The concentration effect on the 'hydrophobic' and 'hydrophilic' behaviour around DMSO in dilute aqueous DMSO solutions. A computer simulation study

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Abstract

We have carried out a molecular dynamics study of dimethyl sulfoxide (DMSO) in water at 298 K at two different densities by simulating two different concentrations: 0.055 and 0.19 mole fraction. We have found an enhancement in the structure of water, an effect that becomes more pronounced as the concentration of DMSO increases. At both concentrations there is a well-defined hydration structure around the oxygen atom of DMSO, which is able to establish strong hydrogen bonds with surrounding water molecules. An increase in the concentration of DMSO depletes the solution of bulk water molecules, reducing the number of hydrogen bonds that water can have in the immediate vicinity of DMSO but increasing the strength of the hydrogen bonds made between the oxygen atom of DMSO and water. There is clear evidence of 'hydrophobic' hydration around the methyl groups of DMSO, which is enhanced as the concentration of DMSO increases.
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Keywords: Molecular dynamics; DMSO; Aqueous solutions; 'Hydrophobic' hydration

1. Introduction

The unique physical and chemical properties of aqueous solutions of dimethyl sulfoxide (DMSO) make them particularly interesting [1,2]. DMSO and water are miscible in all proportions with the excess thermodynamic properties of their solutions exhibiting strong deviations from ideality [3]. The density [4,5], viscosity [5,6], adiabatic and isothermal compressibility [7], relative dielectric permittivity [8,9], surface tension [9,10], heats of mixing [5,11] and other properties exhibit strong non-ideal behaviour. For example, while pure DMSO and water have freezing points of 18.6 and 0 °C, respectively, a 1:3 molar solution of DMSO in water has a very low freezing point: −70 °C [12]. Although there are many experimental observations describing such behaviour, the underlying molecular mechanisms remain unclear.

Aqueous DMSO solutions have been studied with a wide range of experimental techniques, including X-ray and neutron diffraction [13,14], optical [11,15–20], acoustic [7,21], NMR [22] and dielectric [23] spectroscopies. The overall picture arising from these studies is that DMSO enhances the hydrogen-bonding network of water, possibly through the 'hydrophobic' hydration of the methyl groups of DMSO. However, a considerable degree of interpretation of the data has been required to provide such limited structural information.

Computer simulation techniques have provided some detailed information about the thermodynamics, structure and dynamics of aqueous DMSO solutions. Rao and Singh [24] computed the relative free energies of hydration of methanol and DMSO in water. Vaisman and Berkowitz [25] performed molecular dynamics (MD) simulations of dilute aqueous DMSO solutions, finding a sharpening in the water–water pair correlation functions with increasing DMSO concentration as well as the existence of 1DMSO:2H_2O hydrogen-bonded aggregates.

Luzar and Chandler [26] performed MD simulations at higher concentrations, finding that the local tetrahedral structure of water was always preserved. They found that the first hydration shells of DMSO become more structured with increasing DMSO concentration, while

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the average of number of water–water hydrogen bonds decreased, in agreement with their own neutron diffraction data [27,28]. They also found the existence of 1DMSO:2H$_2$O aggregates. These authors also found evidence for the 'hydrophobic' hydration of the non-polar groups of DMSO [26,29]. They also came to the conclusion that the strong DMSO–water correlations observed arise from the strong DMSO–water hydrogen bonds.

Borin and Skaf [30] have performed an MD study at various DMSO concentrations, showing the existence of two kinds of hydrogen-bonded aggregates. The previously identified 1DMSO:2H$_2$O aggregate was seen to predominate in water-rich mixtures, while a 2DMSO:1H$_2$O aggregate was seen to predominate in DMSO-rich mixtures.

In a more recent work, Chalaris and Samios have performed MD simulations of the liquid mixture of DMSO–water at ambient conditions and over the entire composition range using different potentials [31]. Results concerning the accuracy of the tested models in predicting certain properties of such systems have been presented and discussed.

In the present work we have carried out a MD study of the effect that changing the concentration of DMSO has on the hydration structure and hydrogen-bonding properties of its aqueous solutions. We report here our analysis of the thermodynamic, structural and hydrogen-bonding properties of aqueous solutions of DMSO at concentrations of 0.055 and 0.19 mole fraction at 298 K.

