Multiple Time Scales in Solvation Dynamics of DNA in Aqueous Solution: The Role of Water, Counterions, and Cross-Correlations

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Recent time domain experiments have explored solvation dynamics of a probe located inside a DNA duplex, in an effort to gain information, e.g., on the dynamics of water molecules in the DNA major and minor grooves and their environment. Multiple time constants in the range of a few picoseconds to several nanoseconds were obtained. We have carried out 15 ns long atomistic molecular dynamics simulations to study the solvation dynamics of bases of a 38 base-pair long DNA duplex in an aqueous solution containing counterions. We have computed the energy−energy time correlation function (TCF) of the four individual bases (A, T, G, and C) to characterize the solvation dynamics. All the TCFs display highly nonexponential decay with time. When the trajectories are analyzed with 100 fs time resolution, the TCF of each base shows initial ultrafast decay (with $\tau_1 \approx 60-80$ fs) followed by two intermediate components ($\tau_2 \approx 1$ ps, $\tau_3 \approx 20-30$ ps), in near complete agreement with a recent time domain experiment on DNA solvation. Interestingly, the solvation dynamics of each of the four different nucleotide bases exhibit rather similar time scales. To explore the existence of slow relaxation at longer times reported recently in a series of experiments, we also analyzed the solvation TCFs calculated with longer time trajectories and with a larger time resolution of 1 ps. In this case, an additional slow component with a time constant of the order of 250 ps is observed. Through an analysis of partial solvation TCFs, we find that the slow decay originates mainly from the interaction of the nucleotides with the dipolar water molecules and the counterions. An interesting negative cross-correlation between water and counterions is observed, which makes an important contribution to relaxation at intermediate to longer times.

1. Introduction

The study of the dynamics of solvation of a newly created ion or a dipole in macromolecular solution is now a widely used method to obtain molecular level information about the collective solvent response of the solvent molecules around the probe. Solvation dynamics is based on a fluorescent macromolecular probe that has a large dipole moment in the excited state; upon excitation of the probe, the increased electric field associated with the probe can be used to study dynamics of the macromolecule and the surrounding solvent.[1−3] As the excited state is stabilized, the probe's fluorescence shifts to lower frequency, and the solvation dynamics experiment consists of measuring the fluorescence frequency as a function of time after the excitation (the dynamic Stokes shift). Study of solvation dynamics of a polar molecule in liquid water has revealed a wealth of information about the time scale of the polarization relaxation, which has proven useful in understanding crucial chemical processes, like electron and proton-transfer reactions in aqueous solution.

Naturally occurring DNA is a heteropolymer duplex where each strand consists of four different bases. These bases are abundant in nitrogen, oxygen, amide, and carboxylic acidic groups. These atoms and groups are highly polar. Therefore, water plays a crucial role in stabilizing the DNA duplex, and also in the biological function of DNA. Water that surrounds DNA resides in two grooves: minor and major. The dynamical response of water molecules in these two grooves and also in the shell next to the grooves is much sought-after information as these molecules could play an important role in such chemical processes as drug−DNA intercalation and protein−DNA interaction. Solvation dynamics, being partly a local probe that is strongly influenced by the rotational motion of water molecules,[1−6] can provide unique information.

Solvation dynamics is described by the decay of the nonequilibrium time correlation function (TCF) $S(t)$, which is defined as[1,2]

$$S(t) = \frac{\bar{\nu}(t) - \bar{\nu}(\infty)}{\bar{\nu}(0) - \bar{\nu}(\infty)} \tag{1}$$

where $\bar{\nu}(0)$, $\bar{\nu}(t)$, and $\bar{\nu}(\infty)$ denote the observed average emission frequencies at time zero, t, and infinity, respectively. The solvation TCF can be related by linear response theory also to an equilibrium TCF of the energy fluctuation. This is usually termed $C_S(t)$ and defined as

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$$C_S(t) = \frac{\langle \delta E(0)\delta E(t)\rangle}{\langle \delta E(0)\delta E(0)\rangle} \quad (2)$$

where $\delta E(t) = E(t) - \langle E\rangle$ denotes a fluctuation in the solvation energy difference between the excited and the ground state of the solute and $\langle\cdots\rangle$ indicates an equilibrium ensemble average in the ground electronic state. As has been discussed,[3] eqs 1 and 2 represent two somewhat different functions. While $S(t)$ evolves from characteristics of the initial state to that of the final excited state of the probe, $C_S(t)$ refers to the ground state. This difference, as well as the difference of $C_S(t)$ from its excited state analogue, is ignored here.

