Nonlinear effects and thermal expansion as expressed in self-consistent phonon calculations on the temperature dependence of a phase change: Application to the B to Z conformation change in DNA

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(Received 15 October 1993)

The temperature and salt concentration dependence of the B to Z conformation phase change observed in some DNA polymers is calculated using the modified self-consistent phonon approximation theory. The principal modification from more standard self-consistent phonon theory is the incorporation of thermal expansion in the initial determination of the effective force constant. It is this modification that has allowed application of the method to melting temperatures and led to the theory of DNA melting. The temperature dependence of the B to Z transition is shown to depend entirely on the incorporation of the thermal expansion into the theory. The excellent agreement between the predictions of the modified theory with observation indicates the importance of including thermal expansion effects.

PACS number(s): 87.10.+e, 63.20.Dj, 63.70.+h, 87.15.By

I. INTRODUCTION

Calculations of the dynamics of the DNA double helix which involve base pair separation require methods that can deal with very large systems that are very nonlinear. The minimum unit cell for a double helix contains 41 atoms which means that the minimum secular determinant is 123×123 which is fairly large. Any problem that involves bond separation is necessarily highly nonlinear. The usual approach for such a combined problem is to do simulations. Molecular dynamics simulations on reasonable size sections of the DNA helix run for simulated times of tens of picoseconds. It is known from experimental observations of the spin exchange of protons involved in interbase H bonding that the time scale for base pair opening is milliseconds [1,2]. Simulations would have to be carried out for some 10^8 to 10^{10} times longer to investigate problems which involve base pair opening. It is unlikely that simulations relevant to this problem will be possible in the near future.

The problem of large size and large nonlinearity has been explored by the use of an effective phonon theory for the DNA double helix [3,4]. The approach works because the self-consistent phonon approximation (SCPA) theory [5] essentially separates the two elements of the problem. The nonlinearities are incorporated into an effective linear force constant leaving a linear problem to be solved. The large size is then solved by linear harmonic lattice theory which can deal with large systems by simple matrix diagonalization procedures. The diagonalization leads to a normal mode spectrum which can give information on displacement amplitude with the addition of statistical values for mode occupation values. The two elements of the problem are then justified by forcing self-consistency by self-consistent phonon theory. We have found that one needs a modified version we call modified self-consistent phonon approximation (MSPA), which incorporates thermal expansion directly into the determination of the self-consistent force constants to give reasonable results in applying self-consistent phonon theory to the high temperature regime needed for bond disruption studies. The theory has been very successful in calculating the probability of H-bond disruption, the entire base pair separation, and even the cooperative melting of the double helix [6–8]. MSPA is used as a statistical approach and is applicable to the long time scale events such as base pair separation.

This paper investigates a phenomenon that depends critically on the details of the nonlinearities in the system studied and therefore can be used as an example of just how well the MSPA model incorporates thermal expansion and the associated nonlinearities in such an application. The transition studied is the phase change from the B conformation to the Z conformation of certain polymer DNA helices. The change is quite profound as the B conformation is a right handed helix and the Z conformation is left handed. The conformation change is primarily driven by a change in the salt concentration in the medium surrounding the helix; the very high salt version is the Z form and at physiological salt concentration the helix is in the standard B form.

Base pair opening enters into the problem as one of the scenarios for the transition path involves base pair separation. In addition to changing the handedness of the helix the conformation change also requires that each base pair turn over, i.e., the top of the base pair has to rotate to become the bottom. Since the base pairs are wide compared to the spacing between them there is steric hindrance to such a rotation. An assumed path then is that the base pair separates and the separate bases leave the stack. Outside of the stack rotation of the bases is unhindered and the rotation can easily occur. The rotated bases then reform somehow and restack in the altered conformation. The required base pair separation is known to occur with reasonable probability and is studied by analyzing the spin exchange of the protons in the

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interbase H bonding [2,9].

Although the conformation change is primarily driven by changes in salt concentration there is a small temperature dependence to the transition over a small region of salt concentration [10]. It is this temperature dependence which is critically determined by the differing nonlinearities in the different conformations. In this paper we construct a theoretical calculation of the salt and temperature dependence of the transition based on MSPA and show that the temperature dependence arises from the nonlinearities. The MSPA treatment works well enough at incorporating nonlinearities to correctly predict the correct behavior of this subtle effect.