2. Simulation methods and potentials

MD simulations in the canonical ensemble (NVT) were performed using the program MOLDY [32] which makes use of a symplectic integrator to solve the equations of motion, allowing for larger time steps in aqueous systems. Cubic boxes with periodic boundary conditions were applied throughout. A real space cut-off of 10.0 Å was applied to short-range interactions, with standard long-range corrections for molecules at larger separations. Long-range electrostatic interactions were computed using the Ewald sum method [33]. The intermolecular potentials used were the TIP4P model of water [34] and the P2 model of DMSO [26,28], while Lorentz–Berthelot mixing rules were used to calculate cross interaction parameters. The rationale for this choice of water/DMSO potentials used in the present study is the quality of the MD results obtained in comparison with our previous simulation data of this mixture based on other widespread water force fields.

The simulations were performed at constant experimental densities. For the $X = 0.055$ mole fraction concentration, the simulation box contained 28 DMSO molecules and 472 water molecules. For the $X = 0.19$

Table 1
Summary of the simulations for DMSO in water at 298 K

X	ρ (g cm^{-3})	U (kJ mol^{-1})	U_{exp} (kJ mol^{-1})	P (MPa)
0.055	1.0238	−40.86 (0.25)	−42.90	−2.02 (45.3)
0.19	1.0690	−43.89 (0.24)	−45.39	−23.8 (37.5)

X, mole fraction; ρ, density; U, average potential energy; U_{exp}, experimental potential energy and P, average pressure. All values are simulation averages with standard deviations in brackets. Both simulations were performed at an average temperature of 298.1 ± 5.8 K.

mole fraction concentration, the simulation box contained 95 DMSO molecules and 405 water molecules. The initial configurations of the two simulations were obtained from NVT Monte Carlo simulations using the program POLYMC [35], after 3 million trial moves at 298 K. During the MD simulations, the Nose-Poincaré thermostat [36] was used to maintain the required temperature, with a temperature mass parameter of 100 kJ mol^{-1} ps^{-2}. A time step of 2.5 fs was used in both simulations. A period of 25 ps (10 000 time steps) was allowed for equilibration, followed by an additional period of 1.0 ns (400 000 time steps) for the collection of data. The trajectories generated were stored every 25 fs.

3. Results and discussion

In this paper we will analyse the hydration structure of DMSO aqueous solutions at 298 K at two different concentrations: 0.055 and 0.19 mole fraction. We wish to study the effect of concentration (density) on the structure of solutions of DMSO in water. Initially, we will describe the pair correlation functions, which reveal the average structure of the solutions. We will then analyse the structure of water in different regions of the solution and its hydrogen-bonded network.

3.1. Thermodynamic properties

Table 1 presents a summary of the thermodynamic properties of the simulations. In both simulations, the experimental densities were used. The simulated solution at $X = 0.055$ has a small negative pressure, indicating that the simulated and experimental densities match closely. As the concentration is increased to $X = 0.19$, the average pressure drops further, revealing that the simulated density is likely to be slightly higher than the experimental one. The potential energy of the system decreases as the concentration rises, since the density of the solution increases. The potential energy results obtained for the mixture of TIP4P water with P2 DMSO from this study are found to be comparable to those predicted previously by Chalaris and Samios with both SPC water and P2 DMSO and TIPS2 water and P2 DMSO in their previous MD study [31]. Note also that in the case of the calculated pressure the results obtained
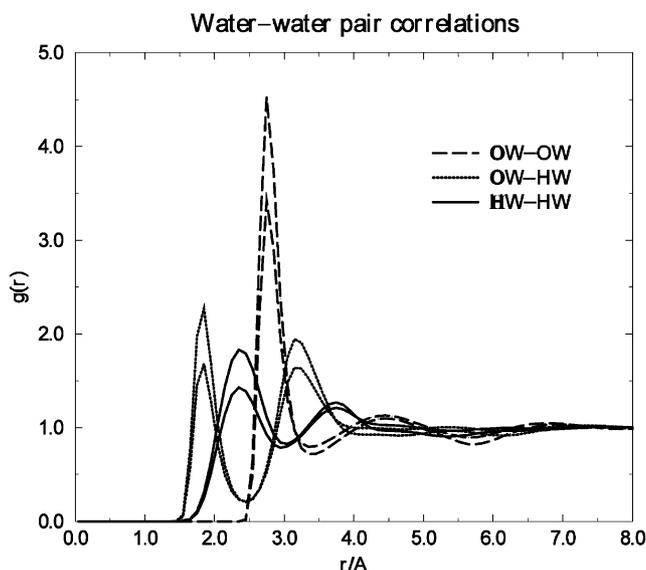
Water–water pair correlations

Fig. 1. Water–water pair correlation functions.

