Multifractal analysis of thermal denaturation based on the Peyrard-Bishop-Dauxois model

S. Behnia*
Department of Physics, Urmia University of Technology, Orumieh, Iran

A. Akhshani
School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia and
Department of Physics, IAU, Orumieh Branch, Orumieh, Iran

M. Panahi and A. Mobaraki
Department of Physics, IAU, Orumieh Branch, Orumieh, Iran

M. Ghaderian
Department of Biotechnology and Plant Breeding, College of Agriculture, Zanjan University, Zanjan, Iran
(Received 7 February 2011; revised manuscript received 15 August 2011; published 19 September 2011)

The theory of DNA dynamics is exceedingly complex and not easily explained. In the past two decades, by adapting methods of statistical physics, the dynamics of DNA in contact with a thermal bath is widely studied. In this paper, the thermal denaturation of DNA in the framework of the Peyrard-Bishop-Dauxois (PBD) model through the Rényi dimension is investigated. As a result, the Rényi dimension spectrum of the melting transition process reveals the multifractal nature of the dynamics of the Peyrard-Bishop-Dauxois model. Also, it can be concluded that the Rényi dimension (D_q) at negative values of q is the characteristic signature of pre-melting and thermal denaturation of DNA. Furthermore, this approach is in excellent agreement with previous experimental studies.

DOI: 10.1103/PhysRevE.84.031918 PACS number(s): 87.14.gk, 05.10.−a, 64.60.al, 87.15.A−

I. INTRODUCTION

DNA is not only an essential object of study for biologists; it also raises very interesting questions for physicists [1]. In the past decade, many analytical studies have been conducted to understand the dynamics of DNA [2–7]. A hierarchy of the most important models for nonlinear DNA dynamics was presented by Yakushevich [8]. DNA is a highly dynamic molecule, and it has a large number of degrees of freedom. Hence, the dynamical properties of the Hamiltonian system are not fully understood. Furthermore, most of the introduced Hamiltonians and the corresponding equations of motion for DNA are extremely nonlinear and highly sensitive to physical parameters, especially the thermal bath temperature. Therefore, it is important to investigate the effects of temperature in the theoretical studies [1]. A very simplified model was proposed in 1989 by Peyrard and Bishop [2] to describe DNA denaturation. Unfortunately, this model does not give rise to a sharp first-order-like denaturation that is observed experimentally. This issue was addressed later by Dauxois, Peyrard, and Bishop [9,10] by the addition of an anharmonic term to the stacking interaction. In this sense, the mechanism of the DNA chain in contact with a thermal bath is investigated by using Langevin molecular dynamics simulations [11,12]. But due to the thermal fluctuations in the DNA molecule, exact solutions for the nonlinear excitations of the DNA model have never existed. Hence, new methods are also required for the investigation of the effect of temperature on DNA dynamics.

In previous studies, multifractal methods have been used to analyze the structure of DNA sequences and proteins [13–18]. In this paper, for a better description of the DNA denaturation temperature in the framework of the Peyrard-Bishop-Dauxois (PBD) model, a method based on the multifractal approach is proposed. The obtained results demonstrate that the Rényi dimension spectrum can be considered a signature of the DNA denaturation temperature in the PBD model. Also, this spectrum can be used to find the pre-melting region of the short DNA sequences that provide important insight into biological processes. Furthermore, this approach is in excellent agreement with the other theoretical and experimental studies [12,19,20].

II. DNA IN A THERMAL BATH

The thermal behavior of DNA denaturation based on the PBD model is investigated. For simulating dynamics of the DNA model with the Hamiltonian in contact with a thermal bath, Langevin molecular dynamics is applied to the PBD model [11,21].

A. The PBD model in the Langevin dynamics framework

In the PBD model, the complexity of DNA is reduced to the study of the dynamics of the N base pairs of the molecule. For each base pair we define the variable y_n associated with the transverse stretching of the hydrogen bonds between complementary bases. The index n labels the base pairs along the DNA chain. The model is defined by the following

*s.behnia@sci.uut.ac.ir

Hamiltonian [11,21]:

$$H = \sum_{n=1}^{N} \left(\frac{1}{2} m \dot{y}_n^2 + V(y_n) + W(y_n, y_{n-1}) \right). \quad (1)$$

The potential energy of the system consists of two parts: the on-site interaction $V(y_n)$ within each base pair and the stacking interaction $W(y_n, y_{n-1})$ between adjacent base pairs. A Morse potential is used for the on-site energy, $V(y_n) = D_n[\exp(-\alpha_n y_n) - 1]^2$, where D_n is the dissociation energy of the nth base pair and α_n denotes the spatial range of the potential. Standard, empirically found base-pair-dependent parameter values are customarily employed: $D_{CG} = 0.075$ eV, $\alpha_{CG} = 6.9$ Å^{-1} for a G-C base pair and $D_{AT} = 0.05$ eV, $\alpha_{AT} = 4.2$ Å^{-1} for an A-T base pair. A nonlinear potential describes the stacking interaction,

$$W(x, y) = \frac{K}{2}(1 + \rho e^{-\beta(x+y)})(x - y)^2, \quad (2)$$

where $K = 0.025$ eV Å^{-2}, $\rho = 2$, and $b = 0.35$ Å^{-1}. A prominent alternative description of DNA denaturation and breathing is the PBD model based on the set of Langevin equations [11],

$$m\ddot{y}_n = -V'(y_n) - W'(y_n, y_{n+1}) - W'(y_{n-1}, y_n) - m\gamma \dot{y}_n + \xi_n(t), \quad (3)$$

where m is the mass of the pair, γ is the effective damping of the system, $\xi(t)$ accounts for thermal noise, $\langle \xi_n(t) \rangle = 0$, and $\langle \xi_n(t)\xi_k(t') \rangle = 2m\gamma k_B T \delta_{nk} \delta(t - t')$, with T as the bath temperature.

