Dynamical Transition of Water in the Grooves of DNA Duplex at Low Temperature

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Dynamical transition in translational and rotational dynamics of water in the grooves of DNA duplex at low temperature

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Abstract

We have simulated structure and dynamics of water in the grooves of a DNA duplex using moleculear dynamics simulations. We find signatures of a dynamical transition in both translational and orientational dynamics of water molecules in both the major and the minor grooves of a DNA duplex. The transition occurs at a slightly higher temperature ($T_{GL} \approx 255$ K) than the temperature ($T_L \approx 247$ K) where the bulk water is conjectured to undergo a dynamical transition. Groove water, however, exhibits markedly different temperature dependence of its properties from the bulk. Entropy calculations reveal that the minor groove water is ordered even at room temperature and the transition at $T \approx 255$ K can be characterized as a *strong-to-strong* dynamical transition. The low temperature water is characterized by pronounced tetrahedral order, as manifested in the sharp rise near 109° in the O-O-O angle distribution. We find that Adams-Gibbs relation between configurational entropy and translational diffusion holds quite well when the two quantities are plotted together in a master plot for different region of aqueous DNA duplex (bulk, major and minor grooves) at different temperatures. The activation energy for the transfer of water molecules between different regions of DNA is found to be independent of temperature.

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I.   INTRODUCTION

Water in the natural world is often found under constrained and/or restricted environments, in the hydration layer of proteins and micelles, within reverse micelles and microemulsions, in the grooves of DNA duplex, within biological cells, to name a few. Properties of water under such constrained conditions can be quite different from those of bulk, neat water [1]. However, it is likely that even under such restricted conditions water retains some of its unique properties. Study of these unique properties of water, especially in the hydration layer of biomolecules, particularly of proteins [1, 2, 3, 4, 5, 6] and DNA [1, 7, 8, 9, 10, 11, 12], has been a subject of great interest in recent times. Hydration layer not only provides the stability of the structure of the biomolecules, but also plays a critical role in the dynamic control of biological activity. The intercalation of anti-tumor drugs, such as daunomycin, into DNA involves active participation of water molecules in the grooves [13, 14].

The low temperature (near 200 K) "glasslike" transition of hydrated protein has drawn a great deal of attention in both experimental and computer simulation studies [15, 16, 17, 18, 19]. Above this transition temperature proteins exhibit diffusive motion and below this temperature the proteins are trapped in localized harmonic modes. An important issue in recent times is to determine the effects of hydration water on this dynamical transition [20, 21, 22, 23, 24]. Recent studies have shown that dynamics of water in the hydration layer of a protein also exhibits strong temperature dependence around the same temperature and it seems to undergo a fragile-to-strong transition which preempts an otherwise expected glass transition at a lower temperature [24, 25, 26, 27].

Study of DNA hydration layer has recently indicated interesting dynamical behavior of water in the grooves [7, 8]. Several recent studies have discussed about the origin of the slow component of the solvation dynamics in DNA hydration layer [11]. However, a detail discussion of this upcoming issue is beyond the scope of this paper.

A recent computer simulation study by Stanley and co-workers has shown that the liquid-liquid (L-L) transition in water induces a *dynamic transition* in DNA which has striking resemblance with that of liquid to glass transition [28]. *This study, however, did not explore*

the dynamics of water in the grooves of DNA.

There are many questions that have remained unanswered regarding dynamics of groove water at low temperature. For example, is there a dynamic transition in the grooves of DNA near the L-L transition of bulk water? Does it in any way resemble the one in protein hydration layer? Note that the remarkable properties of bulk water have recently been attributed to a *highly interesting L-L transition* at around $T_L \approx 247$ K, that is, only 26^oC below the freezing temperature [29, 30, 31]. The effects of the bulk water L-L transition on groove water dynamics have not yet been investigated.

In this article we report our finding that water in the *grooves of a DNA duplex* shows a dynamical transition at a temperature (T_{GL}) slightly higher than the temperature (T_L) where the bulk water undergoes the L-L transition. However, the nature and manifestation of the transition in the grooves are quite different from that in the bulk.

II.   SYSTEM AND SIMULATION DETAILS

The system we studied consists of a *Dickerson dodecamer* DNA duplex (CGC-GAATTCGCG) [32] solvated in 1565 TIP5P water molecules [33]. We have studied the DNA-water system at constant pressure $P = 1$ atm, at several constant temperatures (NPT ensemble) in a simulation box with periodic boundary condition. The molecular dynamics simulations of this aqueous DNA system were performed using the AMBER Force Field [34].

