Temperature-Dependent Signatures of Coherent Vibrational Openings in DNA

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Temperature dependent signatures of coherent vibrational openings in DNA

N. K. Voulgarakis,[1,2] G. Kalosakas,[1] K. Ø. Rasmussen,[1] and A. R. Bishop[1]

[1] *Theoretical Division and Center for Nonlinear Studies, Los Alamos National Laboratory Los Alamos, New Mexico 87545*

[2] *Department of Physics, University of Crete and Foundation for Research and Technology-Hellas, P. O. Box 2208, 71003 Heraklion, Crete, Greece*

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We report numerical simulations of the contribution of the transverse hydrogen bond stretching vibrations in the dynamic structure factor of a DNA sequence. We apply a simple nonlinear dynamical model to a finite segment of the bacteriophage T7 core promoter DNA. The temperature dependence of the dynamic structure factor is investigated. A distinct feature is identified and attributed to localized thermal openings (hot-spots) due to nonlinearity combined with sequence specificity. We present the variation of the position and the width of the corresponding dynamic structure factor feature with temperature. Finally, a strong deviation of the Debye-Waller factor from the usual harmonic form is evaluated.

There are two factors ensuring energy localization at specific sites of a biomolecule, necessary for function: specific inhomogeneity (i.e. base-pair sequence) and nonlinearity. Therefore, combined effects of nonlinearity and inhomogeneity *at finite temperatures* should be fundamental in determining functional biomolecular dynamics. In this direction we present here temperature dependent dynamical properties of a minimal nonlinear model applied to a specific sequence of a a finite region of bacteriophage (T7) core promoter DNA. Although we calculate global physical quantities, such as dynamic structure factors, we isolate effects of sequence-specific, site-selective bubbles in this particular inhomogeneous sequence.

A large number of experimental studies probe the low frequency dynamics of DNA using either optical absorption techniques [1–6] or neutron scattering [7–9]. Raman scattering measurements have investigated the dependence of the spectral region around and below $100\,cm^{-1}$ on the temperature [1, 2, 5] as well as the base-sequence [4]. This part of the spectrum has also been studied by far-infrared absorption at different temperatures and salt conditions [3], while at even lower frequencies submillimeter-wave spectroscopy has been proposed as means of probing DNA sequences due to the sensitivity on the primary structure [6]. Thermal neutron scattering experiments have revealed finite coherence lengths at low energy excitations [7, 8].

Low frequency modes correspond to collective motions of the macromolecule that may be relevant in biological processes, as for example in DNA transcription. Such collective excitations include torsional modes, representing angular motions of base-pairs on planes perpendicular to the backbone axis, and transverse radial modes, which represent stretchings of the hydrogen bonds connecting complementary bases pairs and occurring on the same planes.

Here, we use the Peyrard-Bishop-Dauxois (PBD) model [10, 11] to describe the radial fluctuations y_n (n denotes the position of a base-pair along the DNA sequence) of the base-pairs perpendicular to the helical axis. The advantage of the model is that it effectively takes into account local constraints in the motion of interest, by including appropriate nonlinearities in the stacking interaction [11]. Additionally, to accurately reproduce DNA melting transitions [11, 12], the PBD model has been recently found to provide enhanced probabilities for thermally induced interstrand openings at functionally relevant transcriptional sites [13, 14].

We apply the PBD model to a 70 base-pair DNA sequence, corresponding to a region of of the T7 bacteriophage core promoter around the transcription start site (+1): 5'-ATGACCAGTT GAAGGACTGG AAGTAATACG ACTCAGTATA (+1)GGGACAATGC TTAAGGTCGC TCTCTAGGAC-3'.

The dynamic structure factor $S(q,w)$ is calculated from the spatial and time Fourier transform of the displacements $y_n(t)$ [15, 16]. We simulate finite temperatures by performing Langevin molecular dynamics for nucleotides moving under the influence of i) a nonlinear stacking interaction and ii) an on-site Morse potential. For details regarding the total potential energy of the PBD model see Ref. [11]. The parameter values are the same as those used in Refs. [12] and [14], distinguishing between AT and GC base-pairs along the sequence by modifying the corresponding Morse potential's parameters.

