Available online at www.sciencedirect.com
ScienceDirect
Physica A 384 (2007) 10–14
PHYSICA A
www.elsevier.com/locate/physa

Bubbles in DNA by random force

Rajeev Kapri, Somendra M. Bhattacharjee*

Institute of Physics, Bhubaneswar 751005, India

Available online 8 May 2007

Abstract

We model single strand binding (SSB) proteins as agents exerting randomly oriented force on the bonds in DNA unzipping. The fluctuating force is found to unzip the double stranded DNA (dsDNA) via opening of bubbles along the chain.

Keywords: DNA unzipping; SSB proteins; Random force

1. Introduction

Enzymes like helicases, polymerases, etc. exert force on dsDNA and unzip it to initiate processes like DNA replication or RNA transcription [1]. It was predicted theoretically [2–7] that under the applied pulling force at one end while keeping the other end fixed, the dsDNA unzips to two single strands if the force exceeds a critical value which depends on temperature. Ever since the theoretical prediction of unzipping of DNA [2], various extensions of the basic model have been studied. These include studies of models with intermediate phases [8–11], dependence on pulling directions [12], models with additional features like semiflexibility [13], heterogeneity [14–19], saturation of hydrogen bonding [20], randomness in the medium [21], etc.

The unzipping is a first order phase transition which sets in due to the competition between the binding of the base pairs (to be called monomers) and the orientation of individual links connecting the monomers. However, in a cellular medium there are SSB proteins which bind to single strands thus preventing the strands to get rezipped. The variation in the response of such local regions to force can be modeled by a randomly oriented force which either tries to keep the strands bound or unzip it. In this paper we follow the analysis of Ref. [22] where a single polymer was considered and generalize it to the DNA problem.

2. Model

The Hamiltonian for the DNA, in the continuum, can be written as [2]

$$H = \int_0^N \left[\frac{1}{2}\left(\frac{\partial \mathbf{r}_1}{\partial z}\right)^2 + \frac{1}{2}\left(\frac{\partial \mathbf{r}_2}{\partial z}\right)^2 + V(\mathbf{r}(z)) - \mathbf{g}(z)\cdot\left(\frac{\partial \mathbf{r}_1}{\partial z} - \frac{\partial \mathbf{r}_2}{\partial z}\right)\right] \mathrm{d}z, \tag{1}$$

*Corresponding author.
E-mail address: somen@iopb.res.in (S.M. Bhattacharjee).

0378-4371/$ - see front matter
doi:10.1016/j.physa.2007.04.108

where $\mathbf{r}_i(z)$ is the d-dimensional position vector of a monomer at length z along the contour of the ith strand from the end $z=0$, N is the length of each strand, $V(\mathbf{r})$ is the binding potential, $\mathbf{r}(z)=\mathbf{r}_1(z)-\mathbf{r}_2(z)$, and $\mathbf{g}(z)$ is a random force. Both the strands are anchored at end $z=0$. The first two terms on the right hand side represents the elastic energy or the connectivity of each polymer (taken to be Gaussian). The base pair interaction is for monomers at the same location on the two strands. For the "pure" problem, $\mathbf{g}(z)$ is constant and the force term reduces to the standard form $-\mathbf{g}\cdot\mathbf{r}(N)$. In a discrete form, $\partial\mathbf{r}_i/\partial z$ would represent a link connecting two successive monomers and the force tries to orient the link along it. One may note that on integration by parts the third term gives

$$-\mathbf{g}(N)\cdot(\mathbf{r}_1(N)-\mathbf{r}_2(N))+\int_0^N \frac{\partial\mathbf{g}(z)}{\partial z}\cdot(\mathbf{r}_1(z)-\mathbf{r}_2(z))\,\mathrm{d}z, \tag{2}$$

i.e., a fixed force at the free end plus the gradient of force which acts locally on the strands. Therefore, for a negative force gradient, the two strands stay far apart, thus creating a bubble to minimize the free energy. On a lattice the partition function for the above Hamiltonian can be calculated exactly for a directed polymer via a recursion relation. In $D=1+1$ dimensions the two strands of the DNA are represented by two directed random walks which cannot cross each other and directed along the diagonal of a square lattice. Whenever the strands meet there is a gain in energy $-\varepsilon(\varepsilon>0)$. On each bond between the two consecutive monomers, there is a random force $g(z)=g\zeta(z)$ ($\zeta(z)$ same for a layer) which is always perpendicular to the strands. The magnitude g, related to the standard deviation of the force, is kept fixed but the direction $\zeta(z)=\pm1$ is chosen randomly with equal probability so that the average force, $[g\zeta(z)]_{\mathrm{dis}}=0$. The random force either keeps the strands apart or keeps it close. The schematic diagram of the model is shown in Fig. 1(a).