We have identified the groove water by using the following procedure. We have calculated the radial distribution function (g(r)) of water molecules in the system from the major and minor groove atoms. On the basis of this g(r), a cut-off distance of 3.5Å (the first minima of g(r)) from the groove atoms is used for the selection. For bulk water analysis, we have considered those water molecules which are beyond 15Å from any DNA atoms. We have checked that at 15 Å away, water indeed regains bulk-like behavior.
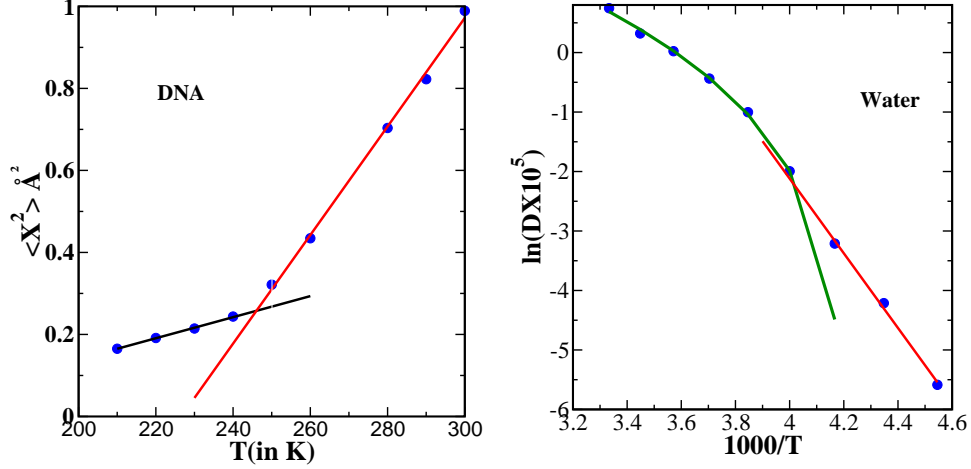
FIG. 1: Mean square fluctuation (MSF) of DNA duplex (left panel) and diffusivity (right panel) of the oxygen atoms of all water in the system. In the left (DNA) panel, MSF of DNA shows a dynamic transition at $T \approx 247$ K. In the right (water) panel, water shows dynamical crossover around same temperature from a high temperature power law behaviour (cyan) to a low temperature Arrhenius behaviour (red).

III. RESULTS AND DISCUSSIONS

A. Mean square fluctuation of DNA and translational diffusivity of water

We first report the calculated mean square atomic fluctuation $\langle X^2 \rangle$ of the DNA atoms starting from 300 K down to 210 K in order to characterize the macromolecular "glass" transition temperature (T_{DNA}). Left panel of **Figure 1** displays the same. We find that the mean square fluctuation (MSF) of DNA slows down dramatically around 247 K and continues to remain slow for the lower temperatures. The onset of the change in slope (near $T_{DNA} \approx 247$ K) of MSF indicates a macromolecular dynamic transition. Right panel of **Figure 1** shows temperature dependence of the diffusivity for all the water molecules in the system. It shows a crossover around the same temperature ($T_L \approx 247$ K) from a high temperature power law form to a low temperature Arrhenius form. From the power law fit to the high temperature region we get a glass transition temperature of 231 K which is in agreement with the earlier simulation study by Stanley and co-workers [28].

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B. Intermediate scattering function

We next discuss the self intermediate scattering function (ISF) of the oxygen atoms of the water molecules in the grooves of DNA for a set of temperatures starting from 300 K to 210 K. The self intermediate scattering function is defined as

$$F_S(k,t) = \langle exp(-ik \cdot (r(t) - r(0))) \rangle = \left\langle \frac{sin|k||r(t) - r(0)|}{|k||r(t) - r(0)|} \right\rangle, \tag{1}$$

where k is the wave vector and $r(t)$ is the position of the oxygen atom of the water molecules. The $|k|$ value taken here is 2.5Å^{-1}. The translational relaxation time (τ_T) is obtained by fitting the two step relaxation of ISF at different temperatures using Relaxing Cage Model (RCM) [35]. The fitting equation used here is given by

$$F_S(k,t) = [1 - A(k)]e^{-(t/\tau_S)^2} + A(k)e^{-(t/\tau_T)^\beta} \tag{2}$$

Here A(k) is Debye-Waller factor, τ_T being the translational relaxation time and β is the stretched exponent.