Time dependent fluorescence Stokes shift (TDFSS) studies have recently been carried out to explore solvation dynamics of aqueous proteins,[4] complex chemical systems,[5,6] and DNA duplexes.[7−13] In a pioneering study, Berg and co-workers[7−11] have studied the solvation dynamics of a 17-mer DNA duplex using a Coumarin102 (C102) probe, which was covalently attached to deoxyribose. It was found that the solvation TCF extracted from the TDFSS exhibits a very slow logarithmic time dependence over three decades of time (40 ps to 40 ns).[7] This study was carried out with a 100 ps temporal resolution, and the authors focused on understanding the slow aspects of dynamics in the DNA−water−counterion system. In a subsequent study, the solvation TCF was fitted to a temporal power law of the form $t^{-\alpha}$.[8]

In another interesting study, Zewail and co-workers[12,13] studied the hydration dynamics at the surface of a DNA dodecamer duplex using femtosecond time resolution. By following the temporal evolution of fluorescence, they observed two well-separated hydration times equal to 1.0 and 10−12 ps[12] (solvation dynamics of a drug−DNA complex showed a slow time constant of about 20 ps[13]). Pal et al.[12,13] concluded that their experimental results could be explained in terms of two general kinds of water molecules, with the slower of these termed "dynamically ordered water". It was conjectured that these ordered water molecules may play an important role in molecular recognition.[14]

The above two experiments probe two different regimes of the solvation TCF. The experiment of Berg and co-workers[7−11] studied the long time dynamics, while the experiment of Zewail and co-workers[12,13] concentrated on the short time dynamics. Thus, these experiments are complementary to each other.

In the present work, we have carried out atomistic molecular dynamics simulations to study the solvation dynamics of DNA bases. We have computed the equilibrium energy−energy TCF of each base of the 38 base-pairs long DNA. The 38 base pair choice is made so that one has a sufficient number of bases of each type to obtain good statistics. In addition, the DNA we used has been standardized and studied earlier.[15−18]

To examine the ultrafast time scales, we have analyzed the trajectory with a 100 fs time resolution. For the long time decay, a separate analysis with 1 ps time resolution of a long simulation (more than 15 ns) was carried out.

In a DNA solvation dynamics experiment an external solute is used since the bases are not fluorescent. Zewail et al.[12] have used 2-aminopurine as an external solute for their solvation dynamics experiment. Berg et al.,[7,8] on the other hand, used Coumarin 102 (C102) as an external probe. Each of these probes replaced a purine base in the DNA. In our simulations, we have instead used each of the DNA bases as an intrinsic probe, i.e., we have calculated energy−energy TCFs for each of the four bases (A, T, G, and C) and compared with the experimental results. Thus, we calculate $C_S(t)$ (defined by eq 2) and *not* $S(t)$ (defined by eq 1) measured in the TDFSS experiments. We anticipate that these will be similar, an expectation borne out by the results reported within. Further, our choice of the bases as probes in the present calculations may limit to some extent a detailed comparison with the above-mentioned experiments which use different probes. Nonetheless, we will find that, for the most part, general (though not complete) agreement with the experimental results is found.

The remainder of the paper is organized as follows. In Section 2, aspects of possible time scales for the problem are discussed. In Section 3, we discuss the details of the simulation. In Section 4, we present the results and discuss their significance. Section 5 contains the concluding remarks.