III. RÉNYI DIMENSION SPECTRUM

From a purely geometric point of view, several methods have been introduced to characterize strange attractors. All the methods rely on concepts developed in the fractal theory [22]. A multifractal structure is characterized by one of two equivalent fractal dimension spectra: (i) the Rényi dimension spectrum D_q or (ii) the spectrum of scaling indices $f(\alpha)$ [23]. Generally, different parts of a strange attractor may be characterized by different values of the fractal dimension.

In the context of dynamical systems theory the Rényi dimensions D_q have been shown to be good candidates to describe the geometric and probabilistic features of the strange attractors [24,25]. The Rényi dimensions are commonly used to characterize the scaling properties of a distribution of points on an M-dimensional space [26,27]. The Rényi dimension spectrum is then given by

$$D_q = \lim_{r \to 0} \frac{1}{q - 1} \frac{\ln \sum_{j=1}^{N(r)} p_j^q}{\ln r}. \quad (4)$$

Note that the Rényi dimension (D_q) involves the probabilities (p_j) raised to the qth power. The definition Eq. (4) was introduced in the context of natural measures occurring in dynamical systems by Grassberger [24] and Hentschel and Procaccia [28]. In practice, almost all calculations of D_q use the generalized correlation sum rather than box-counting method. Therefore, to estimate the Rényi dimension, the generalized correlation sums for various q's is calculated. The generalized correlation sum is defined as [29]

$$C_q(r) = \frac{1}{N} \sum_{j=1}^{N} \left(\frac{1}{N-1} \sum_{(k=1, k \neq j)}^{N} \Theta(r - |x_j - x_k|) \right)^{q-1}. \quad (5)$$

The Rényi dimension (D_q) in terms of the generalized correlation sum can be defined as

$$D_q = \lim_{r \to 0} \frac{1}{q - 1} \frac{\ln C_q(r)}{\ln r}. \quad (6)$$

To estimate the Rényi dimension, the generalized correlation sums for various q's is calculated. We have chosen the interval $q \in [-40,40]$. The resulting Rényi dimension spectrum is a nonincreasing function and is most easily viewed in a D_q vs q plot.

The singularity spectrum $f(\alpha)$ and the generalized dimensions D_q can be derived from each other. The explicit relationship between the set of dimensions D_q and the singularity spectrum $f(\alpha)$ is given by the following Legendre transform [23]:

$$f(\alpha) = \alpha q - \tau(q), \quad \alpha(q) = \frac{d}{dq}\tau(q). \quad (7)$$

There are several physical meanings in the $f(\alpha)$. In particular, the $f(\alpha)$ value at the maximum of the singularity spectrum corresponds to the capacity dimension ($D_{q=0}$). The existence of a phase transition is, however, best indicated by measuring the derivatives of $\tau(q)$ with respect to q [30,31]. By following the thermodynamic formulation of multifractal measures, Canessa showed that the form of C_q resembles a classical phase transition at a critical point [32,33]:

$$C_q \equiv -\frac{\partial^2}{\partial q^2}\tau(q) \approx 2\tau - \tau(q+1) - \tau(q-1). \quad (8)$$

IV. RESULTS

In this paper, the variation of the Rényi dimensions with respect to the system temperature is investigated. In fact, the objective of this study is to evaluate the ability and efficiency of the Rényi dimension spectrum to characterize the DNA denaturation temperature based on the PBD model. The obtained results indicate that the Rényi dimension spectrum is highly sensitive to changes in the temperature of the system. Therefore, the Rényi dimension spectrum can be considered a signature when DNA is denatured. Moreover, this method is more accurate for predicting the critical temperature (denaturation temperature) and interpreting the pre-melting region of short-chain DNA compared to the previous methods [34–38].

Figures 1 and 2 show the calculated D_q for the sequence CCGCCAGCGGCGTTATTACATTTAATTCTTAAGTATTA TAAGTAATATGGCCGCTGCGCC [12] that implies the following results: The Rényi dimensions analysis demonstrated that there is an inverse relationship between D_q and q at a given temperature. In general, for homogeneous fractals $D_q = D_{q'}$ while for multifractals $D_q > D_{q'}$ for $q' > q$ [28]. Therefore, it can obviously be concluded that DNA