Figure 2(a) shows ISF of oxygen atom for the water molecules in bulk, major groove and minor groove at 300 K and 260 K. It is evident from both the figures that water molecules in both the major and the minor groove tend to behave like a liquid at a temperature lower than the bulk. The behavior is more prominent for water molecules in the minor groove. This can be ascribed to the fact that translational motion of water molecules in the minor groove is more constrained owing to the more ordered structure in the minor groove than water molecules in the major groove of DNA. Water molecules in major groove are, in turn, translationally more constrained than bulk water. **Figure 2(b)** shows the temperature dependence of τ_T for water molecules in bulk, major and minor grooves. For both bulk and major groove water the temperature dependence at high temperature region can be fitted to the Vogel-Fulcher-Tammann (VFT) law, $\tau_T = \tau_0 \; exp[DT_0/(T - T_0)]$, where D is a constant measuring fragility and T_0 is ideal glass transition temperature at which relaxation time diverges. In reality, however, the divergence is avoided as below a certain characteristic temperature, the functional dependence of relaxation time switches over to an Arrhenius form which is a signature of a strong liquid. The crossover temperatures for bulk water and major groove water are found to be $T_L \approx 247$ K and $T_{GL} \approx 255$ K, respectively. The
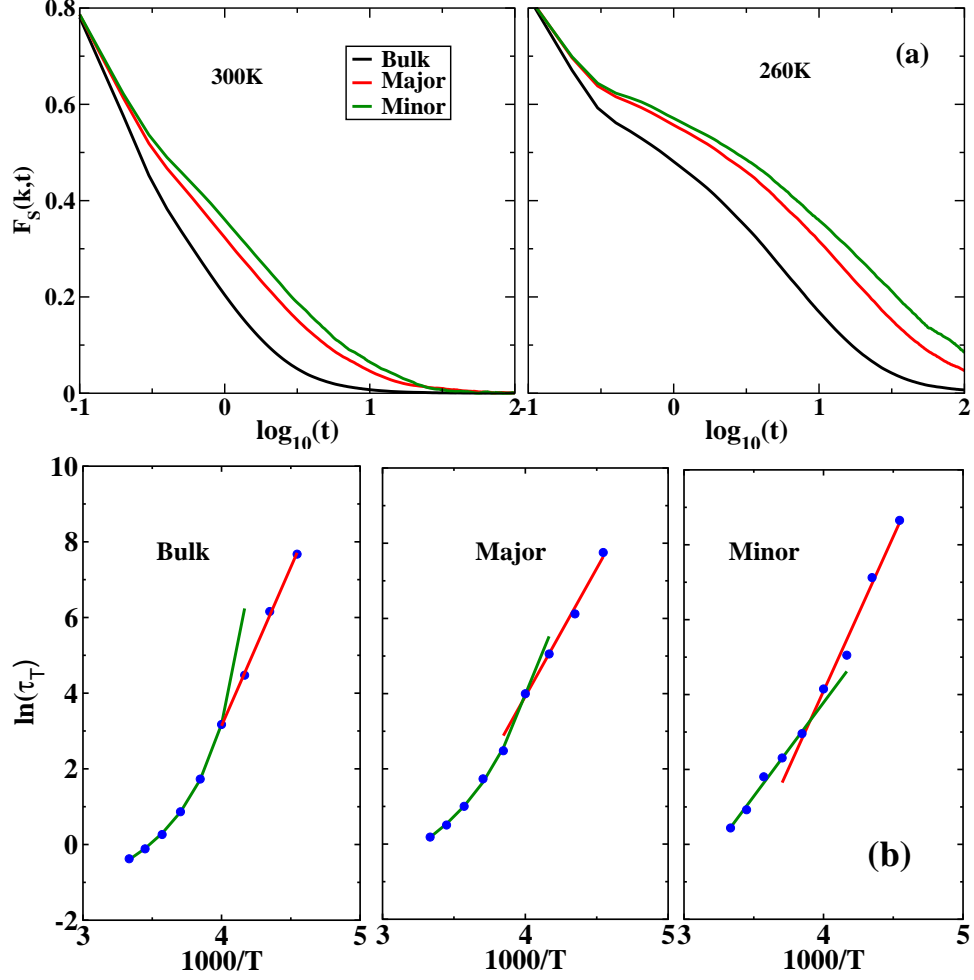
FIG. 2: (a) Intermediate scattering function ($F_S(k, t)$) of the oxygen atoms of the water molecules in bulk, major and minor grooves of DNA duplex at two different temperatures, T = 300 K (left panel) and T = 260 K (right panel) for $|k| = 2.5\text{Å}^{-1}$.(b) Translational relaxation time (τ_T) for bulk (left panel), major groove (middle panel) and minor groove (right panel) water. Bulk and major groove water show dynamical crossover between high temperature VFT behaviour (cyan) and low temperature Arrhenius behaviour (red). Minor groove water shows transition between two Arrhenius behaviours.