In Fig. 1, we display the dynamic structure factor at different temperatures, averaged over 50 different realizations at each temperature. At $T = 10\ K$ (Fig. 1a), we approximately obtain the spectrum of the localized linear modes due to the inhomogeneity, which are concentrated around the AT (lower frequency) and GC (higher frequency) bands of the zero-temperature normal modes. By increasing temperature, these bands are extended toward low frequencies (softening) and they already overlap at $100\ K$. These spectra are typical for finite temperatures and the strongest feature is the central peak centered at $w = 0$ and lower values of q [17]. This cannot

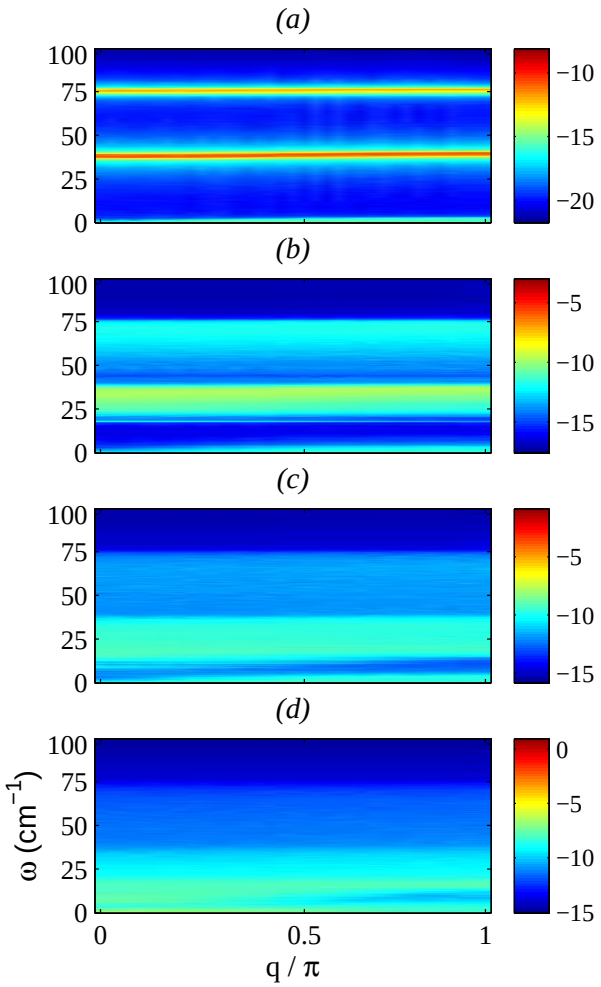

FIG. 1: (Color) Density plot (in logarithmic scale) of the dynamic structure factor $S(q, w)$ for the T7 DNA sequence (see text) at temperatures (a) T=10K, (b) T=100K, (c) T=200K, and (d) T=300K. Different colors correspond to values of the dynamic structure factor according to the color bars at the side of each plot.

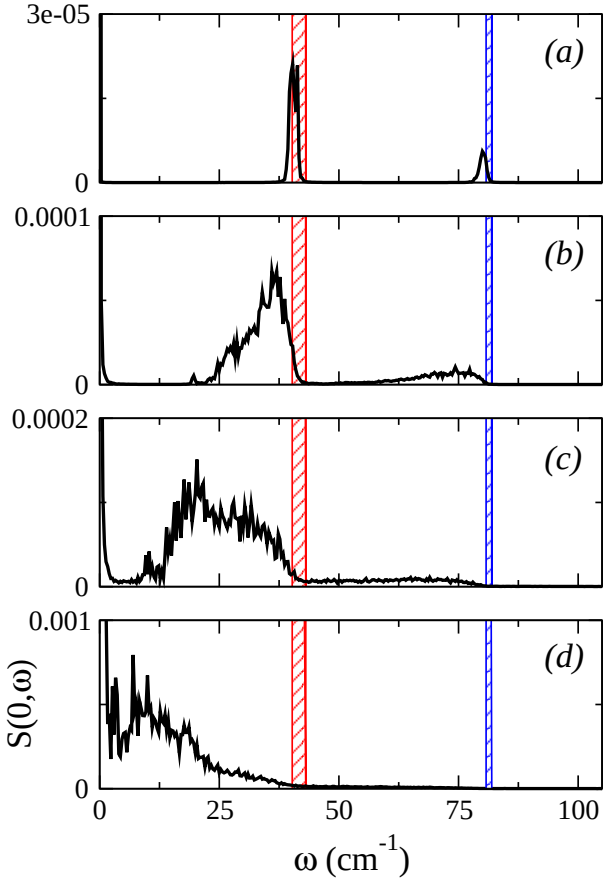

FIG. 2: Frequency dependence of dynamic structure factor at zero wavevector, $S(q = 0, w)$, for the T7 sequence at (a) T=10K, (b) T=100K, (c) T=200K, and (d) T=300K. Shaded areas indicate the zero-temperature linear bands of AT (lower frequency, wider area) and GC (higher frequency, narrower area) sites, respectively.