II. *B* TO *Z* TRANSITION PATHWAYS

Because of possible involvement of *Z* conformation segments in gene expression [11] and recombination [12,13], *Z*-DNA and *B*-*Z* transitions have been the subjects of intense investigations [14]. A fundamental and yet unsolved problem is the determination of the pathway and mechanism of the *B*-*Z* transition. At present there are three different views regarding the mechanism of *B*-*Z* transition. One as discussed above is that the transition involves base pair opening before rotation [15–19]. The second view is that the transition involves nondisruptive transfiguration through a series of correlated internal motions in the backbone and glycosyl bond to facilitate base pair rotation without base pair breakage [20–23]. A third view is that the transition is through an intermediate *A*-type conformation with no disruption of interbase H bonds and without severe sterical interference [24]. While several models of transition mechanism have been proposed, experiments have yet to come up with a conclusive answer.

In an earlier work we proposed a model of *B*-*Z* transition where the transition is facilitated by thermal fluctuational base pair opening [25]. In our model the transition is characterized by domain formation and domain growth rather than an instantaneous transition involving all the segments of DNA. We assume the simultaneous existence of a *B* domain and a *Z* domain separated by a small region with conformation disrupted and unpaired bases. We assume that disrupted pairs are necessary to allow base flip over leading to domain conversion. We further assume that the boundary is most likely to advance into the domain that presents the most fluctuational base pair openings adjoining the boundary. We calculated base pair opening probabilities of both *B*- and *Z*-DNA copolymer Poly *d*(*G*-*C*)·Poly *d*(*G*-*C*) at various salt concentrations and at room temperature. Our calculated probabilities are in agreement with both low salt *B*-DNA measurements and high salt *Z*-DNA measurements [9]. The salt dependence of the calculated probabilities shows a crossover at a salt concentration close to the observed transition concentration.

The conversion between *B* and *Z* conformation requires all bases to rotate 180° from the position they had before conversion [16]. Such a base pair rotation has many elements in common with the spin reversal transitions in magnetic systems. In the spin transition case each spin must reverse its orientation and the transition is characterized by domain formation and domain growth rather than an instantaneous reversal involving all the segments of the system [26]. The instantaneous transition requires an intermediate state of massive disruption of the spin orientation. In domain growth transitions the disruption of the spins is confined to a small region at the domain boundaries. This reduction in the size of disrupted region greatly reduces the energy associated with the disrupted region. This transition is then characterized by the formation of a new domain and the advance of the domain boundary into and through the old domain.

In reality the values of critical concentration and temperature dependence predicted by our analysis cannot be used to argue conclusively that *B*-*Z* conformation change proceeds by base pair disruption. It has been recognized for a long time that the solid liquid melting temperature can be determined by the crossover temperature for the solid vapor pressure curve and the liquid vapor pressure curve. This fact does not imply that melting always takes place via a vapor phase intermediary, only that it could. The situation here is quite similar. The process could occur through open base pairs. The critical values found in this one path give information about the fundamental stability of the two phases that is true even if some other path is more efficient.

III. INCORPORATION OF SALT EFFECT AND THERMAL EXPANSION IN INTERBASE H-BOND STABILITY

The mean length of a thermally equilibrated intact H bond in a large system depends on two factors. One is static forces exerted on the bond that determine the positions of the interatomic potential minima. The second factor is dynamic, i.e., due to the effects of thermal motion in an asymmetric potential (thermal expansion). For a salt dependent theory of interbase H-bond stability in DNA both factors are present and synergistically interact.

The phosphate groups in DNA are charged and these charged groups generate repulsive forces that are balanced by other forces in the system. In particular the cross strand phosphate-phosphate repulsive force generates a tension across the interbase H bonds. This tension together with the tension generated from other nonbonded forces must be compensated for by the generation of a compensating stress in the interbase H bonds so that the interbase H bonds are stabilized at a particular position. The compensating stress arises from an induced strain in the interbase H-bond lengths. Since the charges in the phosphate groups are screened by counterions in the surrounding solvent, the strength of phosphate-phosphate repulsive force changes at varying salt concentrations. Therefore the equilibrium bond length of an interbase H bond is dependent on salt concentration.