dynamical transitions are of fragile-to-strong type, *although the fragility of major groove water is smaller of the two.*

The minor groove water molecules however show a remarkably different translational dynamics. Minor groove water does not show any signature of a fragile liquid in the temperature range studied. Instead, temperature dependence of translational relaxation time for

minor groove water fits well into *two Arrhenius forms* of different slopes with a cross-over temperature around $T_{GL} \approx 255$ K (same as major groove water). This can be understood in the context of difference in the structure of hydration layer in the grooves of DNA. Hydration in the minor groove is more extensive, regular with a *zig-zag* spine of first and second shell of hydration where as hydration in major groove is restricted to a single layer of water molecule [36]. Water molecules in minor groove are thus more structured in comparison with major groove water which results in a strong liquid type of behavior for water molecules in minor groove even in the high temperature region. This explains why in contrast to bulk and major groove water, minor groove water shows a *strong-to-strong* type of dynamical transition.

C. Orientational dynamics

We next analyze orientational (dipole-dipole) time correlation function (TCF) of water molecules in the different regions of aqueous DNA and the TCF calculated is defined as

$$C_\mu(t) = \frac{\langle \mu(0) \cdot \mu(t) \rangle}{\langle \mu(0) \cdot \mu(0) \rangle} \tag{3}$$

where $\mu(t)$ is the dipole moment unit vector of the water molecule at time t and the angular bracket corresponds the ensemble averaging.

Figure 3(a) displays $C_\mu(t)$ for water molecules in bulk, major and minor grooves at 300 K and 260 K, respectively. Similar to the translational motion, rotation of the minor groove water molecules is found to be the most constrained. **Figure 3(b)** shows the temperature dependence of orientational relaxation time (τ_R) as obtained from stretched exponential fitting at long time of dipole-dipole TCF for bulk, major and minor groove water. Bulk water shows a fragile-to-strong transition around the same temperature ($T_L \approx 247$K) as observed for translational relaxation time. However, unlike translational relaxation, orientational relaxation shows a transition between two Arrhenius forms of different slopes with a crossover temperature $T_{GL} \approx 255$ K for *both major and minor groove water*. Strong-to-strong transition observed in the minor groove (both translational and orientational dynamics) can be attributed to the effect of confinement in the minor groove (higher depth and lower width).
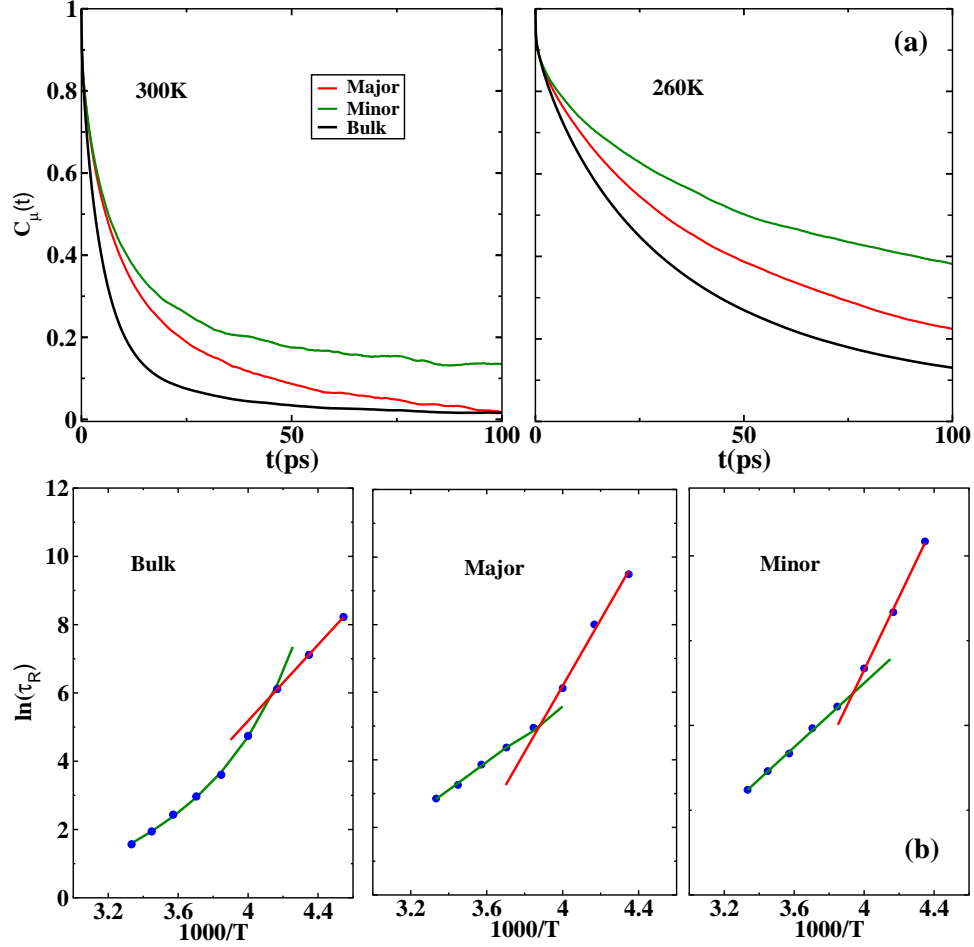
FIG. 3: (a) Dipole-dipole time correlation function ($C_\mu(t)$) of water molecules in bulk, major groove and minor groove of DNA duplex at two different temperatures, T = 300 K (left panel) and T = 260 K (right panel). (b) Rotational relaxation time (τ_R) for bulk (left panel), major groove (middle panel) and minor groove (right panel) water. Bulk water shows a crossover between high temperature VFT behaviour (cyan) and low temperature Arrhenius behaviour (red). Major groove and minor groove water show transition between two Arrhenius behaviour.