Let $D_n(x_1,x_2)$ be the partition function of DNA with nth (or the last) monomers of the two strands at positions x_1 and x_2. For every realization of the randomness, the partition function can be calculated exactly by iterating the recursion relation

$$D_{n+1}^{\{\alpha\}}(x_1,x_2)=\sum_{i,j=\pm1} D_n^{\{\alpha\}}(x_1+i,x_2+j)\mathrm{e}^{(j-i)\beta g\zeta_n^{\{\alpha\}}}[1+(\mathrm{e}^{\beta\varepsilon}-1)\delta_{x_1,x_2}] \tag{3}$$

with $x_2\geqslant x_1$. The superscript α in above expression denotes a particular realization and $\beta=1/T$ in units of $k_{\mathrm{B}}=1$.

The quantities of interest are the distance between the strands at the free end, $[\langle x\rangle]_{\mathrm{dis}}$, given by

$$[\langle x\rangle]_{\mathrm{dis}}=\left[\frac{\sum_x x\mathscr{Z}_N^{\{\alpha\}}(x)}{\sum_x \mathscr{Z}_N^{\{\alpha\}}(x)}\right]_{\mathrm{dis}};\quad \mathscr{Z}^{\{\alpha\}}(x)=\sum_{x_2-x_1=x} D^{\{\alpha\}}(x_1,x_2) \tag{4}$$

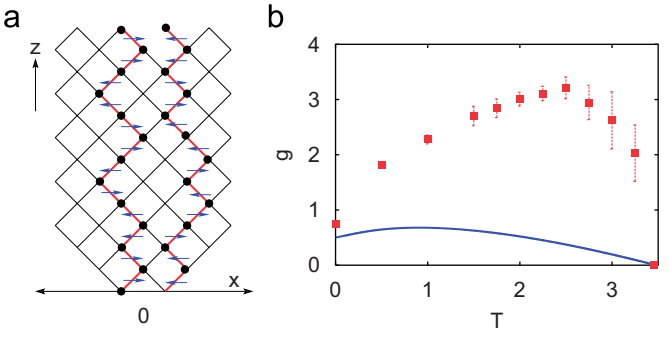

Fig. 1. Schematic diagram for a randomly forced DNA in $D=1+1$ dimensions. The direction of the random force $g\zeta(z)$ is shown by the arrows on each bond.

and the isothermal extensibility, the response to the force, can be expressed in terms of position fluctuation of the end monomers

$$[\chi]_{\rm dis} \equiv \left[\left.\frac{\partial\langle x\rangle}{\partial g}\right|_T\right]_{\rm dis} = (k_{\rm B}T)^{-1}[\langle x^2\rangle - \langle x\rangle^2]_{\rm dis}. \tag{5}$$

3. Results and discussions

For zero force at $T = 0$, the ground state of the DNA is one in which the two strands are completely zipped. On a $D = 1 + 1$ square lattice there can be 2^N degenerate conformations for the zipped DNA of N base pairs contributing an entropy of $S_0(g = 0) = N \ln 2$ for the ground state. The new states can be obtained by flipping the monomers. At any location on the DNA, our model allows flipping of a bound monomer from one of the strands only, because of the non-crossing constraint of the strands. In Fig. 2(a) we have shown four possible force configurations on a particular bound pair of DNA which allows flipping. The mirror images of such configurations also allow flipping. In the presence of a random force these configurations contribute to the entropy. Let n_1, n_2, n_3 and n_4 be the number of such vertices. We have $n_1 + n_2 + n_3 + n_4 = N$. For small g, there is no gain in energy in flipping the monomers of DNA. We gain only for configuration (ii) if $g > \varepsilon/4$. For such cases one sees small bubbles. Below this force, the ground state is unique. For $g > \varepsilon/4$, after flipping all the type (ii) vertices, the average energy is

$$E_0 = -(n_1 + n_3 + n_4)\varepsilon - 4n_2 g = -\frac{N}{4}(3\varepsilon + 4g), \tag{6}$$