In general the mean bond length R_i^{int} of an intact H bond can be given by

$$R_i^{\text{int}} = r_i^0 + dr_i^C + dr_i^T \tag{1}$$

where r_i^0 is the potential minimum, and dr_i^C and dr_i^T are salt induced strain and thermal expansion, respectively. The detailed description of dr_i^C and dr_i^T together with the formulation of our salt dependent MSPA theory, including formulation of the salt screened phosphate-phosphate repulsive force by Soumpasis' potential of mean force (SPMF) approach [27], has been presented elsewhere [28]. In the present work the same formula is employed. Interested readers are directed to Ref. [28].

Thermal fluctuational base pair opening probabilities as well as individual interbase H-bond disruption probabilities are dependent on the mean bond length of the H bonds involved. As a result the thermal stability of these interbase H bonds are dependent on salt concentration and thermal expansion. The salt dependence can be analyzed within the framework of the MSPA theory [25,28] in that the stress induced strain in the interbase H bonds can be calculated by a simple consideration of balance of forces across the interbase H bonds. The calculated strain or the change of bond length can then be incorporated into the MSPA self-consistent formalism and this MSPA theory then becomes a salt dependent theory.

IV. RESULTS AND DISCUSSIONS

A. Determination of nominal salt concentrations

In the salt dependent MSPA theory a nominal salt concentration is defined as the concentration at which the interbase H bonds in a particular DNA structure can be regarded as unstrained. That is to say at this salt concentration the equilibrium bond length of an interbase H bond can be determined by that particular H-bond potential and no further static force correction is necessary in the calculation. The change in the bond length at a different salt concentration is then determined by the differences in the cross strand static forces with respect to the forces at the nominal salt concentration. In MSPA we use a Morse potential as the potential for an interbase H bond. This potential is an effective potential for the bond end atoms. Our Morse parameters were determined using experimental data obtained from B-DNA samples. They were fitted assuming that the H bonds were in equilibrium at the x-ray determined positions at room temperature. The nominal salt concentration should then correspond to the conditions under which the experiments were carried out. The exact value of this nominal salt can be determined as that concentration at which the salt shielded Coulomb strains across the H bonds from the phosphate groups are exactly canceled by other cross H-bond nonbonded interactions and the H-bond reaction forces at the x-ray determined configuration at room temperature. Our calculations give a value of $0.05M$ NaCl for both AT and GC base pairs in B conformation in agreement with the range of salt concentrations reported for the samples used in the x-ray analysis and the Raman and ir analyses.

In the calculation of the Z-form DNA polymers we use the same Morse parameters as those of the B-form GC pairs we used earlier. Because of significant structural differences in the backbones the cross strand SPMF force, the solvent averaged cross strand phosphate-phosphate repulsive force, in a Z-form DNA differs significantly from that in a B-form DNA. Therefore one expects the nominal salt concentration of a Z-form DNA to be different than the nominal salt concentration of a B-form DNA. For the Z-form Poly d(G-C)·Poly d(G-C) we calculate the value of its nominal salt concentration by the use of the same formula as that used for B-form DNA polymers. Our calculation gives a value of $\sim 0.25M$ NaCl for both fiber and crystal coordinates. This value is different from the value of $0.05M$ NaCl for the B-form DNA polymers. The difference arises because the phosphate-phosphate repulsion is stronger as the charges are closer in Z-DNA than that in B-DNA. As a result additional counterions are needed to shield the phosphate repulsion in Z-DNA polymers. It is interesting to note that our calculated Z-DNA nominal salt is actually close to the salt concentrations used in both fiber [29] and crystal [16] studies from which our coordinates for Z-form Poly(dG-dC)·Poly(dG-dC) are obtained.