2. Time Scales Involved in the Solvation Dynamics

The solvation energy of a probe located at the *i*th base of the DNA sequence at time is given by sum of three individual contributions

$$E_P^{(i)}(t) = E_{P,DNA}^{(i)}(t) + E_{P,ion}^{(i)}(t) + E_{P,W}^{(i)}(t) \quad (3)$$

where $E_P^{(i)}(t)$ is the total energy of the probe and $E_{P,DNA}^{(i)}(t)$, $E_{P,ion}^{(i)}(t)$, and $E_{P,W}^{(i)}(t)$ are the energies of the interaction of the probe with the DNA, counterions, and water molecules, respectively. Therefore, the total solvation TCF $C_S(t)$ consists of three self (DNA−DNA, ion−ion, and water−water) and three cross (DNA−water, DNA−ion, and ion−water) TCFs. It is the fluctuation of $E_P^{(i)}(t)$ that enters in eq 2. To avoid possible confusion, we add a note as to our notation. For example, the ion−ion self-TCF involves the initial and time t values of the fluctuation of the interaction energy of the ion with the probe, not the self-interaction energy between the ions. Similarly, and for example, the ion−water cross TCF involves the initial time value of the fluctuation of the interaction energy of the ions with the probe and the time t value of the fluctuation of the interaction energy of the water molecules with the probe, not the interaction energy between the ions and the water molecules.

It is useful for perspective to discuss various time scales anticipated for the problem. For a naturally occurring long DNA, the self-term from the DNA chain itself can make an important contribution to the time dependence of the energy and give rise to a slow component in the solvation dynamics.[19] However, the experiments of Berg et al.[7−11] and Zewail et al.[12,13] have used a small section of DNA. Since the persistence length of DNA is ∼500 Å, the DNA employed in these experiments behaves as a rigid rod. Therefore, the contribution from the DNA is expected to be negligible.

A slow component can certainly arise from counterions,[20−24] since ion atmosphere relaxation (τ_{atm}) is a slow process. The time scale of relaxation for an electrolyte solution can be given by the well-known Debye−Hückel (DH) relation[21−23]

$$\tau_{atm} = \frac{1}{D_{ion}\kappa_D^{\,2}} \quad (4)$$

where D_{ion} is the diffusion coefficient of the counterions, and κ_D is the inverse Debye screening length. κ_D can be written as

$$\kappa_D^{\,2} = \frac{4\pi}{\epsilon k_B T}\rho_{ion} q_{ion}^{\,2} \quad (5)$$

where ϵ is the static dielectric constant of the medium, q_{ion} and ρ_{ion} are respectively the charge of an ion and bulk number density, k_B is the Boltzmann constant, and T is the absolute

temperature. For a typical 0.001 M solution of 1:1 salt, $\tau_{atm} \approx$ 100 ns, and for a 0.01 M solution, $\tau_{atm} \approx 10$ ns. Since the energy of both the negatively charged phosphate groups and the bases of DNA can be quite sensitive to ion atmosphere fluctuations, one may expect a very slow time scale of relaxation from the ion atmosphere. A more generalized DH theory developed recently on the basis of mode coupling theory shows that ion atmosphere relaxation should be considered to be nonexponential.[21]

In addition, a slow relaxation component can arise from the movement of the quasibound counterions along the DNA chain.[24] This slow contribution of the counterions can particularly be understood from the dielectric relaxation (DR) of polyelectrolyte solutions,[24] which generally shows highly nonexponential decay at a long time scale, attributed to counterion movement along the DNA axis.[24]

While the ultrafast component in the solvation dynamics certainly originates at least partly from water, the water contribution on the intermediate to long time scale is not yet clear. In such a situation, computer simulations are quite useful in differentiating between different contributions. Several groups[25−31] have carried out molecular dynamics simulations to study the structure and dynamics of aqueous DNA solutions. In an important simulation study, Makarov et al.[27] investigated water diffusion around a DNA. These authors found that the overall solvent diffusion rate at the interface is lower than in the bulk. The rate is higher than average in the direction parallel to the solute surface and is lower in the direction normal to the surface. The rate was also found to be lower in the solvation shells of the macromolecules, producing characteristic depressions in the radial profiles of the diffusion coefficient correlated with peaks in the corresponding radial distribution functions. In another simulation study, Bonvin et al.[31] examined the structure and dynamics of a hexadecamer duplex by 1.4 ns MD simulation in water. The DNA hydration was characterized in terms of hydrogen bond percentage and the corresponding residence time. These authors calculated the residence times of those water molecules within a distance of 0.35 nm from the DNA nonexchangeable protons and compared their results with NMR studies. The average residence time of hydrogen-bonded water molecules was only 11($\pm$11) ps with a maximum of 223 ps.[31] However, neither of the above-mentioned computer simulation studies explored the microscopic aspects of DNA solvation and the role of water and counterions.

