COMMUNICATIONS IN COMPUTATIONAL PHYSICS
Vol. **6**, No. 3, pp. 577-585

Commun. Comput. Phys.
September 2009

A Solution to a Single Molecular Experiment Problem

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Received 18 July 2008; Accepted (in revised version) 13 November 2008

Communicated by Wei Cai

Available online 6 February 2009

Abstract. Recently Hari Shroff and his collaborators [Nano Letters 5 (2005)] developed a nanoscopic force sensor, but the force which they measured in their single molecular experiment was much lower than the theoretical critical value. In order to fix this problem, we investigate the micromechanics of dsDNA based on the worm-like chain model and flexible hinge model by using Monte Carlo algorithm. The simulation results not only address Hari Shroff's experiment difficulty reasonably, but also provide strong support for flexible hinge mechanism put forward recently by Yan and Marko [Phys. Rev. Lett. 93 (2004)].

AMS subject classifications: 65Z05, 92-08, 65Y99, 68W99

Key words: Monte Carlo algorithm, worm-like chain (WLC) model, flexible hinge model, single molecular experiment, micromechanics of double-stranded DNA (dsDNA).

1 Introduction

Double-stranded DNA (dsDNA) mechanics is essential to understand the DNA organization in cell, since the DNA is tightly folded in cell. The current understanding of DNA mechanics is based on the single molecule stretching experiments for DNA larger than one micrometer ($1\mu m$) or the cyclization experiments for DNA larger than 230 base pairs (bp). Based on the force extension curve and the cyclization probability measurement of long DNA, DNA is understood to be semi-flexible, WLC model, in agreement with these

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experiments with the choice of one parameter, persistence length. It has been widely accepted by biophysicists.

But compared with DNA packaged in cell, the DNA is less bent in experiments mentioned above. Recently there have been more evidences that challenge the worm-like chain model when local bending is too sharp. Cloutier and Widom reported that DNA with length around 100 bp has looping probability several orders of magnitude larger than the prediction of traditional WLC model at temperature 30 degree Celsius [2, 3]; their results do not conflict with earlier experiments because this regime of sharp DNA bending was not investigated by experiments. Later Du and coworkers found that the looping probability of DNA about 100bp is consistent with prediction of the WLC model with 47 nm persistence length at lower temperature 21 degree Celsius [4].

Two experiments above trigger the interests of the theoretical biophysicists. The excited flexible hinge model was proposed to explain the unusual bending elasticity found in Cloutier and Widom's experiment. Traditionally, in physiological conditions, the stiffness of double stranded DNA is considered to be a result of double helix structure, which is made robust by base-pairing and the stacking interactions. By comparison, the covalently bonded sugar-phosphates are completely flexible, characterized by a persistence length of about 1nm. It suggests a mechanism for generations of localized regions of extreme flexibility along the double helix: local disruption of bases interaction, called flexible hinge, may give rise to regions where the double helix can be bent easily. Such disruptions might occur by thermal fluctuations which open bases in localized regions of double helix and explain Cloutier and Widom's experiment successfully. Because the excitation energy to form a hinge defect should be dependent on the temperature, the model does not contradict the results of Du and coworkers in reference [4].

Some other experiments are challenging WLC model further, all of them indicate that the sharp bending of DNA is much easier than WLC model. It is found that spontaneous large-angle bending is more prevalent than predicted by the WLC model [5]. Shroff and coworkers found that short DNA could be bent by force much smaller than the theoretical value predicted by the WLC model [6]. Especially in another recent work by Du and Vologodskii, they also reported that the disruption of base pairs was found in the minicircle with its length shorter than $70nm$ [7]. By comparison, the flexible hinge is noharmonic sharp bending, and the semi-flexible WLC model based on linear elasticity of a continuous material or on harmonic bending of base steps, so it can not solve the problem presented by the experiments mentioned above.

The common features of the recent experiments are that the DNA is sharply bent which challenges the traditional worm like chain model. Motivated by these experiments, we construct two simple models: (I) dsDNA is connected by hard spring; (II) dsDNA is connected by single stranded DNA (ssDNA) and the flexible hinge model is introduced to dsDNA. For model (I), the Euler instability of dsDNA is to be investigated. For the model (II), a comparison will be made between the worm like chain model and the flexible hinge model to identify the reasons that caused the difficulty mentioned in Shroff's work and show some insights into the sharp bending in other experiments.