B. Temperature dependence of the base pair opening probability

We carry out a calculation to calculate base pair opening probability P^{op} of the fiber B-form, fiber Z-form, and crystal Z-form Poly d(G-C)·Poly d(G-C). The fiber coordinates can be found from Ref. [31] and the crystal coordinates can be found from Ref. [30]. The calculated P^{op}'s of the three structures at different NaCl concentrations and at several temperatures are given in Figs. 1 and 2. We find that our calculated P^{op}'s of both the B-structure at lower salt concentration and the two Z-structures at high salt concentrations are in fair agreement with available experimental estimates. For example the P^{op} for the B-form Poly d(G-C)·Poly d(G-C) at $0.1M$ NaCl is 4.65×10^{-6} at 308 K. This is in fair agreement with the observed value of 2.5×10^{-6} for the base pairs in a B-DNA oligomer $d(CG)_{12}$ from imino proton exchange measurement at the same salt concentration and same temperature [9]. At $4M$ NaCl the calculated P^{op} of the Z-form Poly d(G-C)·Poly d(G-C) is 1.61×10^{-6} for the fiber coordinates and 7.78×10^{-7} for the crystal coordinates at 308 K. These are within a factor of 3 of the estimate of 5×10^{-7} for the base pairs in the Z-form $d(CG)_{12}$ from imino proton exchange measurement at that salt concentration and temperature [9].

From Figs. 1 and 2 one finds that at low salt concentrations our calculated P^{op}'s of the two Z structures are higher than that of the B structure. At high salt concentrations the P^{op}'s of both Z structures are lower than that of the B structure. The cross over salt concentration C_{B-Z} for the curves is also close to the observed B-Z transition concentrations. For example at 293 K our calculated C_{B-Z} is $2.54M$ NaCl for the fiber structure and $1.44M$ NaCl for the crystal structure. These are compared to the observed value of $2.28M$ NaCl for a 100 bp oligo(dC-dG) from a uv measurement at 295

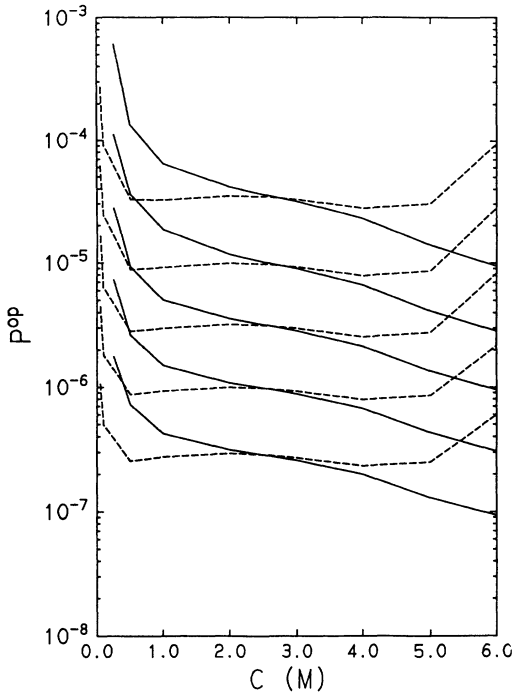

FIG. 1. Comparison of base pair opening probability P^{op} of fiber Z and fiber B DNA Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ at various NaCl concentrations and at several temperatures. The solid lines are for the Z structure and the dashed lines are for the B structure. The uppermost solid (dashed) line corresponds to the calculation at 353 K, the second solid (dashed) line at 333 K, the third solid (dashed) line at 313 K, the fourth solid (dashed) line at 293 K, and the lowest solid (dashed) line at 273 K.

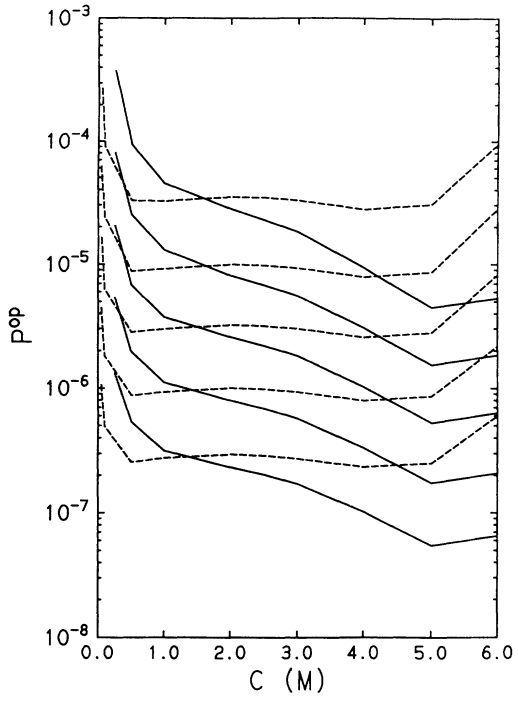

FIG. 2. Comparison of base pair opening probability P^{op} of crystal Z and fiber B DNA Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ at various NaCl concentrations and at several temperatures. The solid lines are for the Z structure and the dashed lines are for the B structure. The uppermost solid (dashed) line corresponds to the calculation at 353 K, the second solid (dashed) line at 333 K, the third solid (dashed) line at 313 K, the fourth solid (dashed) line at 293 K, and the lowest solid (dashed) line at 273 K.