taking all the four possible vertices to be equally probable. Equating this with the energy of the unzipped state, $-2Ng$, in which the DNA favors a configuration where each bond of both the strands get oriented in the local force direction, we get the critical value of the force, $g_c = 3\varepsilon/4$. This simple analysis shows that there is a critical force fluctuation above which the DNA favours the unzipped state at $T = 0$. Let us calculate the ground state entropy for $g = \varepsilon/4$. Notice that the flipping of vertex (ii) does not cost any energy if $g = \varepsilon/4$. On an average there are $N/4$ such twofold degenerate vertices. Same number of twofold degenerate vertices is also contributed by the mirror image of vertex (ii). Therefore, the entropy of the ground state for $g = \varepsilon/4$ is $S_0(g = \varepsilon/4) = (N/2)\ln 2$ which is half the entropy of the ground state in the absence of force.

A typical configuration of DNA of length $N = 64$ is shown in Fig. 2(b) for three different force values at $T = 0.5$. At each force the configuration shows bubbles which grow in size with increase in force fluctuation and finally the two strands get separated at some critical force which is realization dependent.

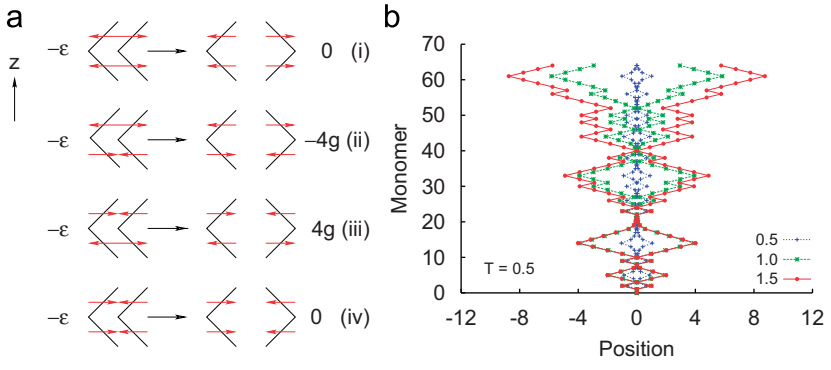

Fig. 2. (a) Energy cost in flipping a monomer of DNA. (b) Typical configurations of DNA for three different g at $T = 0.5$. The length of the DNA is $N = 64$.

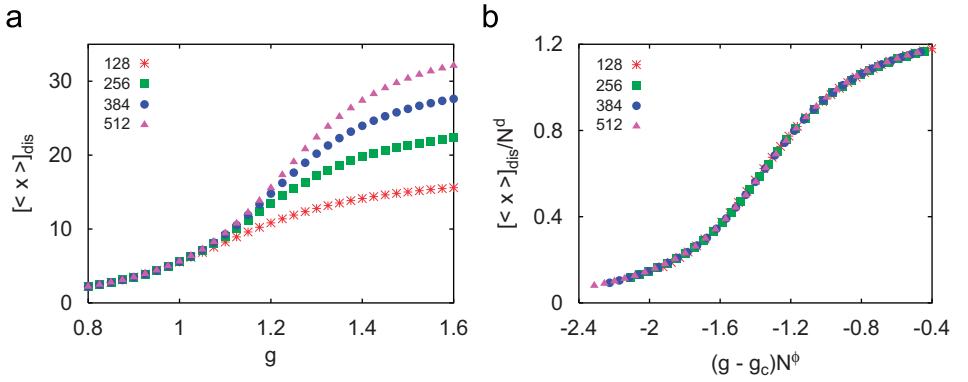

Fig. 3. (a) $[\langle x\rangle]_{\rm dis}$ vs g at $T = 0.5$ for various chain lengths. (b) Data collapse of above data.

For a fixed pulling force at the free end we have $\mathbf{g}(z) = \mathbf{g}$ which is equivalent to choosing $\zeta(z) = 1$ in Eq. (3). For such a case, the above recursion relation can be solved exactly giving the phase boundary

$$g_c(T) = \frac{T}{2}\cosh^{-1}\left[\frac{1}{2}\frac{1}{\sqrt{-e^{-\beta\varepsilon}+1}-1+e^{-\beta\varepsilon}}-1\right] \tag{7}$$

with a purely temperature driven (zero force) denaturation at $T_c = \varepsilon/\ln(4/3)$. The phase boundary is shown by the solid line in Fig. 1(b). The critical force increases with temperature reaching to a maximum and then decreases till it becomes zero at T_c, thus showing reentrance at low temperatures. The reentrance is attributed to the entropy gain of the bound strands which wins over the entropy of two stretched single strands. Below $g_c(T)$ the DNA is in the zipped phase whereas above $g_c(T)$ the DNA is in the unzipped phase with the average distance between the free strands $\langle x\rangle \sim N$. The unzipping transition is of first order with a discontinuity in $\langle x\rangle$ at the phase boundary, i.e., $\langle x\rangle/N \sim |g - g_c|^{-1}$.