OS–water pair correlations

Fig. 2. OS–water pair correlation functions.

with TIP4P model are found to be slightly better compared to other water models.

3.2. Solution structure

Pair correlation functions $g(r)$ were computed during the 1.0 ns data collection periods. Fig. 1 shows all pair correlations for the intermolecular water sites: OW–OW, OW–HW and HW–HW. No graphical distinction is made between the two densities simulated, but the higher concentration of DMSO induces water in the solutions to become more structured, as revealed by a significant sharpening of the peaks. Even at the lowest concentration of $X=0.055$, the height of the peaks reveals an enhancement of water structure with respect to bulk water [37,38], as reported earlier [25,26,28–30]. Fig. 2 shows the two pair correlations between the oxygen in the sulfonyl group of DMSO and the water sites: OS–OW and OS–HW. Here too the increase in DMSO concentration produces a significant sharpening of the peaks of the pair correlations. We can also see that the pair correlations at both concentrations show that water molecules establish a linear hydrogen bond to the OS atom in DMSO, as the first peak in the OS–HW $g(r)$ is observed at a distance of 1.55 Å, while the first peak in the OS–OW $g(r)$ is observed at a distance of 2.55 Å. At these concentrations of DMSO, it is to be expected that the structure of the solutions corresponds to the existence of predominant 1DMSO:2H$_2$O aggregates [25,26,30].

Fig. 3 shows the two pair correlations between the methyl groups of DMSO and the water sites: Me–OW and Me–H. We can also see here that an increase in DMSO concentration induces an enhanced structuring
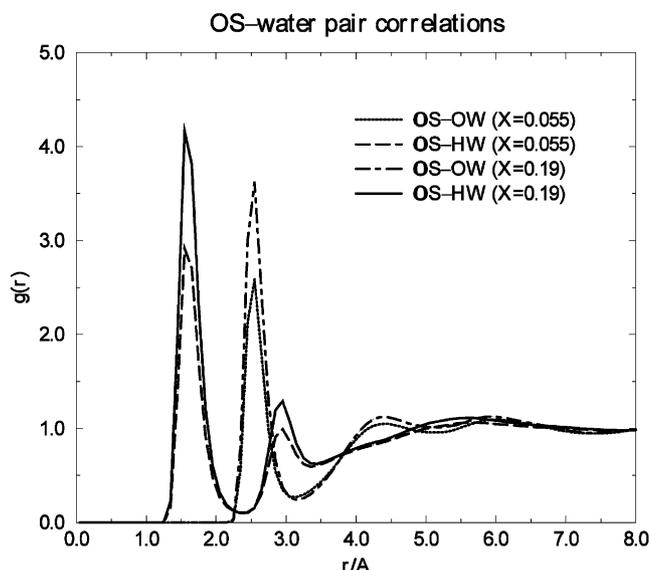
of water around such non-polar groups, as revealed by a sharpening of the peaks of the pair correlations. All the first peaks have similar positions, indicating a nearly tangential arrangement of water molecules around the methyl groups, as was reported earlier for the methyl groups of ethane in water [37]. Such a geometric arrangement around non-polar groups is characteristic of 'hydrophobic' hydration, allowing for water–water hydrogen bonds to be maintained albeit at an entropic cost.
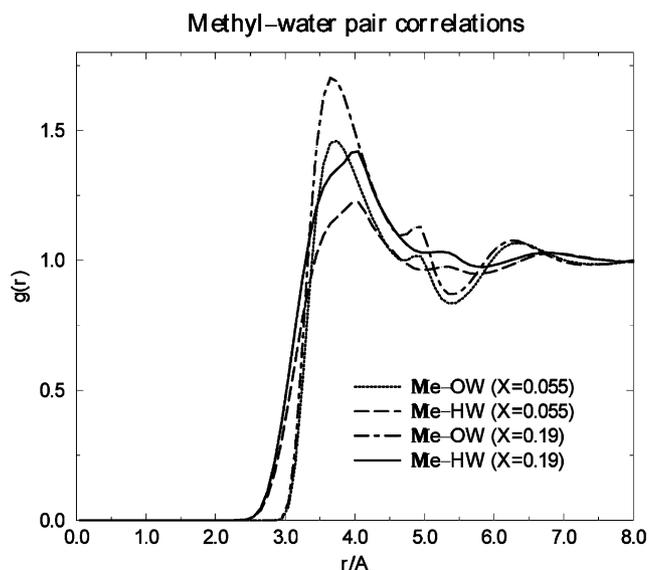
Methyl–water pair correlations
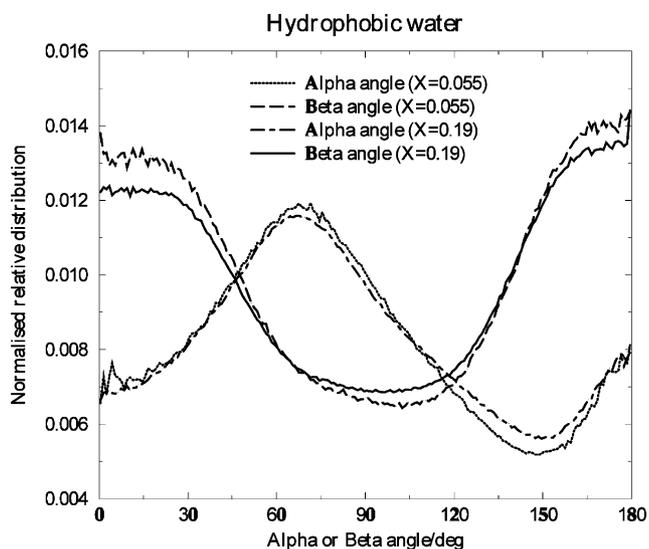