be seen in the density plots of Fig. 1 because it corresponds to a very thin feature at zero frequency (see Fig. 2). Figure 2 shows cuts of these dynamic structure factors along the $q = 0$ line. We see that, in contrast to the band at higher frequency that smears out quickly with increasing temperature, the lower frequency band remain a distinct broad spectral feature. Both its position and its width exhibits a characteristic evolution with temperature (see below). Cocco and Monasson [18] have theoretically studied a model similar to ours (an extension of the PBD model including additional degrees of freedom, which introduces additional low frequency acoustic modes), using a different approach, named instantaneous normal modes, where a Gibbs-weighted normal modes spectrum has been averaged over different configurations of the molecule. However the peak found in that work does not evolve with temperature, which the authors attribute to the use of homogeneous sequence in their calculation. We find softening of the peak with increasing T (see Fig. 4 below), which is consistent with the weakening of the feature observed experimentally [1], as it moves toward the resonant Raman response.

In order to explore the nature of the peak at high temperatures we examine single realizations of our simulations. A typical realization is displayed in Fig. 3a, showing the time evolution of a particular simulation at 300 K. The darker color represents regions where nonlinear effects dominate due to large values of y_n. We observe that the vibrational hot-spots are persisting for very long times (relative to characteristic time-scales of the phonons of the system, at thermodynamic equilibrium [19–21]. In Refs. [19, 20], due to the translational invariance of the studied systems, the positions of the spontaneously emerging hot-spots were randomly selected along the DNA chain. In our simulations of the inhomogeneous T7 sequence the hot-spots (bubbles) are site-specific, and

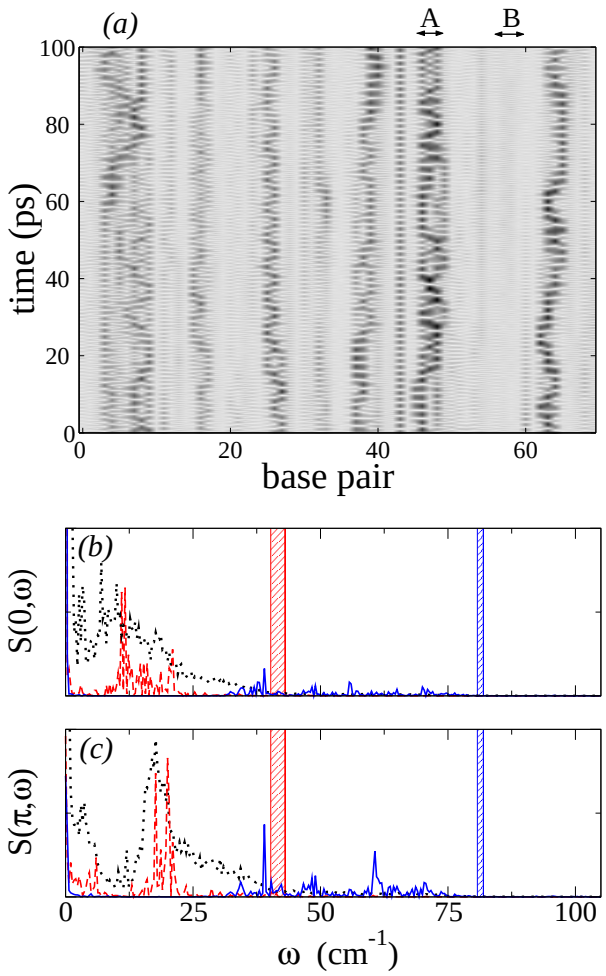

FIG. 3: (Color) (a) Density plot of y_n as a function of time for the $T7$ sequence at temperature $T = 300K$. The darker regions correspond to larger values of y_n. (b) Spectral function versus frequency for $q = 0$ and $T = 300K$. Solid blue line corresponds to phonons (region B of (a)) [for clarity we show $10 \times S(0,\omega)$ and $10 \times S(\pi,\omega)$ in this case], dashed black line to vibrational hot-spots (region A of (a)), and dotted red line to the full dynamic structure factor presented in Fig.2 (d). Shaded areas represent the $T = 0K$ linear bands, as in Fig. 2. (c) The same as in (b) for $q = \pi$.

the selectivity is determined by the interplay of disorder, entropy (through temperature) and nonlinearity [14].

To determine possible contributions of vibrational hot-spots to the dynamic structure factor, we show in Figs. 3b and 3c the corresponding power spectra of the displacements restricted to the region A (covered by a large amplitude bubble), or B (occupied by phonons), and compare them with the full shape of the spectrum, shown in Fig. 2d. From this comparison, both at $q = 0$ and $q = \pi$, it is evident that vibrational hot-spots are exclusively responsible for the distinct peak of the spectra observed in Fig. 2, as the characteristic phonon frequencies have higher values and are well separated from this peak. This result holds independently of the wavevector q. Therefore, these results clearly demonstrate that the distinguished peak in the dynamic structure factor at higher temperatures constitutes a signature of large amplitude vibrations (breathers) localized over a few base-pairs and around specific sites of the sequence.