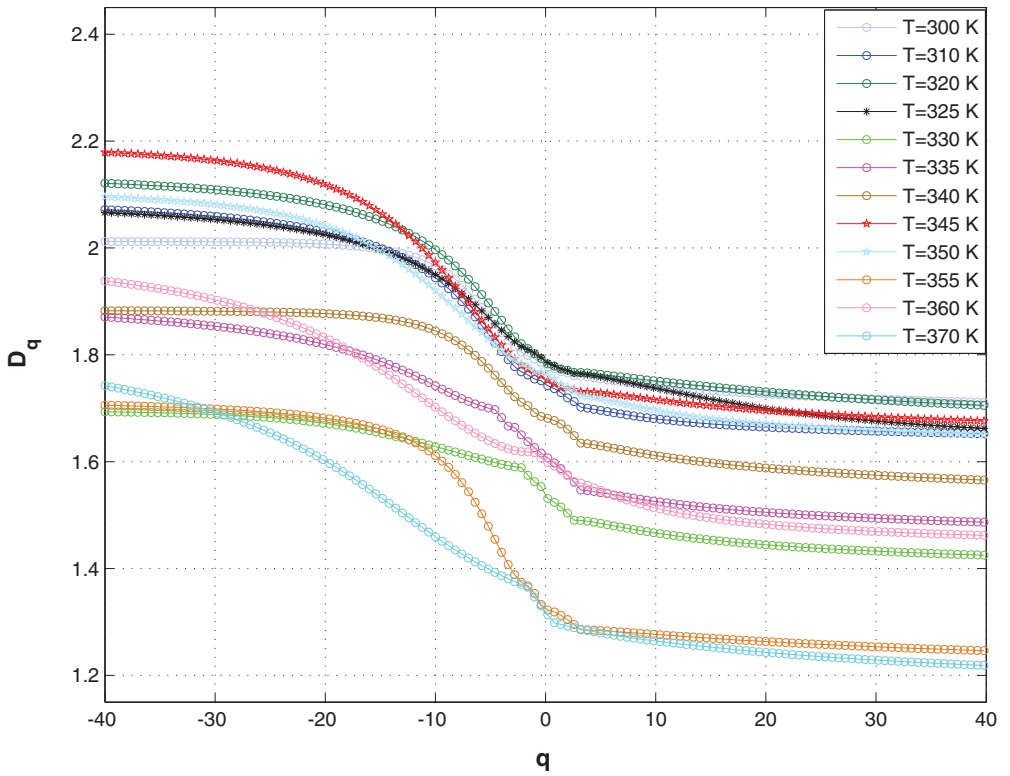


FIG. 1. (Color online) The Rényi dimensions spectrum.

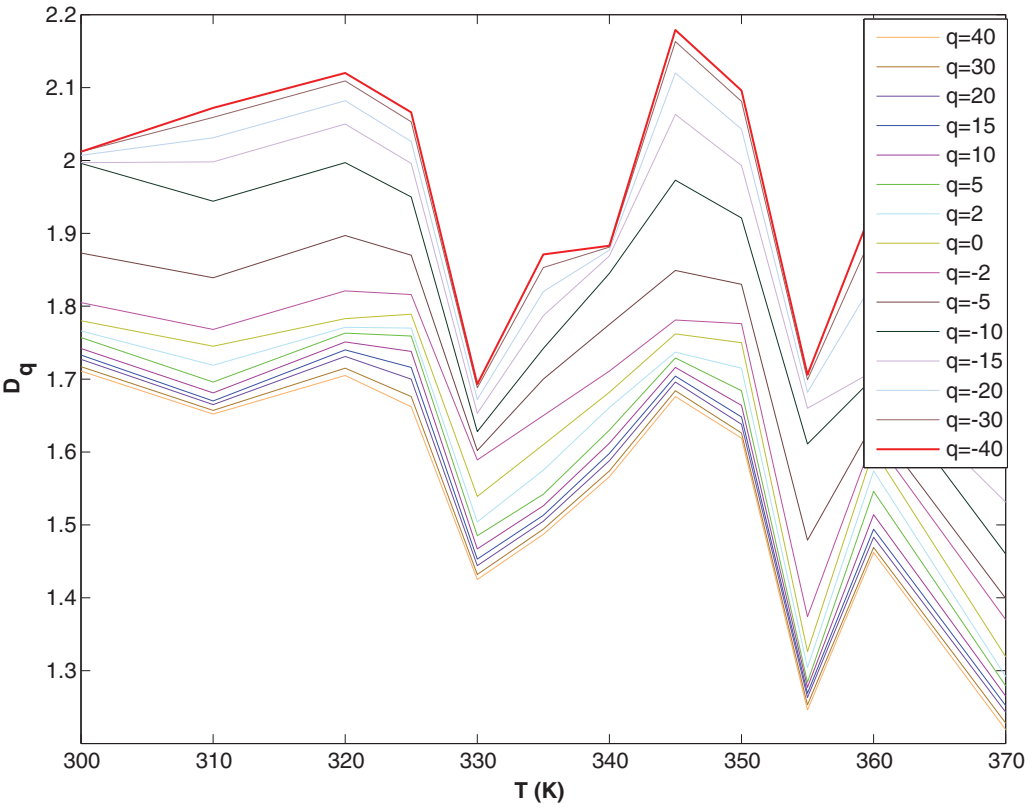


FIG. 2. (Color online) The Rényi dimensions spectrum at various temperatures..