Fig. 3. Me–water pair correlation functions.

Fig. 4. α(alpha)- and β(beta)-angle distributions at $X = 0.055$ and $X = 0.19$ for 'hydrophobic' water molecules.

3.3. Water structure

The above results suggest that water molecules can establish an effective hydrogen-bonded network around the DMSO molecule. We thus decided to look at the orientational correlations between water molecules in the hydration shell of the Me ('hydrophobic' water) and OS ('hydrophilic' water) groups of DMSO. The vector that joins either the methyl or OS groups of DMSO to the water oxygen (OW) subtends an angle α with the water dipole moment vector and an angle β with a vector perpendicular to the H–O–H molecular plane.

Fig. 4 shows the normalised distributions of the α- and β-angles for 'hydrophobic' water at the two concentrations studied. The peaks at approximately 70° for the α angle and the preferred nearly parallel/antiparallel orientations of the β-angle correspond to a nearly tangential orientation of water molecules in the first hydration shell, as already discussed in our analysis of the Me–water pair correlations. Such arrangement in the vicinity of a non-polar group allows water molecules to straddle the surface of the group and retain nearly tetrahedral hydrogen-bond coordination [37–39]. An increase in the concentration of DMSO from 0.055 to 0.19 mole fraction produces a slight flattening of the distributions, suggesting that the enhanced structuring of water in the vicinity of the methyl groups is not necessarily paralleled by a more geometrically-ordered arrangement of water molecules.

In the case of the 'hydrophilic' water molecules, Fig. 5 shows that the α- and β-angle distributions indicate the existence of a defined solvation pattern around the sulfonyl group, consistent with hydrogen-bonding between this group and the neighbouring water mole-

cules. These angular distributions are consistent with the oxygen of the sulfonyl group accepting nearly linear hydrogen bonds from neighbouring water molecules, as expected [29]. An increase in DMSO concentration seems to indicate that there is a sharpening of the distributions, although the noise level is high. This reveals that the hydrogen-bonded DMSO–water aggregates are strongly held together and that the orientational preferences of such aggregates are enhanced as the concentration of DMSO increases from 0.055 to 0.19 mole fraction.