It is known that a confined liquid is comparatively less fragile than in the bulk [37, 38] and this eventually gives rise to a Arrhenius temperature dependence of the relaxation times (signature of strong liquids) *even at the higher temperature region*. The reason for the different behavior of major groove water is thus probably due to the fact that rotation probes local environment more faithfully than translation.

IV.   MICROSCOPIC CHARACTERIZATION: O-O-O ANGLE DISTRIBUTION

To understand how the structure of groove water changes across the dynamical transition, we have calculated the O-O-O angle distribution inside the first coordination shell of a water molecule. Angle distributions at three different temperatures (300K, 250K and 230K) for groove water molecules are displayed in **Figure 4**. At all the temperatures, the distribution has a two peak character. While the peak at lower angle is the signature of the presence of interstitial water molecules inside the first hydration shell, higher angle peak characterizes the degree of tetradehrality present. As it is evident from this **Figure**, with decreasing temperature the degree of tetrahedrality increases (higher angle peak height increases) with the removal of interstitial water molecules (lower angle peak height decreases) from the first hydration shell. Structural change of this kind with decreasing temperature and increasing order (as discussed further below) responsible for the dynamical transition for groove water molecules.

Bulk water also exhibits a dynamical transition near 250K. The signatures are, however, weaker in the case of bulk water than what are observed in the grooves. The role of confinement in fostering the transition of tetraedral water can be understood in the following fashion. In the confined state, water molecules gain in energy but lose entropy (see next section). The tetrahedrally coordinated water is a low entropy state of the system. Confinement thus favours the crossover/transition to the tetrahedral state.