For the random force case, the g vs $[\langle x\rangle]_{\rm dis}$ isotherms, averaged over 40,000 force realizations at $T = 0.5$ for $N = 128, 256, 384, 512$ and its collapse are shown in Fig. 3((a) and (b), respectively). The Bhattacharjee–Seno procedure [23] for data collapse yields a scaling form

$$[\langle x\rangle]_{\rm dis} = N^d \mathcal{G}((g - g_c)N^\phi) \tag{8}$$

with exponents $d = 0.53 \pm 0.007$, $\phi = 0.1326 \pm 0.0002$ and $g_c = 1.81 \pm 0.03$. Therefore the quenched average distance between the end monomers $[\langle x\rangle]_{\rm dis}/N = |g - g_c|^{(1-d)/\phi} \sim |g - g_c|^{3.5}$, increases continuously with increase of force making it a continuous transition. Using the above procedure we obtain the critical force at various temperatures. The g vs T phase boundary thus obtained for the random force case is shown in Fig. 1(b) by points. The critical force increases with temperature and starts decreasing only close to T_c where it becomes zero.

4. Conclusions

We have studied the unzipping of DNA by a random force which acts locally on each bonds of the DNA. We found that depending on the strength of the force, bubbles can be developed in the DNA even at $T = 0$ (ground state). The size of these bubbles increases with increase of the force fluctuation, and the DNA gets unzipped when the random force exceeds a critical value. In contrast to the case of pulling at the end where the DNA unzips discontinuously as the pulling force exceeds a critical value, the unzipping via bubbles by random force is a continuous transition.

References

[1] J.D. Watson, et al., Molecular Biology of the Gene, fifth ed., Pearson, Benjamin Cummings, San Francisco, 2003.
[2] S.M. Bhattacharjee, J. Phys. A 33 (2000) L423 (condmat/9912297).

[3] K.L. Sebastian, Phys. Rev. E 62 (2000) 1128.
[4] D. Marenduzzo, A. Trovato, A. Maritan, Phys. Rev. E 64 (2001) 031901.
[5] D. Marenduzzo, et al., Phys. Rev. Lett. 88 (2001) 028102.
[6] Y. Kafri, D. Mukamel, L. Peliti, Eur. Phys. J. B 27 (2002) 135.
[7] A.V. Tkachenko, Phys. Rev. E 70 (2004) 051901.
[8] R. Kapri, S.M. Bhattacharjee, Phys. Rev. Lett. 93 (2004) 248102.
[9] R. Kapri, S.M. Bhattacharjee, J. Phys. Condens. Matter 18 (2006) S215.
[10] S. Kumar, D. Giri, S.M. Bhattacharjee, Phys. Rev. E 71 (2005) 051804.
[11] N. Singh, Y. Singh, Eur. Phys. J. 17 (2005) 7.
[12] S. Kumar, D. Giri, Phys. Rev. Lett. 98 (2007) 048101.
[13] J. Kierfeld, Phys. Rev. Lett. 97 (2006) 058302.
[14] D.K. Lubensky, D.R. Nelson, Phys. Rev. E 65 (2002) 031917.
[15] Jeff Z.Y. Chen, Phys. Rev. E 66 (2002) 031912.
[16] H. Zhou, e-print cond-mat/0007015.
[17] A.E. Allahverdyan, et al., Phys. Rev. E 69 (2004) 061908.
[18] Pui-Man Lam, J.C.S. Levy, H. Huang, Biopolymers 73 (2004) 293.
[19] Pui-Man Lam, J.C.S. Levy, Biopolymers 79 (2005) 287.
[20] D. Giri, S. Kumar, Phys. Rev. E 73 (2006) 050903.
[21] R. Kapri, S.M. Bhattacharjee, Phys. Rev. E 72 (2005) 051803.
[22] R. Kapri, S.M. Bhattacharjee, Phys. Rev. Lett. 98 (2007) 098101.
[23] S.M. Bhattacharjee, F. Seno, J. Phys. A 34 (2001) 6375.