Finally, in an earlier study,[15] we have reported the differing water dynamics at the major and minor grooves of aqueous DNA. We found that the rotational time correlation function of surface water dipoles is markedly nonexponential with a slow time component of the order of 200 ps. Translational motion of the water molecules present in the minor groove is found to be subdiffusive.[15] The hydrogen bond lifetime correlation function of the water molecules present in the minor groove shows slower dynamics than those in the major groove. The averaged lifetime of the hydrogen bond between the minor groove water molecule and the DNA base is found to be 50 ps with a longest time component of 115 ps.[16] On the other hand, the averaged lifetime of the hydrogen bond between the water molecules in the major groove and the DNA base is found to be 20 ps with a longest time component of 35 ps.[16] These time constants are about an order of magnitude slower than that for the water molecules in the bulk.

3. Simulation Details

The sequence of the 38 base pair DNA used in the simulation is (GCCGCGAGGTGTCAGGGATTGCAGCCAGCATCTCG-TCG), taken from the earlier work of Goddard and coworkers.[17,18] During the simulation study, DNA was found to be stable (see the Supporting Information); furthermore, it does not collide with its periodic image. The present MD simulations used the AMBER7 software package with the all-atom AMBER95 force field (FF).[32] AMBER95 FF has been validated for Molecular Dynamics (MD) simulations of B-DNA in explicit water with salt, starting from the crystal structure.[17,18] The electrostatic interactions were calculated with the Particle Mesh Ewald (PME) method.[33] By using the LEAP module in AMBER, the DNA structure was immersed in a water box with use of the TIP3P model for water.[34] The box dimensions were chosen to ensure a 10 Å thick solvation shell around the DNA structure. In addition, some waters were replaced by Na^+ counterions to neutralize the negative charge on the phosphate groups of the backbone of the DNA structure. This procedure resulted in solvated structures containing 25 081 atoms which include 2405 DNA atoms, 74 counterions (Na^+), and 7534 water molecules in a simulation box of lengths 42, 42, and 142 Å along the three axes. Details of the simulations can be found elsewere.[15−18]

For the calculation of the solvation TCFs eq 2, two different sets of simulations were carried out to examine shorter and longer time scales probed in the experiments, as explained in Section 1. To capture the short time behavior, simulation was carried out for 5 ns where the coordinates and velocities were stored for every 100 fs time interval. A second set of simulations was carried out for 15 ns where coordinates and velocities were stored for every 1 ps time interval.

The energy of each base was calculated by using the ANAL module of the AMBER program.[32] The DNA studied here consists of 25 G-C pairs and 13 A-T pairs. We excluded four terminal bases (4 base pairs from the 5′ end and four base pairs from the 3′ end) to avoid the end fluctuation of the DNA and considered only 30 base pairs for the energy calculations.

4. Solvation Time Correlation Functions

Motivated by the experiments mentioned in the Introduction, we have studied the equilibrium energy−energy TCF for each of the four nucleotides in the DNA model. That is, we have used individual bases as the probe in their solvation dynamics. As mentioned earlier in Section 2, the energy of the *i*th base at time *t* consists of three parts: the contributions to the total interaction energy of the probe with the rest of the DNA ($E_{P,DNA}$), with the ions ($E_{P,ion}$), and with the water ($E_{P,W}$); i.e., the specification of eq 3 for the probe as a base i is

$$E_B^{(i)}(t) = E_{B,DNA}^{(i)}(t) + E_{B,ion}^{(i)}(t) + E_{B,W}^{(i)}(t) \qquad (6)$$

where $E_B^{(i)}(t)$ is the time dependent energy of the *i*th base.