3.4. Hydrogen-bonding structure

We also performed an analysis of the structural properties of the hydrogen bonds of water molecules in the vicinity of the 'hydrophobic' (Me) and 'hydrophilic' (OS) groups of DMSO. This analysis was carried out only on those water molecules in the first hydration shell of the above groups, as defined by the position of the first minimum in the previously calculated pair correlation functions. All remaining water molecules were defined as bulk water. It is important to mention that at a DMSO concentration of $X = 0.055$ there is an average of just over 18 water molecules in the bulk environment, while at a concentration of $X = 0.19$ the average is less than 0.3 (hence reported structural properties have lower statistical significance and are shown for completeness). Water molecules were considered for possible hydrogen-bonding if their oxygens were $\leqslant 3.5$ Å apart [37,38,40]. The hydrogen bond between two such neighbouring water molecules was the one having the minimum OW⋯HW distance (*hydrogen-bond length*) among the four possible combinations of intermolecular OW⋯HW distances. Accordingly, a
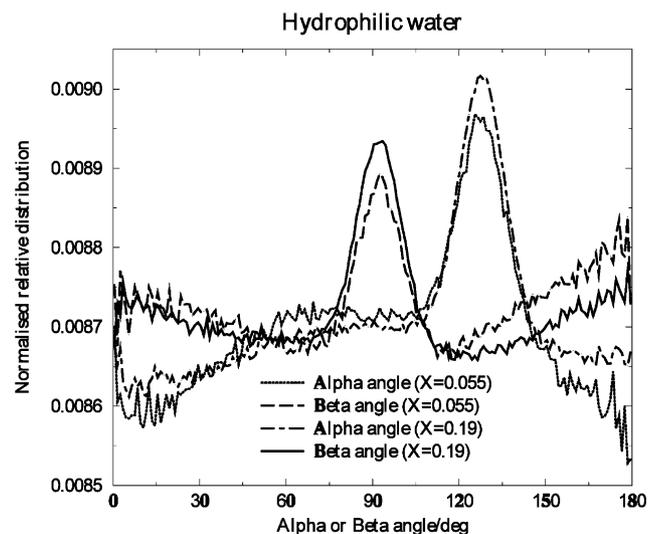

Fig. 5. α(alpha)- and β(beta)-angle distributions at $X = 0.055$ and $X = 0.19$ for 'hydrophilic' water molecules.

hydrogen-bond angle was then defined as the angle formed between the OW–HW bond vector of one water molecule and the intermolecular OW···HW hydrogen-bond vector with another water molecule. Finally, a hydrogen bond was defined to exist if it had a maximum length (H···O) of 2.5 Å and a hydrogen-bond angle between 130° and 180°. Within this definition, 'strong' hydrogen bonds are shorter in length and closer to a linear geometry (an angle of 180°). In the following analysis, hydrogen bonds made between water molecules of a different category (bulk, 'hydrophilic' or 'hydrophobic') are taken into account twice: once for each water category.

We have observed that as the DMSO concentration increases, bulk water shows no changes in the distribu-
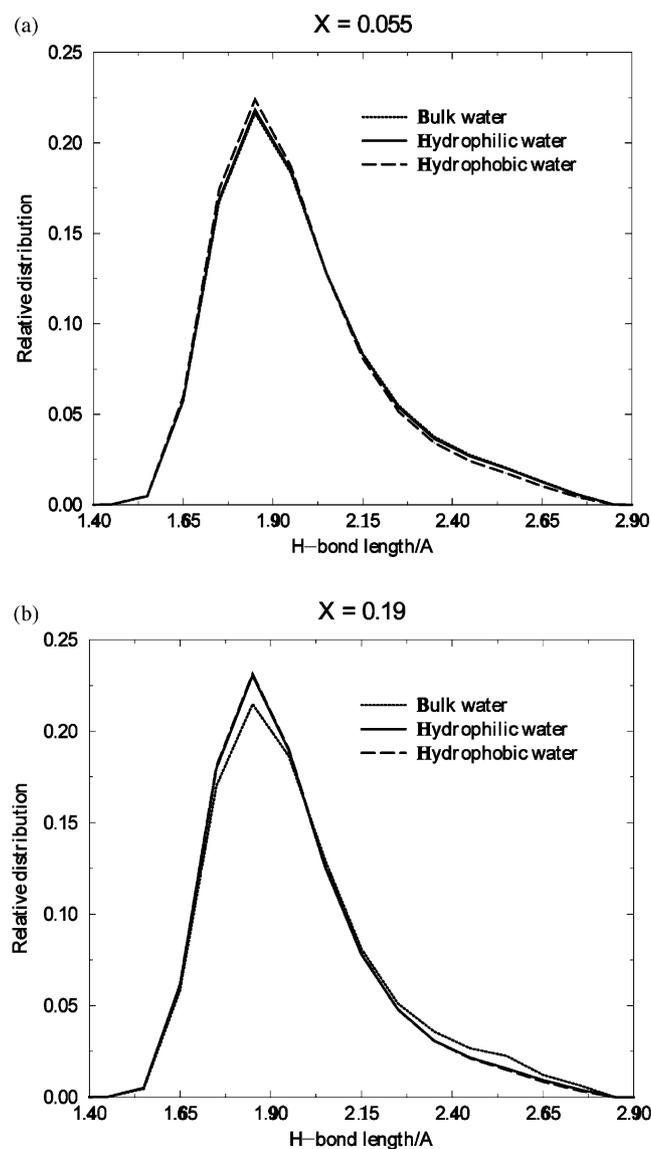
(a)