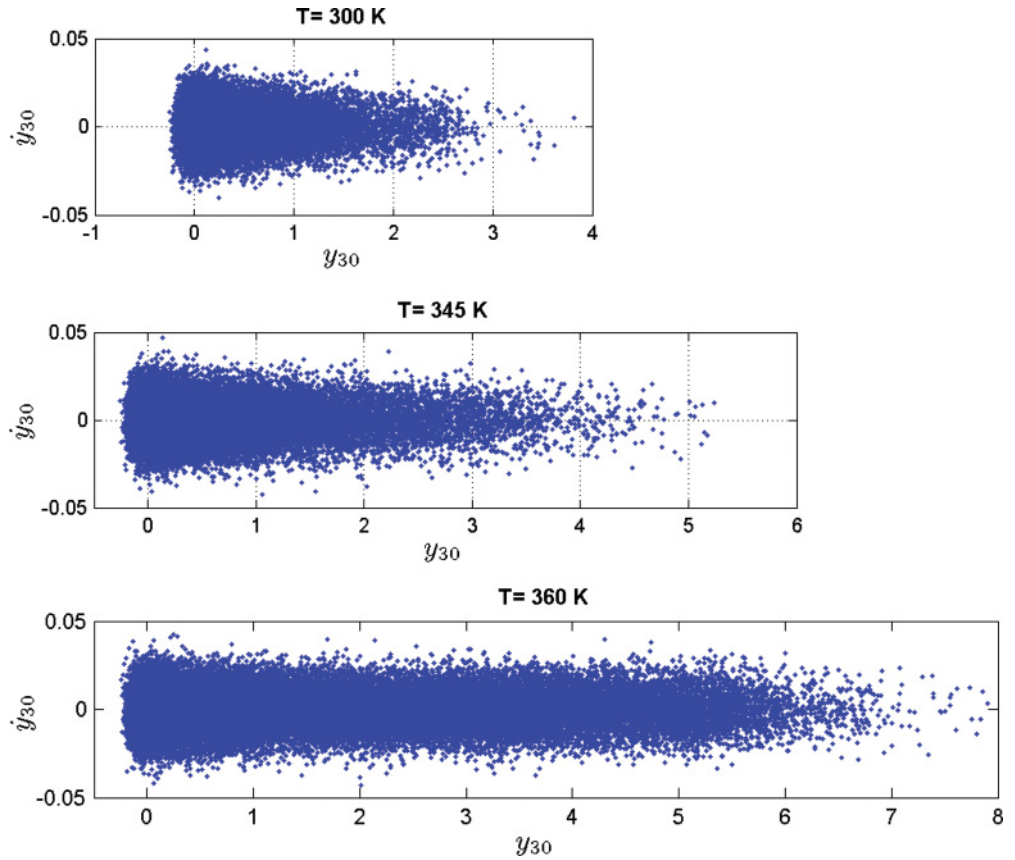


FIG. 3. (Color online) Phase space diagram for 30th base pair.

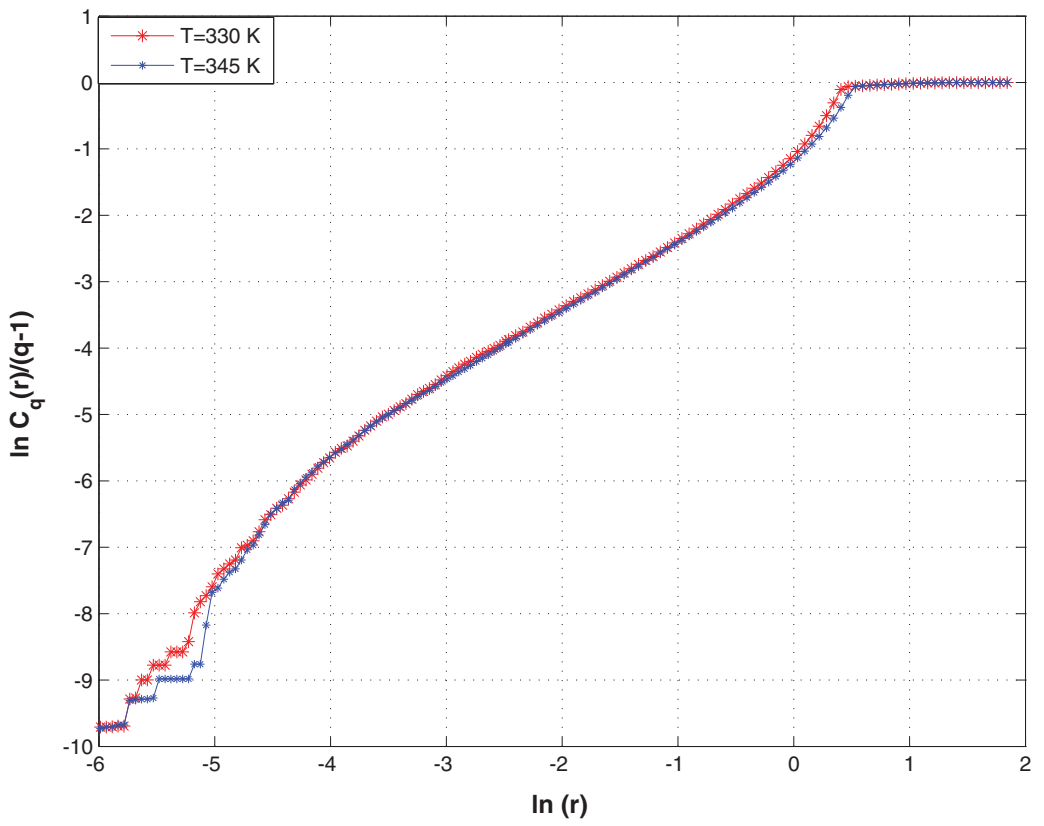


FIG. 4. (Color online) Generalized correlation sum for different temperatures at $q = -40$.