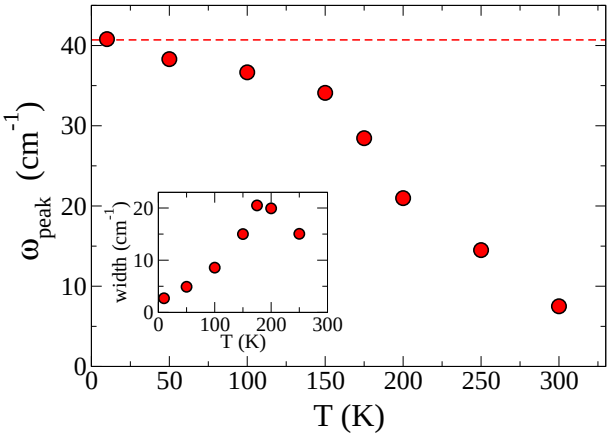

FIG. 4: The position of the distinct peak in the dynamic structure factor at $q = 0$ as a function of temperature. The horizontal dashed line indicates the peak position at zero temperature (lower edge of the AT linear phonon band). In the inset the temperature dependence of the full width at half maximum is plotted.

In Figure 4 we present the temperature dependence of the position of the $q = 0$ peak, as well its width. A substantial softening occurs, which continue through the highest temperatures studied (approaching the melting transition), as long as we can distinguish it from the central peak. We observe that the slope of the variation of the peak position distinctly increases (i.e., enhanced softening) in the region around 150 K. This seems likely to be related to the increasing influence of hot-spots that become more dominant. The width of the peak (full width at half maximum) increases with temperature up to 180 K. Above this temperature, because of the close proximity to the central peak, we cannot infer the full width at half maximum from the plot of $S(q = 0, w)$. We note that such a softening of a mode with strong hydrogen bond breathing character, has been reported in Ref. [22]. However, in that work the temperature variation is indirectly represented by varying the hydrogen bond force constants.

Apart from the signatures of the strong nonlinearities of the system in the dynamic structure factor, they strongly affect in the effective Debye-Waller factor. This factor modifying the scattered intensities will be exponentially dependent on the average squared displacements $\langle y^2 \rangle$. In Fig. 5 we plot $\langle y^2 \rangle$ averaged over time, space, and different statistical ensembles as a function of temperature. We observe a significant deviation from the linear dependence, expected in harmonic approximations. The divergence is strongly increased with T and

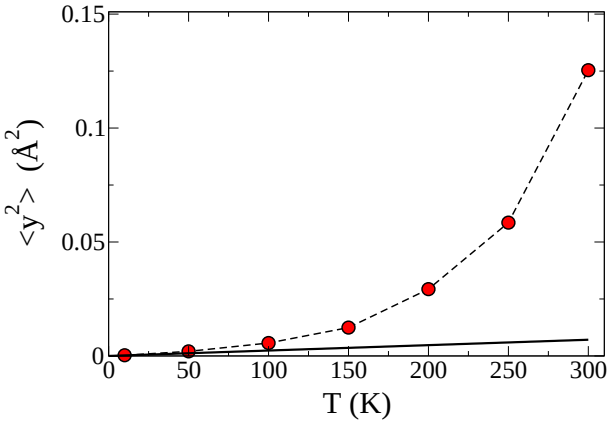

FIG. 5: Temperature dependence of the averaged squared displacements $\langle y^2 \rangle$ entering in the Debye-Waller factor. The continuous line at the bottom of the plot corresponds to the expected value, as obtained from the equipartition of the energy in the harmonic approximation of the potential. The dashed line is a guide to the eye only.

the actual $\langle y^2 \rangle$ becomes an order of magnitude larger than its harmonic counterpart in the extended melting precursor regime, with significant increase developing for $T \geq 150K$.

In conclusion, we have presented temperature effects in a dynamical model describing the radial stretchings of the hydrogen bond within base-pairs. As a concrete example we have examined a segment of the T7 bacteriophage promoter DNA. We find that thermal fluctuations increasingly explore the nonlinearity of the system in the extended melting precursor regime. Thermally induced hot-spots (i.e breather-like bubble openings) are responsible for a distinct feature in the dynamic structure factor occurring at low frequencies and in a wave-vector range reflecting the (inverse) bubble width. We have followed in detail the temperature dependence of the corresponding peak. The effective Debye-Waller factor is also strongly affected by these hot-spots. These signatures of coherent, functional base-pair dynamics should be amenable to experimental conformation with, e.g. inelastic scattering.

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