V.   ENTROPY CALCULATION

In order to understand the origin of the large observed differences between the dynamics of water molecules in the minor groove and in the bulk, we have calculated the entropy of water molecules in the respective regions [8, 39] at two different temperatures (300 K and 280 K). In both the temperatures, minor groove water molecules have substantially lower entropy than bulk. At 300 K the difference is $\sim 60\%$ of the latent heat of fusion of bulk water. Entropy is usually found to be closely correlated with diffusion coefficient and structural relaxation time, in **Figure 5**, we show the correlation between TS_{Conf} and translational
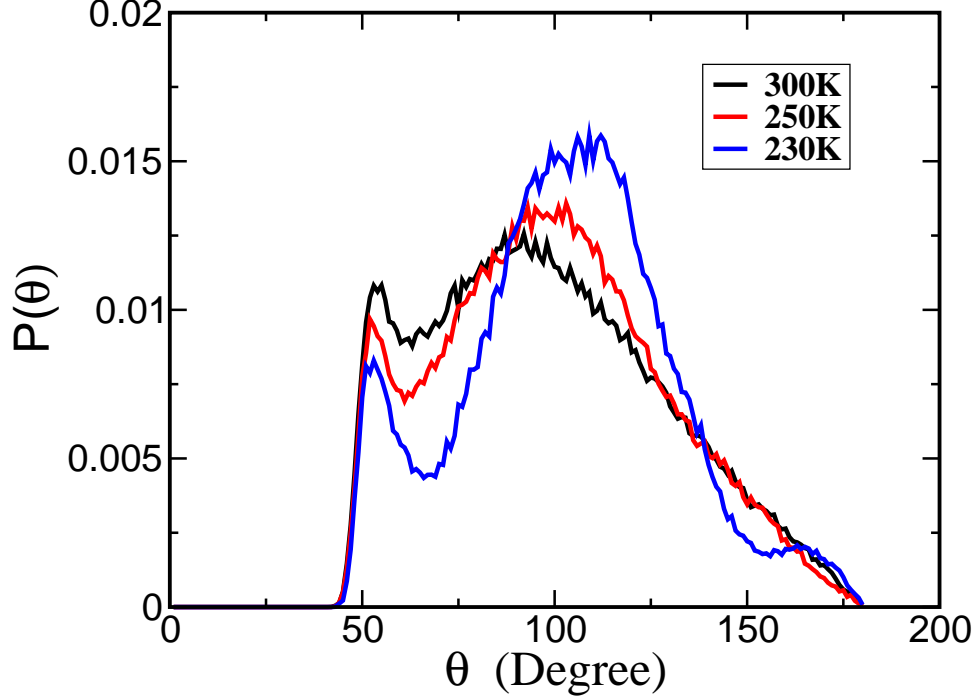
FIG. 4: O-O-O angle distribution of the groove water molecules inside the first coordination shell at 300K, 250K and 230K . Note the decrease of lower angle (interstitial) peak and increase of higher angle (degree of tetrahedrality) peak height with decreasing temperature.

diffusivity and show that the *Adam-Gibbs relation* remains valid for the different regions of DNA. Interestingly, we find that the Adams-Gibbs plot for the two different temperatures collapse on a single curve which can be fitted to a straight line. This seems to indicate that the activation energies for the transfer of water molecules between different regions of aqueous DNA are at most weakly dependent on temperature above the L-L transition. Dynamics below the L-L transition is too slow to allow a comprehensive study. The present calculation of entropy is semi-quantitatively reliable as the entropy of bulk water is correctly (within 5 %) reproduced and also the chemical potentials of bulk water and groove water are found to be the same, as expected for systems in equilibrium.

In a thermodynamic co-existence between two phases, a discontinuous change in entropy signals the presence of latent heat and a first order phase transition. However, in the present case, the large difference in entropy between bulk and minor groove water molecules should be regarded as a signature in the difference in structure between the two phases. Because of the small number ($\sim$65 for major groove and $\sim$30 for minor groove) of water molecules
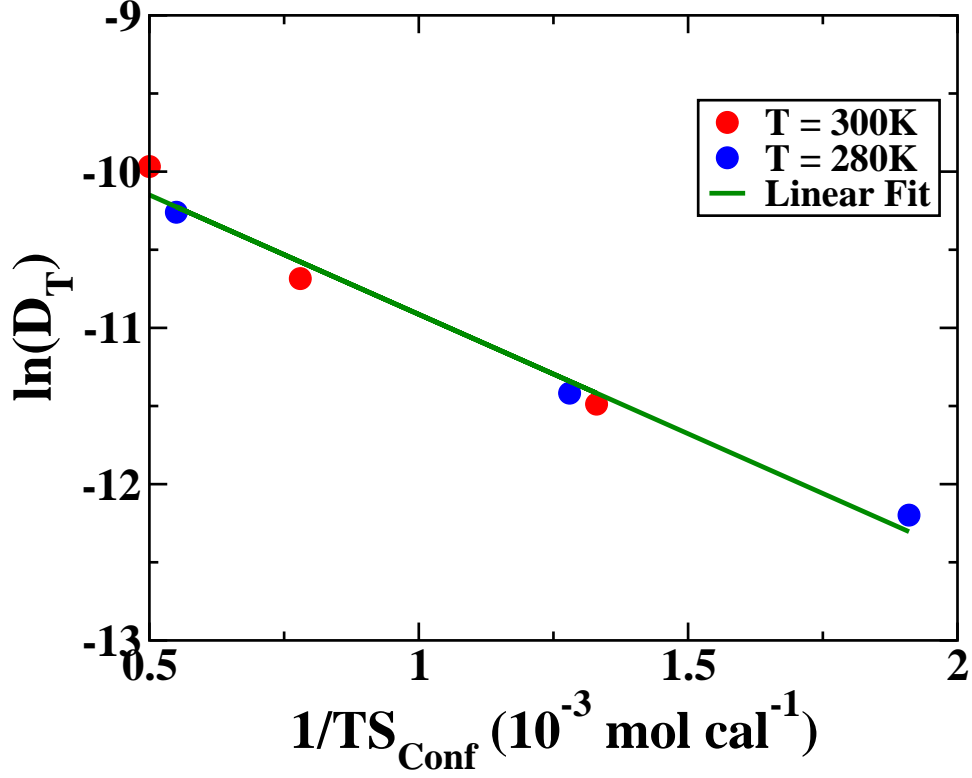
FIG. 5: Adam-Gibb's plot of translational diffusivity ($\ln(D_T)$) vs $1/TS_{Conf}$ for water molecules in the different regions of DNA duplex (major groove, minor groove and bulk) at two different temperatures, T = 300 K and T = 280 K.

