した。本稿では、クロマチンの基本構造である、ヌクレオソーム (nucleosome) 構造について物理的な視点からの研究を紹介したい。

## 1 Introduction

A polymer chain exhibits plural number of length-scales, such as contour length  $L$ , persistence length  $\lambda$ , and width  $d$ . When  $L \gg \lambda \gg d$ , we call the chain as semi-flexible. In usual genomic DNA molecules,  $L \sim \text{cm}$ , whereas double stranded DNA structure is characterized as  $\lambda = \text{ca. } 50 \text{ nm}$ , and  $d = \text{ca. } 2 \text{ nm}$ . It is obvious that genomic DNA molecules are classified as semi-flexible chain.

A semi-flexible chain exhibits unique properties.[1, 2] i) A single chain undergoes large discrete transition between elongated coil and folded compact states. ii) The transition is classified as a first-order phase transition under the criterion of Landau. iii) The compact state exhibits poly-morphology, rich variety of steric structures are found such as toroid, rod, spool-like, pearling.

In eukaryotic cells, DNA is compactly stored in a small cell nucleus by assuming a highly organized and hierarchical structure, which is called chromatin. The structure and dynamics of chromatin are considered to be essential for fundamental functions of DNA, such as transcription, replication, and duplication under the actions of various proteins and enzymes. Therefore, it has been and is an important challenge to elucidate the structure as well as the mechanism of the formation of chromatin. The minimum elementary repeating unit of chromatin is the nucleosome, in which DNA is wrapped around a positively charged core particle, histone octamer, about 1.75 times in a left-handed manner. Therefore, understanding the stability and dynamics of the nucleosome is an important first step that could lead to elucidation of the higher-order functions of chromatin.

One of the most striking aspects of the nucleosome structure is the uniformity of the direction of wrapping, wrapping chirality. In particular, DNA is wrapped around the nucleosome core particle exclusively *in a left-handed manner* in living cells on the earth. It would be very interesting to explore the origin of this chiral selection from the viewpoint of the intrinsic elasticity of DNA. The elasticity of DNA has been extensively investigated through, for example, mechanical stretching experiments. We adapt the approximation of worm-like chain as a model of DNA. We adapt a model by taking into account of the coupling of twisting with stretching

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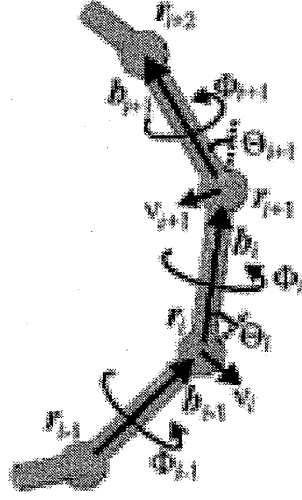


Figure 1: A schematic picture that shows the definitions of the position vectors  $r_i$  of respective monomeric units, the bond vectors  $b_i$ , the bending vectors  $v_i$ , the bending angles  $\Theta_i$ , and the dihedral angles  $\Phi_i$ .

and also bending. By reflecting the right-handed helical structure on the double-stranded DNA, it is expected that coupling between bending and twisting should be highly asymmetric. In this paper, we present dynamical evidence that the asymmetric coupling between bending and twisting of DNA gives rise to the selection of the direction of wrapping by using the Langevin dynamics at the coarse-grained level.[3]

## 1.1 Modeling[3]

In Fig.1 is shown the model we have adapted in the present study. As for the detail, please see reference [3]. We have introduced the coupling between bending twisting,  $V_{bend,twist}$

$$V_{bend,twist} = \sum_{i=2}^{n-1} \frac{1}{2} \kappa_i (s_{i-1}, s_i, t_{i-1}, t_i) \Theta_i^2. \quad (1)$$

The solvent environment is simulated by the underdamped Langevin dynamics. Basic equations of motion are given by

$$\begin{aligned} m \frac{d^2 r_i}{dt^2} &= -\zeta v_i - \nabla_{r_i} V + g_i(t), \\ m_c \frac{d^2 r_c}{dt^2} &= -\zeta_c v_i - \nabla_{r_c} V + g_c(t). \end{aligned} \quad (2)$$

## 2 Results and Discussion

Figure 2 exemplified the time-dependent change on the warping process of a semi-flexible chain. From the systematic numerical study based on such simplified model, we have confirmed that asymmetric coupling between the bending and twisting of DNA plays a predominant role in determining the direction of wrapping of DNA around a core particle. The basic assumption of

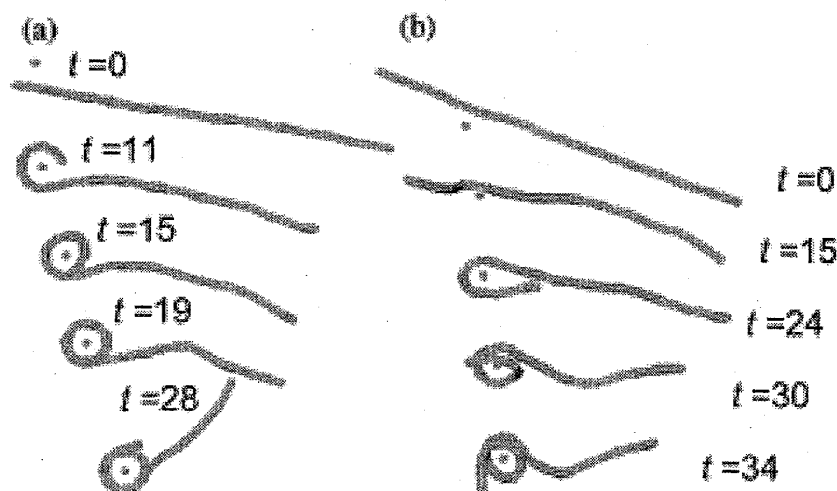


Figure 2: Two typical time evolutions of the model system that consists of a DNA-like polymer and a core particle. The center of the core particle is shown with a small sphere. Time goes on from the top to the bottom in both (a) and (b) as indicated. In (a), the system achieves the proper left-handed wrapping, while in (b), the system undergoes the improper right-handed wrapping.

our model is that DNA has a general tendency to twist in a left-handed manner. This bending-twisting coupling makes DNA select left-handed wrapping with high accuracy, provided that the size of the core is appropriate. If the core is too large, this chiral selection is not accurate enough. On the other hand, if the core is too small, DNA cannot wrap around the core for a sufficient number of turns. This is because the energy cost of bending exceeds the stabilization effect due to the adsorption of DNA on the core surface. If the core size is set within an appropriate range, DNA can select the proper left-handed wrapping with an accuracy of 90%-95%, or even higher. Our results suggest that nature has selected a histone core particle of the appropriate size so that the asymmetric nature of the coupling between bending and twisting of DNA can be effectively used in chiral selection in wrapping. It is expected that in chromatin, which has a poly-nucleosome structure, a cooperative effect between neighboring nucleosomes will enhance the chiral selectivity to be 100%. [3]

The above mentioned numerical results correspond well to our recent results on the experimental observation concerning the interaction between DNA and artificial positively charged spheres. [4, 5] It was found that regular winding around a cationic sphere is performed only when the diameter of the sphere is on the order of persistence length of DNA. When the size of the nano-sphere is larger, DNA interacts with the sphere in an irregular manner. Whereas, for the smaller sphere, DNA never winds around the sphere, instead, it collects the spheres from the environment.

We believe that such unique characteristics of DNA, together with the packing property, should play an important role on the mechanism of self-regulation of genetic information in living cells. Detailed discussion along this line, please check the articles. [6, 7]

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