K [17]. At 298 K the calculated cross over concentration is $2.57M$ NaCl for the fiber structure and $1.46M$ NaCl for the crystal structure. These are compared to the observed values of $2.56M$ NaCl from a uv measurement [17,32] and $1.67M$ NaCl from a circular dichroism (CD) measurement [17,32] for Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ at the same temperature.

We point out that although the P^{op} of a base pair in both the B and Z form Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ is small, the observed lifetimes of these GC pairs are well within the range of observed B-Z transition relaxation times. For example, the lifetime of a B-DNA GC pair is in the range of 10 milliseconds [2] and that of a Z-DNA GC pair is in the range of a few tenths of a second [9]. In comparison the observed relaxation times of B-Z transition are in the range from tens to hundreds of seconds per base pair [14,15,19]. The B-Z transition relaxation time is a measure of the time scale associated with the transition. This comparison indicates that thermal fluctuational base pair opening is fast enough to facilitate B-Z transition.

Our calculated C_{B-Z}'s show a temperature dependence in agreement with observations. Experimental measurement has shown [10] that in a certain range of NaCl concentration there exists a temperature such that Poly $d(G\text{-}C)$·Poly $d(G-C)$ adopts the Z form below the temperature and it adopts the B form above the temperature. This temperature increases as the salt concentration increases. The range of NaCl concentration where this phenomenon can be observed at experimentally accessible temperatures is narrow. It is between $2.3M$ and $2.5M$ [Na^+]. Below and above these limits only B and Z forms are observed, respectively. A similar behavior was observed in high concentrations of KCl and CsCl. From Fig. 3 we find that our calculated C_{B-Z}'s of both fiber and crystal structures show the same behavior. The calculated C_{B-Z} of the fiber structure increases from $2.49M$ NaCl at 273 K to $2.78M$ NaCl at 333 K. It decreases slightly as temperature further increases. It reduces to $2.76M$ NaCl at 353 K. The increment between the calculated C_{B-Z} at high temperature and that at the freezing temperature is $\sim 0.29M$ NaCl which is close to the observed increment of $0.2M$ NaCl in Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ [10]. Assuming that the transition occurs from fiber form B-DNA to fiber form Z-DNA and vice versa the predicted critical salt concentration and its temperature dependent behavior is close to observation. The C_{B-Z} of the crystal structure also increases from $1.36M$ NaCl at 273 K to $1.63M$ NaCl at 333 K. As the temperature further increases the C_{B-Z} again decreases slightly. It is reduced to $1.61M$ NaCl at 353 K. The largest increment between the calculated C_{B-Z} at high temperature and that at the freezing temperature is $\sim 0.27M$ NaCl

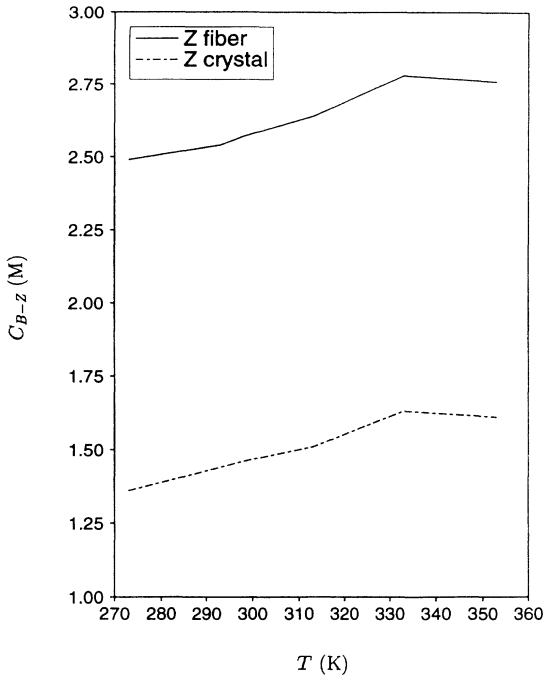

FIG. 3. Calculated cross over concentration C_{B-Z} of Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ as a function of temperature.

which is again in fair agreement with experimental measurements.