present in the groove region, a detailed quantification of microscopic structural arrangement is hard to perform.

Because the numbers of water molecules in the two grooves of the dodecamer are rather small, we have also simulated a large system with a standardized 38 base pair DNA and 8,000 water molecules interacting with TIP3P potential [40]. This system is known to sustain a stable double helix over a long time period [40]. Interestingly, we obtained qualitatively similar results for the groove water molecules, but transitions (around 245 K in the grooves) are not as prominent since TIP3P is known not to be a good network forming liquid and the *L-L transition is largely suppressed in the bulk phase.* Nevertheless, we do find similar kind of transition in the grooves in two different systems with two different water models which strengthens the generality of the results obtained in the present study.

VI.   CONCLUSIONS

In conclusion, we have studied both translational and rotational motions of water in the grooves of a DNA duplex . We find that groove water shows a remarkable dynamical transition which can explain the transition observed in DNA duplex itself. *The fact that this transition occurs at not too deeply supercooled water ($T_{GL} \approx 255$ K) suggests that this can be of importance in natural world.*

VII.   ACKNOWLEDGEMENT

[1] Bagchi, B. *Chem. Rev.* **2005**, *105*, 3196-3219.; Nandi, N.; Bhattacharyya, K.; Bagchi, B. *Chem. Rev.* **2000**, *100*, 2013-2045.

[2] Cheng, Y.-K.; Rossky, P. J. *Nature (London)* **1998**, *392*, 696-699.

[3] Tarek, M.; Tobias, D. J. *Phys. Rev. Lett.* **2002**, *88*, 138101.

[4] Nelson, D. L.; Cox, M. M. In *Lehninger Principles of Biochemistry*; Worth: New York, 2000.

[5] Tarek, M.; Tobias, D. J. *Biophys. J.* **2000**, *79*, 3244-3257.

[6] Murarka, R. K.; Head-Gordon, T. *J. Phys. Chem. B* **2008**, *112*, 179-186.

[7] Pal, S.; Maiti, P. K.; Bagchi, B. *J. Chem. Phys.* **2006**, *125*, 234903.

[8] Jana, B.; Pal, S.; Maiti, P. K.; Lin, S.-T.; Hynes, J. T.; Bagchi, B. *J. Phys. Chem. B* **2006**, *110*, 19611-19618.

[9] Berg, M. A.; Coleman, R. S.; Murphy, C. J. *Phys. Chem. Chem. Phys.* **2008**, *10*, 1229-1242.

[10] Andreatta, D.; Sen, S.; Perez Lustres, J. L.; Kovalenko, S. A.; Ernsting, N. P.; Murphy, C. J.; Coleman, R. S.; Berg, M. A. *J. Am. Chem. Soc.* **2006**, *128*, 6885-6892.

[11] Sen, S.; Andreatta, D.; Ponomarev, S. Y. Beveridge, D. L.; Berg, M. A. *J. Am. Chem. Soc.*

(Submitted).

[12] Jayaram, B.; Beveridge, D. L. *Annu Rev Biophys. Biomol. Struct.* **1996**, *25*, 367-394.

[13] Qu, X.; Wan, C.; Becker, Hans-Christian; Zhong, D.; Zewail, A. H. *Proc. Natl. Acad. Sci.* **2001** *98*, 14212-14217.

[14] Mukherjee, A.; Lavery, R.; Bagchi, B.; Hynes, J. T. *J. Am. Chem. Soc.* **2008**, *130*, 9747-9755.

[15] Ringe, D.; Petsko, G. A. *Biophys.Chem.* **2003**, *105*, 667-680.

[16] Hartmann, H.; Parak, F.; Steigemann, W.; Petsko, G. A.; Ponzi, D. R.; Frauenfelder, H. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 4967-4971.