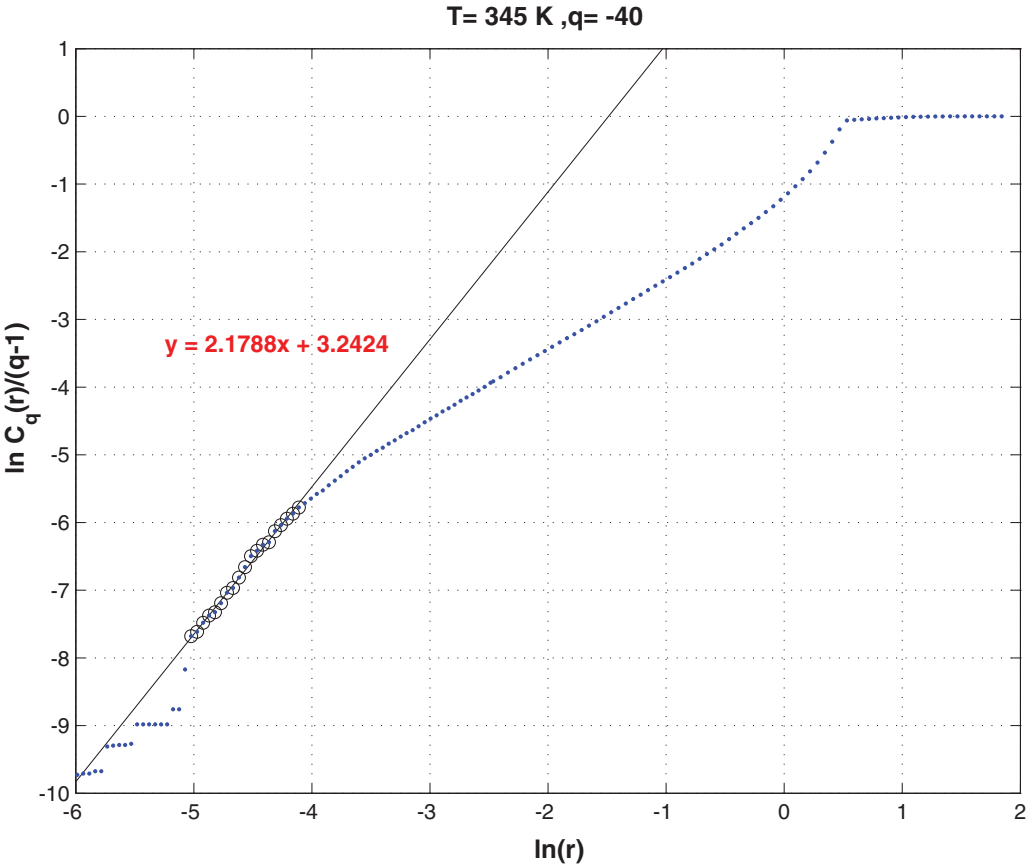


FIG. 5. (Color online) Scaling of the generalized correlation sum for $T = 345$ K, $q = -40$.

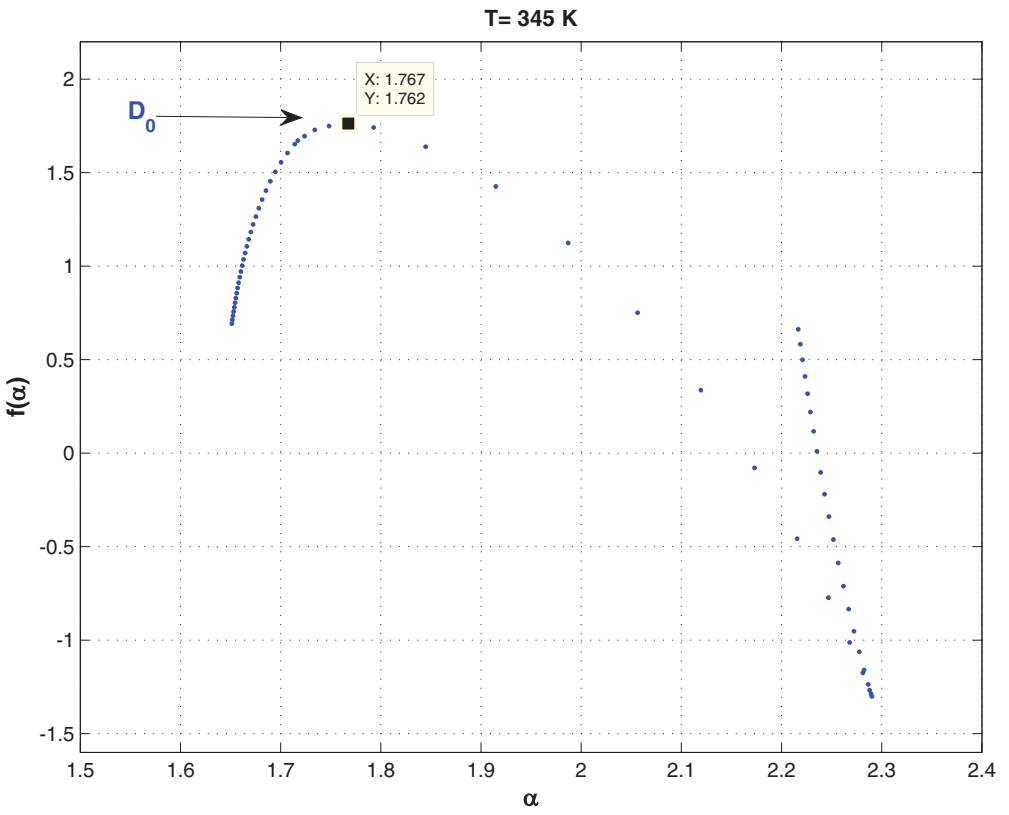
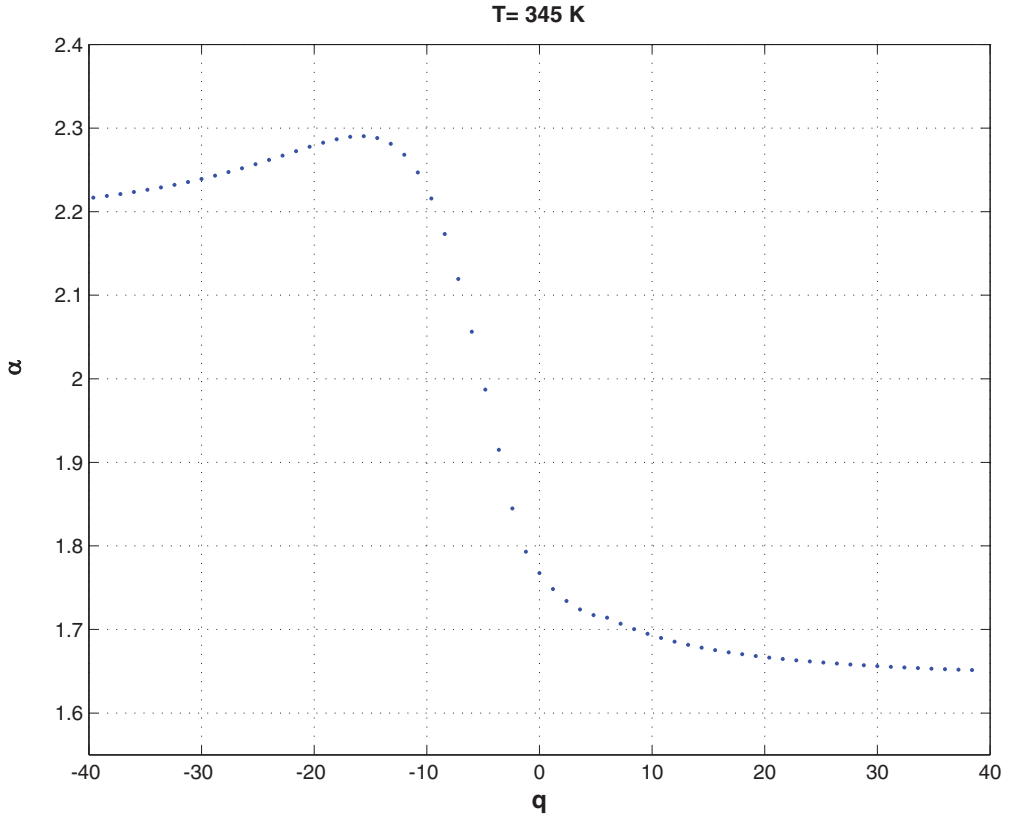