We have calculated the equilibrium energy−energy time correlation function ($C_S^i(t)$) using eq 2, whose specification for each probe base i is

$$C_S^i(t) = \frac{\langle \delta E_B^i(0)\, \delta E_B^i(t) \rangle}{\langle \delta E_B^i(0)\, \delta E_B^i(0) \rangle} \qquad (7)$$

Thus, the total solvation TCF contains three direct and three cross terms; we refer the reader to the discussion below eq 3 for the meaning of our terminology for such terms.

We have calculated all the partial, both direct and cross, TCFs. To examine the short time relaxation, we have calculated the TCFs with a time resolution of 100 fs on a 5 ns trajectory. To

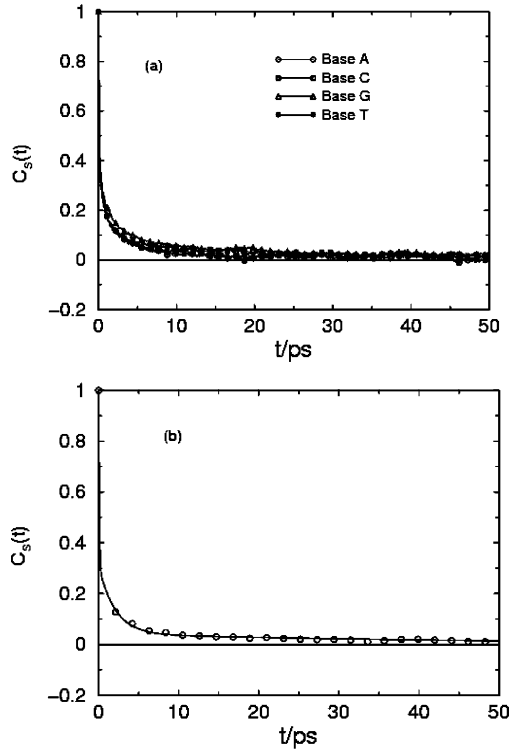

Figure 1. (a) Plot of the time dependence of the total solvation energy time correlation function (TCF) for all the four different bases. The TCFs are calculated with 100 fs time resolution. The symbols are the data points (shown infrequently for clarity) obtained from simulations, and the continuous line is the multiexponential fit. Fitting parameters are provided in Table 1. (b) Plot of the time dependence of the averaged total solvation time correlation function (TCF). The average has been taken over all four TCFs shown in panel a. The symbols are the simulation data points (shown infrequently for clarity) and the continuous line is the multiexponential fit. The fitting parameters for individual bases (panel a) are given in Table 1.

obtain the longer time dynamics, we have calculated the TCFs with a 1 ps time resolution on a 15 ns trajectory.

In Figure 1a, we show the time dependence of $C_S(t)$ calculated with 100 fs time resolution for all four bases and in Figure 1b the solvation TCFs averaged over all these bases are shown. A noticeable feature of this figure is the ultrafast decay (∼40% of the total initial function) of the solvation TCFs of all the bases. This type of ultrafast solvation is of course well-known in the solvation dynamics of charged and dipolar species in water.[2] We have fitted the computed solvation TCFs (Figure 1a) to a multiexponential form, with the fitted parameters shown in Table 1. We find three time scales: one ultrafast component (∼60−80 fs), a fast component (1−2 ps), and an intermediate component (∼20−30 ps). The average solvation time (defined as $\tau = \int_0^\infty dt\, C_S(t)$) for all the bases is also provided in Table 1.

To gain a microscopic understanding of the origin of the observed time scales, we have decomposed the total solvation TCF into pure (DNA−DNA, water−water, and ion−ion) and cross (DNA−ion, DNA−water, and ion−water) TCFs according to the decomposition eq 3 of the interaction energy of the DNA, the water, and the counterions with the base. In Figure 2a, we show all three direct (DNA−DNA, ion−ion, and water−water) and three cross (DNA−ion, DNA−water, and ion−water) TCFs for a base of type G (the other bases give similar results). The un-normalized TCFs are displayed so that their relative magnitudes are evident. The cross correlation functions are multiplied by a factor of 2, reflecting their proper contribution to the total TCF.