[17] Lee, A. L.; Wand, A. J. *Nature (London)* **2001**, *411*, 501-504.

[18] Rasmussen, B. F.; Stock, A. M.; Ringe, D.; Petsko, G. A. *Nature (London)* **1992**, *357*, 423-424.

[19] Doster, W.; Cusack, S.; Petry, W. *Nature (London)* **1989**, *337*, 754-756.

[20] Vitkup, D.; Ringe, D.; Petsko, G. A.; Karplus, M. *Nat. Struct. Biol.* **2000**, *7*, 34-38.

[21] Tarek, M.; Tobias, D. J. *Biophys. J.* **2000**, *79*, 3244-3257.

[22] Zanotti, J. -M.; Bellissent-Funel, M. -C.; Parello, J. *Biophys. J.* **1999**, *76*, 2390-2411.

[23] Sokolov, A. P.; Grimm, H.; Kahn, R. *J. Chem. Phys.* **1999**, *110*, 7053-7057.

[24] Norberg, J.; Nilsson, L. *Proc. Natl. Acad. Sci. USA.* **1996**, *93*, 10173-10176.

[25] Lagi, M.; Chu, X.; Kim, C.; Mallamace, F.; Baglioni, P.; Chen, S. -H. *J. Phys. Chem. B.* bf 2008, *112*, 1571-1575.

[26] Chen, S. -H.; Liu, L.; Chu, X.; Zhang, Y.; Fratini, E.; Baglioni, P.; Faraone, A.; Mamontov, E. *J. Chem. Phys.* **2006**, *125*, 171103.

[27] Mellamace, F.; Chen, S. -H.; Broccio, M.; Corsaro, C.; Crupi, V.; Majolino, D.; Venuti, V.; Baglioni, P.; Fratini, E.; Vannucci, C.; Stanley, H. E. *J. Chem. Phys.* **2007**, *127*, 45104.

[28] Kumar, P.; Yan, Z.; Xu, L.;Mazza, M. G.; Buldyrev, S. V.; Chen, S. -H.; Sastry, S.; Stanley, H. E. *Phys. Rev. Lett.* **2006**, *97*, 177802.

[29] Harrington, S.; Zhang, R.; Poole, P. H.; Sciortino, F.; Stanley, H. E. *Phys. Rev. Lett.* **1997**, *78*, 2409-2412.

[30] Meyer, M.; Stanley, H. E. *J. Phys. Chem. B***1999**, *103*, 9728-9730.

[31] Xu, L.; Kumar, P.; Buldyrev, S. V.; Chen, S. -H.; Poole, P. H.; Sciortino, F.; Stanley, H. E. *Proc. Natl. Acad. Sci. USA.* **2005**, *102*, 16558-16562.

[32] Drew, H. R.; Wing, R. M.; Takano, T.; Broka, C.; Tanaka, S.; Itakura, K.; Dickerson, R. E. *Proc. Natl. Acad. Sci. USA.* **1981**, *78*, 2179-2183.

[33] Mahoney, M. W.; Jorgensen, W. L. *J. Chem. Phys.* **2000**, *112*, 8910-8922.

[34] Case, D. A. *et al.*, AMBER 8 (University of California, San Francisco, 2004).

[35] Chen, S. H.; Liao, C.; Sciortino, F.; Gallo, P.; Tartaglia, P. *Phys. Rev. E* **1999**, *59*, 6708-6714.

[36] Subramanian, P. S.; Ravishanker, G.; Beveridge, D. L. *Proc. Natl. Acad. Sci. USA.* **1988**, *85*, 1836-1840.

[37] Riggleman, R. A.; Yoshimoto, K.; Douglas, J. F.; de Pablo, J. J. *Phys. Rev. Lett. 2006*, *97*, 045502.

[38] Soles, C. L.; Douglas, J. F.; Wu, W. -L.; Dimeo, R. M. *Phys. Rev. Lett.* **2002**, *88*, 037401.

[39] Lin, S. -T.; Blanco, M.; Goddard III, W. A. *J. Chem. Phys.* **2003**, *119*, 11792-11805.

[40] Maiti, P. K.; Pascal, T. A.; Vaidehi, N.; Goddard III, W. A. *Nucleic Acids Res.* bf 2004, *32*, 6047-6056.; Maiti, P. K.; Pascal, T. A.; Vaidehi, N.; Heo, J.; Goddard III, W. A. *Biophys. J.* **2006**, *90*, 1463-1479.