C. Effect of normal mode frequency, cross strand SPMF force, and thermal expansion on the *B-Z* cross over concentration

The effect of temperature on base pair opening probability and the cross over concentration is determined by three factors. One is the temperature induced changes in the normal mode frequencies of the system. The normal mode frequencies determine the vibrational free energy of the system. The temperature induced changes in the frequencies of the normal modes, however, have a rather limited effect on the temperature dependence of the mean vibrational amplitudes and thermal expansion of the interbase H bonds. Since P^{op} is determined by mean vibrational amplitudes and thermal expansion of the bond, one expects the effect associated with the change in the normal mode frequencies is negligible.

The second factor is the temperature dependent strain in the interbase H bonds induced by the cross strand solvent averaged phosphate-phosphate interactions. The SPMF polyelectrolyte *B-Z* free energy difference shows little temperature dependence in the region around cross over concentration. This polyelectrolyte effect enters our MSPA calculation in derivative form. In our calculation this derivative has sizable but almost identical temperature dependence for *B* and *Z* conformation. The temperature dependence of the transition depends on differences in the individual temperature dependences and little transition temperature dependence results. That this is so can be seen in Fig. 4 where the force from SPMF labeled δf_p is shown as a function of temperature for several salt concentrations for both conformations. The force δf_p is defined as the change of the SPMF force at concentration C with respect to that at the nominal salt concentration C_0, i.e., $\delta f_p = f_p(C) - f_p(C_0)$. This is the force that enters into MSPA formalism.

The slope of the lines in Fig. 4 are nearly identical for all cases. The change in the differences in δf_p between conformations is relatively unaffected by change in temperature. There is some small systematic shift in slopes between the conformations. The *Z* conformation force decreases faster, i.e., goes to a larger negative value with increasing T. Since negative force compresses the helix, larger negative force stabilizes the helix. The net effect of temperature on the polyelectrolyte forces in the helix is to shift to more stability for *Z* at higher temperature. This effect is negligibly small at room temperature and only becomes significant at very high temperatures.

The spacing between lines for different salt concentrations is quite different for the two conformations. The effect of changes in salt on the change in δf_p is large and therefore the Coulomb shielding effect is most important to the conformation change at a given temperature.

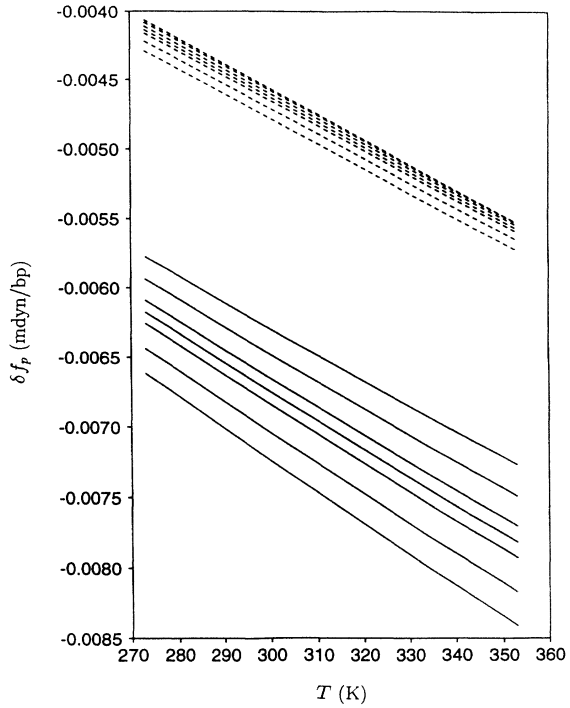

FIG. 4. Calculated cross strand SPMF force $\delta f_p = f_p(C) - f_p(C_0)$ of Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ as a function of temperature and NaCl concentration. C is the NaCl concentration and C_0 is the nominal salt concentration. The force is in units of mdyn/bp (1 mdyn=10^{-8} newton; bp stands for base pair). The solid lines are for the fiber *B* structure and the dashed lines are for the fiber *Z* structure. The uppermost solid (dashed) line corresponds to calculation at C=2.0M NaCl, the second at 2.2M NaCl, the third at 2.4M NaCl, the fourth at 2.5M NaCl, the fifth at 2.6M NaCl, the sixth at 2.8M NaCl, and the lowest solid (dashed) line at 3.0M NaCl.