Fig. 6. Hydrogen-bond length distributions for all kinds of water molecules: (a) at $X = 0.055$ and (b) at $X = 0.19$.
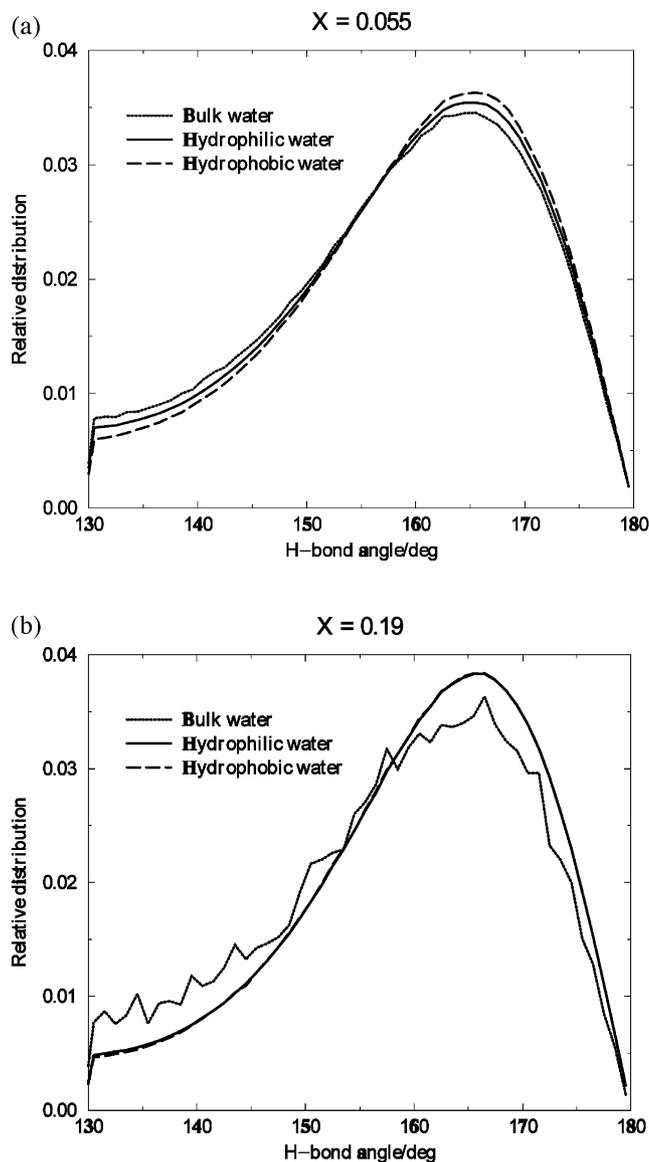
(a)

Fig. 7. Hydrogen-bond angle distributions for all kinds of water molecules: (a) at $X = 0.055$ and (b) at $X = 0.19$.

tion of its hydrogen-bond lengths, while there are some subtle changes for 'hydrophilic' and 'hydrophobic' water molecules, as seen in Fig. 6a and b. For both 'hydrophilic' and 'hydrophobic' water, the increase in DMSO concentration produces a sharpening of their distributions (which become nearly indistinguishable), indicating a slight shortening of their average hydrogen-bond lengths. The most likely water–water hydrogen-bond length of approximately 1.8 Å remains the same at both DMSO concentrations. As a consequence, when comparing the different kinds of water molecules, an increase in DMSO concentration induces 'hydrophilic' and 'hydrophobic water molecules to exhibit a slight enhancement of their structure (more short, strong hydrogen bonds).