TABLE 1: Parameters of the Multiexponential Fit to the Solvation Time Correlation Function for Different Bases (Figure 1a)[a]

base	time constant (ps)	amplitude (%)	av time constant (ps)
G	0.08	65	2.8
	1.8	27	
	28.3	8	
C	0.06	64	2.2
	1.2	29	
	25.6	7	
A	0.08	68	2.0
	2.0	27	
	28.8	5	
T	0.06	69	1.7
	1.9	26	
	23.6	5	

[a] The solvation time correlation functions were calculated with 100 fs time resolution.

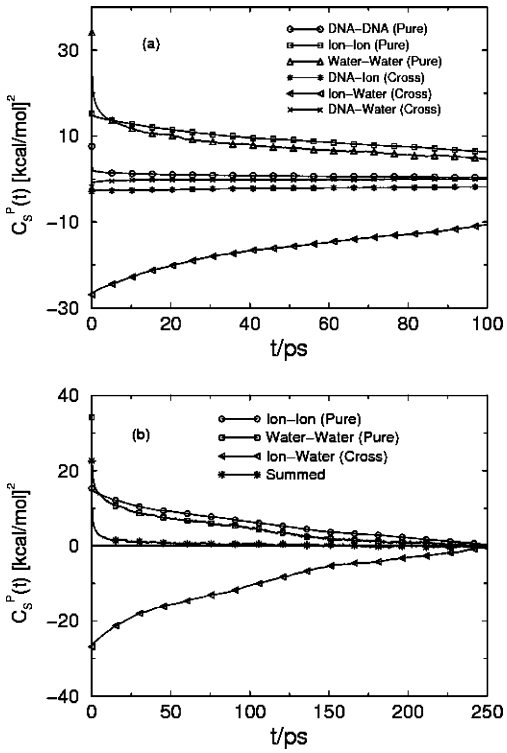

Figure 2. (a) Decay of the partial solvation time correlation functions (direct and cross) $C_S^P(t)$ for a base of type G. The other bases show a similar behavior. The correlation functions were calculated with 100 fs time resolution. They are not normalized. (b) Plot of the ion−ion (pure), water−water (pure), ion−water (cross), and the summed (unnormalized) time correlation functions versus time. The latter is obtained by adding the ion−ion, water−water, and ion−water correlation functions.

Among the three pure TCFs, the direct DNA−DNA TCF is small, as anticipated in Section 2, leaving only the direct water−water and ion−ion TCFs as significant. The cross correlation functions are found to be negative. The ion−water cross correlation function is dominant compared to the other two cross correlation functions. Overall, any TCF involving the DNA energy is negligible and the important contributions arise from the interaction of water and the counterions with the nucleotides and these contributions exhibit slow dynamics, as anticipated in Section 2. Another important point is that while the ultrafast

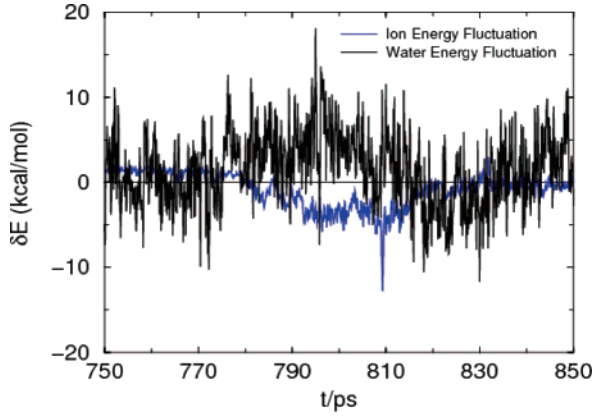

Figure 3. The time-dependent fluctuation in the energy contribution from ions and water molecules as a function of time along an MD trajectory for a G base showing the negative cross-correlation between the water and ionic contributions over a segment of trajectory.

sub-100 fs decay is almost entirely due to water,[2] the subsequent slow decays of the water and ionic contributions display similar rates.