FIG. 6. (Color online) Singularity spectrum $[f(\alpha)]$ for $T = 345$ K.



.

FIG. 7. (Color online) The plot of the function α vs q for $T = 345$ K.

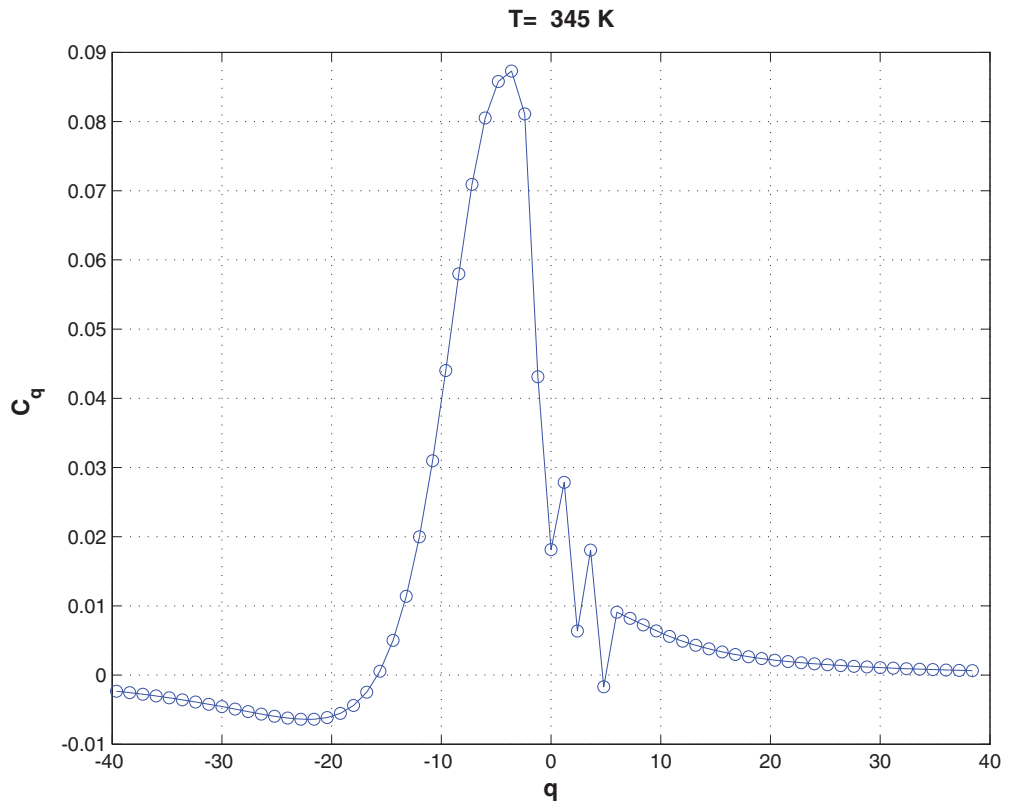


FIG. 8. (Color online) C_q curve for $T = 345$ K.

thermal denaturation in the Peyrard-Bishop-Dauxois model exhibits multifractal scaling behavior. It is worthwhile noting that for negative values of q, there is a maximum value for the Rényi dimensions (D_q) at the denaturation temperature ($T = 345$ K) and sharp changes in the behavior of the Rényi dimensions for the pre-melting region ($320\ \text{K} < T < 335\ \text{K}$). For positive moments $q > 0$, the results of the analysis indicate that there were no significant changes in the values of D_q with respect to q. In general, negative q is important for revealing the geometry of low-density regions [39].

Moreover, the phase space reconstruction of the 30th base pair of the sequence at some selected temperatures is shown in Fig. 3: $T = 300$ K before denaturation; $T = 345$ K during denaturation, and $T = 360$ K after denaturation. These figures confirm that the size of the attractor and the phase space density distribution directly depends on the temperature.

Figures 4 and 5 show, respectively, the generalized correlation sums and the scaling regions for some selected temperatures for different q's. These plots clearly show that there is a region of scaling for some selected temperatures, but to quantify this scaling range more clearly the local slope of $\frac{\ln C_q(r)}{q-1}$ vs $\ln(r)$ is determined.