Table 2
Average numbers of hydrogen bonds

X	Nhb (bulk)	Nhb ('hydrophilic')	Nhb ('hydrophobic')
0.055	3.78257 (0.17985)	3.54668 (0.04056)	3.24932 (0.14240)
0.19	3.84211 (0.71487)	2.85280 (0.04699)	2.30477 (0.11255)

X, mole fraction; Nhb, average number of hydrogen bonds (standard deviations in brackets).

The increase of DMSO concentration has a similar effect on the average hydrogen-bond angle distributions of the different kinds of water molecules, as can be seen in Fig. 7a and b. As the DMSO concentration increases, 'hydrophilic' and 'hydrophobic' water molecules exhibit a sharpening of their distributions, while bulk water seems unaltered. Furthermore, the most likely hydrogen-bond angle goes from 165° at $X = 0.055$ to 166/167° at $X = 0.19$. We can then conclude that, when comparing the different kinds of water molecules, an increase in DMSO concentration enhances the structure (more linear, strong hydrogen bonds) of 'hydrophilic' and 'hydrophobic' water.

The properties of the hydrogen-bond lengths and angles of the various kinds of water molecules in the solutions reveal that the polar OS group of DMSO acts as a strong hydrogen-bonding group, promoting an enhancement in the structure of water. This view is created by the presence of shorter and more linear hydrogen bonds between water molecules in the vicinity of this group. The non-polar Me groups of DMSO produce a further enhancement of the structure, as hydrogen bonds between water molecules are even longer and more linear than in the bulk of the solution. We can conclude that both the 'hydrophilic' and 'hydrophobic' groups of DMSO are seen to enhance the structure of water. An increase in DMSO concentration does not modify this picture; however, 'hydrophilic' and 'hydrophobic' water are equally enhanced in structure by DMSO at $X = 0.19$.

We also computed the average number of hydrogen bonds (Nhb) for the different kinds of water molecules, as in earlier studies of non-polar substances in water [40–42]. The results at each of the two DMSO concentrations for the different aqueous regions can be seen in Table 2. We can see that as the DMSO concentration increases, the average Nhb increases for bulk water, indicating that fewer hydrogen bonds are broken at $X = 0.19$. By contrast, as the DMSO concentration increases, the average Nhb decreases for both 'hydrophilic' and 'hydrophobic' water, the effect being slightly more pronounced on the latter. These observations reveal that increasing the DMSO concentration, which effectively depletes the system of bulk water molecules, decreases as a consequence the average Nhb in both 'hydrophilic' and 'hydrophobic' water. This is explained by noting that counting the Nhb in these regions of the solutions also takes into account hydrogen bonds made across to the remaining bulk of the solutions, where there are now significantly fewer water molecules.

4. Conclusions

The MD simulations of DMSO in water that we have carried out at concentrations of 0.055 and 0.19 mole fraction at 298 K reveal an enhancement in the structure of water, which is more pronounced at the higher DMSO concentration. At both concentrations there is a well-defined hydration structure around the OS group of DMSO, which establishes well-defined directional hydrogen bonds with surrounding water molecules. The formation of such hydrogen bonds compensates for the loss of some hydrogen bonds of these water molecules with other neighbouring water molecules. Increasing the concentration of DMSO depletes the solution of bulk water molecules, decreasing the number of water molecules in the vicinity of both 'hydrophilic' and 'hydrophobic' water molecules and decreasing the average Nhb of the latter two, but increasing the strength of the hydrogen bonds between the OS group of DMSO and water.

The formation of an ordered hydration structure around the Me groups of DMSO provides clear evidence of 'hydrophobic' hydration. Increasing the concentration of DMSO enhances the structure of water around the Me groups of DMSO, with stronger water–water hydrogen bonds. There is, however, no evidence of enhanced geometrical ordering.

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