At high salt concentrations where the cross over occurs the net Coulomb forces become negligibly small and the hard sphere interactions become dominant in SPMF. Our calculation indicates that at concentrations higher than $2M$ NaCl for the fiber Z structure or $1M$ NaCl for the crystal Z structure, the Z structure appears to be more commensurate with the optimal positions for negative ions in the salt structure. This can be seen by the smaller value of SPMF force of the Z structures as shown in Fig. 5.

The third factor that can affect the temperature dependent behavior of the P^{op} and cross over concentration is the thermal expansion and its effect on nonlinearities in the interbase H bonds. From the definition

$$P^{op} = \prod_i A_i \int_{L_i^{max}}^{\infty} dr \exp[-(r - R_i)^2/2D_i] , \qquad (2)$$

one finds that P^{op} depends sensitively on the mean bond length R_i of the interbase H bonds. Here i is the index of the interbase H bonds in a base pair and the product runs over all the interbase H bonds in a base pair. R_i, D_i, and L_i^{max} are mean bond length, mean square vibrational amplitude, and maximum stretch length of an H bond, respectively. A_i is a normalization factor. In MSPA the R_i of an interbase H bond is given by the sum of the potential minimum r_i^0 and a thermal expansion term. The thermal expansion term is determined by the mean vibrational square amplitude D_i. Therefore the temperature behavior of D_i determines the temperature behavior of thermal expansion and in turn determines the temperature behavior of P^{op}.

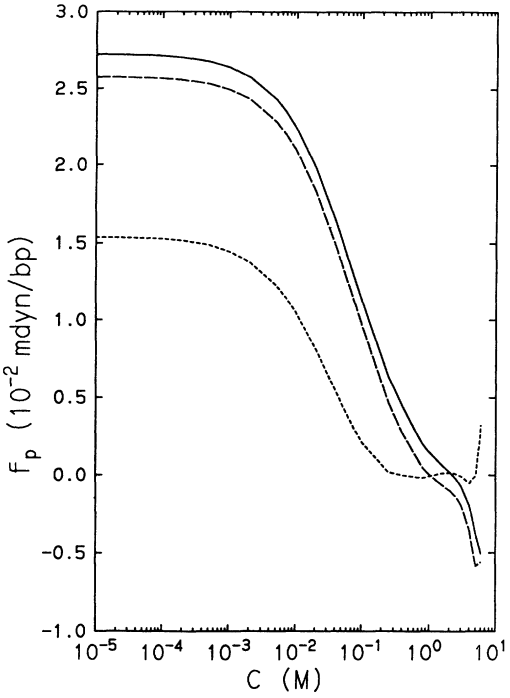

FIG. 5. Calculated cross strand SPMF force f_p of Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ as a function of NaCl concentration at room temperature (293 K). The force is in units of mdyn/bp (1 mdyn=10^{-8} newton). The solid line is for the fiber Z structure, the long dashed line is for the crystal Z structure, and the short dashed line is for the B structure.

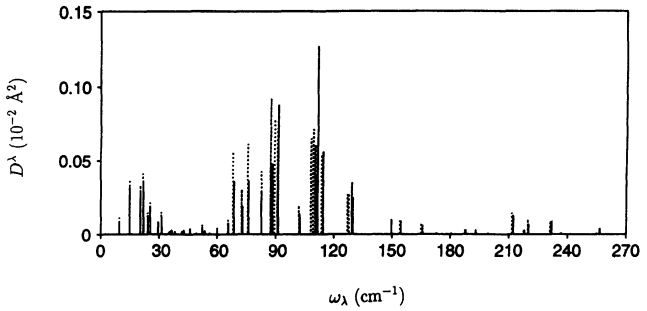

FIG. 6. Calculated mean interbase stretch square vibrational amplitudes D^λ of individual band of normal modes of B-form Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ as a function of the band zone center frequency ω_λ. The solid lines correspond to calculation at 293 K and the dashed lines correspond to calculation at 333 K. The lines are located at the respective zone center frequencies of the bands.