Selected examples of singularity spectra, $f(\alpha)$ vs α and α vs q for $T = 345$ K, are shown in Figs. 6 and 7, respectively. We find that for $q = 0$, the capacity dimension $D_{q=0} = 1.762$, which is equal to the maximum of the singularity spectrum. In all temperatures, the dimension of the support of the measure $D_{q=0} = f_{\max}(\alpha)$ is lower than 2, ranging from 1.319 to 1.789. As shown in Fig. 6, there is a double back for the domain of large α. The technical reason for this is because the D_q plot saturates quickly for the negative q, resulting in a rising hump in the α vs q plot (see Fig. 7). Two different values of q produce the same α in the rising hump region of Fig. 6; consequently, two different values of q produce the same $f(\alpha)$, since $f(\alpha) \simeq (\alpha, q)$ [40]. A reason for why D_q saturates early for negative q may be the absence of low-probability subsets in the data [41]. The existence of a phase transition is, however, best indicated by measuring the derivatives of $\tau(q)$ with respect to q. According to Fig. 8, this may be an indication of some sort of phase transition [30–32].

V. CONCLUSIONS

DNA denaturation is one of the interesting issues for biologists and physicists [1,2,8,42–47]. Denaturation temperature and the pre-melting phenomenon are very important questions for experimental and theoretical studies from a biological point of view. For instance, UV-Vis absorption spectroscopy or the hyperchromic effect and laser light scattering have been reported in the literature [43,48–50].

Accurate prediction of DNA thermal denaturation is very important for several bimolecular techniques including polymerase chain reaction, sequencing by hybridization, antigen targeting, and southern blotting [51]. Also, DNA thermal denaturation plays an important role in DNA sequencing by denaturation, which is a very significant development in sequencing techniques [52]. Furthermore, the %GC content of the DNA has determined from the denaturation temperature [49,53].

In experimental studies, the actual melting temperature (T_m) of a given piece of the DNA depends on several factors, such as the length of the DNA sequence, the base composition of the DNA, the topological structure, and the salt concentration [48]. Because of the reasons stated above, various denaturation temperatures are reported in the literature [48].

Recently, very advanced and powerful methods have been developed to study the denaturation temperature and melting dynamics of DNA [54–56]. Concerning DNA denaturation temperature, previous methods based on nonlinear Schrödinger equations or classical partition functions are very complex [2,8,57], and sometimes they have reported temperatures far from experimental results [57]. Also, in the mentioned methods, the results would appear to highlight the computational difficulties associated with the partition function [56]. To overcome these difficulties and improve the computational methods, Theodorakopoulos proposed a novel approach based on matrix multiplication [55,56]. The results are in good agreement with the experimental reports [56,58].

In this paper, the multifractal nature of the dynamics of the PBD model is studied, and the Rényi dimension spectrum is reported as a signature for DNA denaturation temperature. Although no approximation has been done in the original model (the PBD model), using multifractal analysis, the critical temperature falls in a range that is in very good agreement with experimental and theoretical reports [12,19,20]. The proposed method has these advantages: it is straightforward, simple to deal with, and more accurate to predict the critical temperature compared to the previous methods [34–38]. In this method, the obtained results are directly derived from the main equation [Eq. (4)], and there is no need to use any approximation methods.

Another important aspect of the PBD model is its potential ability to describe local openings (denaturation bubbles) of the double helix [59]. As shown in Fig. 2 it can be concluded that the results obtained by use of the Rényi dimension spectrum are in very good agreement with previous theoretical and experimental studies [12,19,20].

In conclusion, it seems that multifractal analysis of the PBD model can be an informative index for this model, yet far from fully understood; the results described here are mostly concerned with thermal denaturation. Many aspects are still to be discussed.

In the future, it would be of interest to explore the link between the Rényi dimensions as a measure and %GC content of a chain. Because each G-C base pair has three hydrogen bonds, it is more stable than an A-T base pair, which has only two hydrogen bonds [60,61]. Moreover, the values of the Morse potential parameters in the PBD model are different for G-C and A-T pairs [12,62], and it depends on the proportion of G-C base pairs.

ACKNOWLEDGMENTS

The authors would like to thank Professor Michel Peyrard for valuable comments and Mr. R. Tapia-Rojo for helpful discussions.