To more clearly assess the contributions of water and the counterions, we have calculated the summed TCF, shown in Figure 2b, which is the sum of the ion−ion and water−water direct terms and the ion−water cross correlation, i.e., the terms found dominant in Figure 2a. It is seen that much of the slow decay evident in the individual contributions in Figure 2a disappears because of the cancellation due to the cross-correlation term. This important negative ion−water cross correlation has been further explored via an analysis of the trajectories of individual bases, which provide more detail than does a TCF. The contribution of the water molecules and the counterions to the total energy of interaction with a base and the fluctuation in the contributed energy has been calculated. Figure 3 shows these energy fluctuations, again for base G, with the other bases showing a similar behavior. The most noticeable feature is the anti cross correlation between the counterion and water energy fluctuations. Over a range of time, when the water energy fluctuation is positive, the counterion energy fluctuation is negative and vice versa, which is of course reflected in the water−ion TCF in Figure 2a.

Some physical understanding of the negative cross-correlation between the interaction energy fluctuations in the contributions of the water and the counterions may be provided by the following illustrative and simplified argument. Let us consider a positively charged "probe" ion at the center of a small sphere (of a few angstroms diameter) in a solution of water and counterions. An equilibrium configuration will involve the oxygen atoms of the water molecules pointing toward the central positive ion. The counterions will be largely in periphery, with an excess of negative over positive ions. In this equilibrium configuration, the interaction energy of the central ion with the water molecules will be negative (i.e., attractive) and that with the counterions will also be negative but screened by the intervening water. We imagine a fluctuation in which, e.g., an outward motion of the water molecules surrounding the central probe ion occurs. The change in the probe−water interaction energy will be positive, as the attraction is decreased. At the same time, the change in the net probe−counterion interaction energy will be negative, as the probe−counterion attraction is enhanced by the reduced screening. Thus, the fluctuations in the water−probe and ion−probe interaction energies are anti-correlated. Variants of the above argument can be constructed and provide the same conclusion.

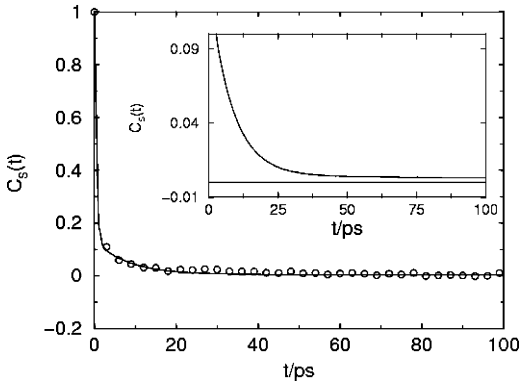

Figure 4. The calculated average solvation time correlation function with 1 ps time resolution. The circles are the data simulation points (shown infrequently for clarity) obtained from simulation, and the continuous line is the multiexponential fit. The inset shows the fitted curve with a magnified scale. The parameters of the multiexponential fit are provided in Table 2.

TABLE 2: Parameters of the Multiexponential Fit to the Average Solvation Time Correlation Function (Figure 4)[a]

time constant (ps)	amplitude (%)	av time constant (ps)
0.4	84	
8.3	12	10.8
235.8	4	

[a] The solvation time correlation function was calculated with 1 ps time resolution.

Finally, as mentioned in the Introduction, recent solvation dynamics experiments on DNA by Berg and co-workers[7,8] reveal an existence of a very slow solvation dynamics component (40 ns). To capture such a slow component in the solvation TCF, we have carried out another set of simulations with 1 ps time resolution. We have first calculated the average TCF for the four individual bases (similar to Figure 1a) and then finally averaged over the four TCFs (similar to Figure 1b). The average TCF result is shown in Figure 4, with the multiexponential fitted curve on a magnified scale shown in the inset and the fitting parameters shown in Table 2. The average TCF is highly nonexponential and shows the existence of a very slow component with a time constant ∼250 ps. Despite the finding of this slow component, the present simulations fail to recover the ultraslow, power law decay observed by Berg and co-workers,[7,8] a point to which we return in the next section.