Figures 6 and 7 show the calculated mean square vibrational amplitude D^λ from an individual normal mode band (λth band) as a function of zone center frequency ω_λ of that band. Here λ is the index of the normal mode band. D^λ is the average of the D_i^λ's of the interbase H bonds. D_i^λ is defined such that the sum of D_i^λ gives the total D_i: $D_i = \sum_\lambda D_i^\lambda$. In Figs. 6 and 7 the amplitudes D^λ's are represented by solid (at 293 K) and dashed (at 333 K) lines located at their respective zone center frequencies of the bands. In this calculation the SPMF induced strain in the interbase H bonds is ignored. In an earlier work we have shown that the bulk of base

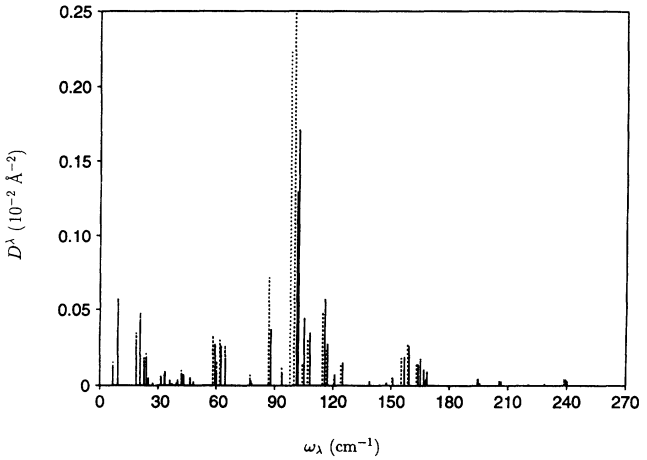

FIG. 7. Calculated mean interbase stretch square vibrational amplitudes D^λ of individual bands of normal modes of fiber Z-form Poly $d(G\text{-}C)$·Poly $d(G\text{-}C)$ as a function of the band zone center frequency ω_λ. The solid lines correspond to calculation at 293 K and the dashed lines correspond to calculation at 333 K. The lines are located at the respective zone center frequencies of the bands.

pair disruption motion comes from several vibrational modes whose character is best described as basic breathing motion across the interbase degrees of freedom [33]. The breathing modes can be identified as those modes which contribute significantly to the interbase breathing mean square amplitude. The breathing modes of the B structure are distributed in a frequency range between 70 cm^{-1} and 115 cm^{-1}. The breathing modes of the Z structure are distributed in a much narrower region which is concentrated around 100 cm^{-1}. The zone center frequency of the breathing modes of both structures decreases slightly with temperature in a similar way. However, the amplitudes of the breathing modes of the two structures show different behavior. We find that the D^{λ} of the breathing modes of the Z structure increases with temperature much more significantly than that of the breathing modes of the B structure. There is a collapse of character into H-bond breathing motion for these modes and this amplifies the effect of their drops in frequency. As a result the P^{op} of the Z structure increases faster than that of the B structure. One then expects that the difference in the effect of thermal expansion and associated nonlinearities of the two structures would cause the cross over concentration shifting towards higher concentration at increasing temperature. A similar behavior is also found in the crystal Z structure calculation.

The opposing effects of thermal expansion and cross strand SPMF force on the temperature dependence of the cross over concentration interact, resulting in our calculated behavior. At lower temperatures, where the difference between the decreasing rate of SPMF force of the B and Z structure is small, the effect of thermal expansion plays a dominant role in the determination of temperature dependence of the cross over concentration. As a result the cross over concentration shifts toward higher concentration when temperature is increased. As the temperature increases, the increases in both cross over concentration and temperature result in a larger and larger difference between the decreasing rate of the SPMF force of the B and Z structure. At a sufficiently high temperature the effect associated with the SPMF force is expected to become so strong that it outweighs the effect associated with the thermal expansion. As a result the cross over concentration stops increasing and even begins to decrease somewhat as shown in Fig. 3. The overall net effect of thermal expansion and SPMF force on the temperature dependence of the cross over concentration is relatively small as seen both from our calculation and from observations.

ACKNOWLEDGMENT

This work was supported in part by ONR Grant No. N00014-92-K-1232.

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