[1] M. Peyrard, Nonlinearity **17**, R1 (2004).
[2] M. Peyrard and A. R. Bishop, Phys. Rev. Lett. **62**, 2755 (1989).
[3] J. De Luca, E. Drigo Filho, A. Ponno, and J. R. Ruggiero, Phys. Rev. E **70**, 026213 (2004).
[4] S. Zdravkovic and M. V. Sataric, Phys. Lett. A **373**, 126 (2008).
[5] S. Zdravkovic and M. V. Sataric, Phys. Lett. A **373**, 2739 (2009).
[6] M. Ghorbani and F. Mohammad-Rafiee, Phys. Rev. E **78**, 060901(R) (2008).
[7] S. Behnia, M. Panahi, A. Mobaraki, and A. Akhshani, Phys. Lett. A **375**, 1092 (2011).
[8] L. V. Yakushevich, *Nonlinear Physics of DNA* (Wiley-VCH, Weihheim, Germany, 2004).
[9] T. Dauxois and M. Peyrard, Phys. Rev. E **51**, 4027 (1995).
[10] M. Joyeux and S. Buyukdagli, Phys. Rev. E **72**, 051902 (2005).
[11] B. S. Alexandrov, L. T. Wille, K. O. Rasmussen, A. R. Bishop, and K. B. Blagoev, Phys. Rev. E **74**, 050901(R) (2006).
[12] B. Alexandrov, N. K. Voulgarakis, K. Ø. Rasmussen, A. Usheva, and A. R. Bishop, J. Phys.: Condens. Matter **21**, 034107 (2009).
[13] Z.-G. Yu, V. Anh, and K.-S. Lau, Phys. Rev. E **64**, 031903 (2001).
[14] Z.-G. Yu, V. Anh, and K.-S. Lau, Phys. Rev. E **68**, 021913 (2003).
[15] Y. Zhou, Z.-G. Yu, and V. Anh, Phys. Lett. A **368**, 314 (2007).
[16] J.-Y. Yang, Z.-G. Yu, and V. Anh, Chaos Solitons Fractals **40**, 607 (2009).
[17] S.-M. Zhu, Z.-G. Yu, and V. Anh, Chinese Physics B **20**, 010505 (2011).
[18] A. Provata and C. Beck, Phys. Rev. E **83**, 066210 (2011).
[19] Y. Zeng, A. Montrichok, and G. Zocchi, J. Mol. Biol. **339**, 67 (2004).
[20] Y. Zeng, A. Montrichok, and G. Zocchi, Phys. Rev. Lett. **91**, 148101 (2003).
[21] T. Dauxois, M. Peyrard, and A. R. Bishop, Phys. Rev. E **47**, R44 (1993).
[22] R. Badii and A. Politi, Phys. Rev. A **35**, 1288 (1987).
[23] T. C. Halsey, M. H. Jensen, L. P. Kadanoff, I. Procaccia, and B. I. Shraiman, Phys. Rev. A **33**, 1141 (1986).
[24] P. Grassberger, Phys. Lett. A **97**, 224 (1983).
[25] P. Grassberger and I. Procaccia, Physica D **13**, 34 (1984).
[26] A. Guerrero and L. A. Smith, Phys. Lett. A **318**, 373 (2003).
[27] A. Renyi, Acta Math. Acad. Sci. Hung. **6**, 285 (1955).
[28] H. G. E. Hentschel and I. Procaccia, Physica D **8**, 435 (1983).
[29] R. C. Hilborn, *Chaos and Nonlinear Dynamics: An Introduction for Scientists and Engineers* (Oxford University Press, USA, 2000).
[30] M. H. Jensen, A. Levermann, J. Mathiesen, and I. Procaccia, Phys. Rev. E **65**, 046109 (2002).
[31] R. Rangel and L. E. Guerrero, Phys. Rev. A **43**, 669 (1991).
[32] E. Canessa, J. Phys. A: Math. Theor. **33**, 3637 (2000).
[33] Z. G. Yu, V. V. Anh, K. S. Lau, and L. Q. Zhou, Phys. Rev. E **73**, 031920 (2006).
[34] R. A. Dimitrov and M. Zuker, Biophys. J. **87**, 215 (2004).
[35] T. Das and S. Chakraborty, Europhys. Lett. **85**, 68004 (2009).
[36] D. L. Hien, N. T. Nhan, V. T. Ngo, and N. A. Viet, Phys. Rev. E **76**, 021921 (2007).
[37] T. Garel and C. Monthus, J. Stat. Mech. (2005) P06004.
[38] F. de los Santos, O. Al Hammal, and M. A. Muñoz, Phys. Rev. E **77**, 032901 (2008).
[39] G. Falkovich, K. Gaęwdzki, and M. Vergassola, Rev. Mod. Phys. **73**, 913 (2001).
[40] M. Wolf, Phys. Rev. A **43**, 5504 (1991).
[41] H. Atmanspacher, H. Scheingraber, and W. Voges, Phys. Rev. A **37**, 1314 (1988).
[42] T. Dauxois and M. Peyrard, *Physics of Solitons* (Cambridge University Press, Cambridge, United Kingdom, 2006).
[43] R. Thomas, Gene **135**, 77 (1993).
[44] G. Altan-Bonnet, A. Libchaber, and O. Krichevsky, Phys. Rev. Lett. **90**, 138101 (2003).
[45] M. Rosa, R. Dias, M. da Graca Miguel, and B. Lindman, Biomacromolecules **6**, 2164 (2005).
[46] J.-X. Xiao, J.-T. Lin, and B.-G. Tian, Phys. Rev. E **50**, 5039 (1994).
[47] R. Tapia-Rojo, J. J. Mazo, and F. Falo, Phys. Rev. E **82**, 031916 (2010).
[48] D. W. Ussery, in *Encyclopedia of Genetics*, edited by S. Brenner and J. H. Miller (Academic, New York, 2001), pp. 550–553.
[49] V. T. Verdree, S. Pakhomov, G. Su, M. W. Allen, A. C. Countryman, R. P. Hammer, and S. A. Soper, J. Fluoresc. **17**, 547 (2007).
[50] R. K. Dubey and D. N. Tripathi, Indian J. Biochem. Biophy. **42**, 301 (2005).
[51] L. Dagdug and E. Vázquez-Contreras, Rev. Mex. Fis. S **48**, 0168 (2002).
[52] Y.-J. Chen and X. Huang, Analytical Biochemistry **384**, 170 (2009).
[53] J. Marmur and P. Doty, J. Mol. Biol. **5**, 109 (1962).
[54] G. Weber, N. Haslam, N. Whiteford, A. Prugel-Bennett, J. W. Essex, and C. Neylon, Nat. Phys. **2**, 55 (2006).
[55] N. Theodorakopoulos, Phys. Rev. E **82**, 021905 (2010).
[56] N. Theodorakopoulos, J. Nonlin. Math. Phys. **18**, 429 (2011).
[57] T. Lipniacki, Phys. Rev. E **64**, 051919/1 (2001).
[58] A. Wildes, N. Theodorakopoulos, J. Valle-Orero, S. Cuesta-López, J.-L. Garden, and M. Peyrard, Phys. Rev. Lett. **106**, 048101 (2011).
[59] B. S. Alexandrov, V. Gelev, Y. Monisova, L. B. Alexandrov, A. R. Bishop, K. Ø. Rasmussen, and A. Usheva, Nucl. Acids Res. **37**, 2405 (2009).
[60] H. F. Lodish, *Molecular Cell Biology* (W. H. Freeman, San Francisco, 2000).
[61] B. Lewin, *Genes IX* (Jones and Bartlett, Burlington, Massachusetts, 2008).
[62] A. Campa, Phys. Rev. E **63**, 021901 (2001).