5. Concluding Remarks

In conclusion, we have carried out long atomistic molecular dynamics simulations to study the solvation dynamics of DNA bases for DNA immersed in an aqueous solution containing counterions. The solvation time correlation functions (TCFs) are similar for all the bases and are highly nonexponential. Several time constants with values of a few tens of femtoseconds and several tens of picoseconds were obtained, in general agreement with experimental results.[12] The longer time scale found here (24 ps) is twice that found in the experiments in ref 12. This difference may arise due to the differents probe used here and in those experiments, as noted in the Introduction. It may also be due to the fact that the DNA used in refs 12 and 13 was 12 base pairs long, while in the present work, the DNA is 38 base pairs long, chosen to allow the formation of a definable hydration layer. The chain length dependence of the solvation dynamics is worth pursuing in the future. We address

below the issue of the nanosecond ultraslow decay found experimentally.[7,8]

Our analysis of partial solvation TCFs reveals that (a) the ultrafast component is dominated by the self-TCF associated with the water−base interaction energy and (b) the slower decay originates mostly from the interaction of the DNA base with the water molecules and the counterions and not from the interaction of the base with the rest of the DNA.

The water contribution to the solvation dynamics results in a contribution at least an order of magnitude slower than in bulk water. This result can be put into perspective in connection with several recent experiments and computer simulations on the solvation dynamics of proteins.[4−6] In these studies, the probe is on the protein surface or buried in the core, thereby studying the hydration layer or buried water dynamics, respectively. These investigations have repeatedly found a significant slow component in the solvation time correlation function which is at least an order of magnitude slower than the solvation time in the bulk (as in the present DNA results). The origin and nature of this observed slow component is a subject of considerable debate.[5,6] A model in terms of a dynamic equilibrium between "bound" and "free" water molecules has been proposed that explains some aspects of the observed dynamics.[6,35] Such a mechanism should also be present in the DNA case. A preliminary analysis of hydrogen bond lifetime dynamics[16] indeed provides evidence of "bound" water molecules in the grooves of DNA.

We have found that the ions play an important role in solvation dynamics for DNA—this ionic contribution is largely absent in protein solvation. In fact, it is the time scale of the motion of ions as seen by the DNA bases that is a subject of great interest in the context of DNA dynamics. We find that the ion−ion TCF indeed gives rise to a slow contribution to the solvation energy relaxation. However, this contribution to the slow relaxation is cancelled by a large negative cross-correlation between the ion and water contributions.

Finally, while the present simulations have found a slow ∼250 ps decay, they fail to recover the ultraslow, power law decay observed by Berg and co-workers.[8] We think that there could be several different reasons for this. First, the different probes in those experiments and the present simulations (see the Introduction) may conceivably be relevant here, although the following two reasons now discussed seem more likely to us. Second, it is likely that the present simulations are not sufficiently long to capture any ultraslow fluctuations in energy due to the collective motion of the ions (as noted in the Introduction, the size of DNA used by Berg et al.[7,8] is rather small, so that it is unlikely that the slow contribution can come from the motion of DNA itself). Indeed, it is known that ion atmosphere relaxation can give rise to a fractional frequency dependence of frequency dependent electrolyte friction[21−23] at low frequency or equivalently long times for the time dependent electrolyte friction. The present simulations certainly cannot address this issue because of the absence of free negative ions in the simulation box, such that there is no question of the formation of an ion atmosphere. Therefore, the present simulation does not include the slow dynamics due to ion atmosphere relaxation. Third, another probable reason is that the experimental time dependent fluorescence studies measure a nonequilibrium response function, which has been approximated here in terms of an equilibrium, ground electronic state, TCF (cf. Section 1). Subsequent to the creation of a new charge distribution in the excited electronic state, the time dependent rearrangement of ion and water molecules around the probe may involve a very slow ionic contribution that could be absent in the equilibrium simulations. Such nonequilibrium effects are known to be important at longer times.[21,3] Thus, the experimental nanosecond scale ultraslow component remains to be clarified. We hope to address some of these issues in the future.

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Supporting Information Available: Root-mean-square deviation (rmsd) of the DNA with respect to the initial canonical structure and with respect to the averaged solution structure. This material is available free of charge via the Internet at http://pubs.acs.org.

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