Polarizable force field for water-dimethyl sulfoxide systems: II properties of mixtures by molecular dynamics simulations

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ARTICLE INFO

ABSTRACT

A consistent polarizable force field for dimethyl sulfoxide (DMSO) with the TIP4P-FQ (fluctuating charge) water model was developed to explore the properties of pure DMSO liquid and the DMSO–water mixtures in this work. The DMSO–water mixtures at a range of concentrations of DMSO were selected to explore the unusual properties of them at 298 K and 1 atm. The radial distribution functions of neat DMSO liquid from the simulations with the current model are more excellently consistent with data from a neutron diffraction experiment than the additive models. More reasonable results for the static (radial distribution function, density, excess volume, heat of vaporization and mixing heat) and dynamic properties (lifetime of hydrogen bond, reorientational relaxation time and self-diffusion coefficient) of the mixtures over a range of composition were obtained by the current model and parameters than the previous additive models. The interaction between methyl hydrogen and water oxygen is mainly characteristic of weak hydrogen bond interactions and weaker than that between methyl hydrogen and DMSO oxygen. The hydrated methyl is more preferred than the methyl–methyl association. The enhanced structure of water and DMSO within the first shell is due to decrease of the water number in the hydrogen bond chain of DMSO–$n$water–DMSO. The distributions and fluctuations of dipole moment can well reflect the polarization effect and the microscopic configures in the mixtures. The static dielectric permittivities of the DMSO–water mixtures are in well agreement with the corresponding experimental values.

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1. Introduction

Aqueous DMSO solutions have been paid more attention, not only because of the extensive applications as a cryoprotective agent [1], or in studies involving the folding or unfolding of proteins [2], membrane permeability or cell fusion [3,4], as well as a potential drug [5,6], but also the microscopic mechanism behind them. For the simple mixtures of DMSO and water, a combination of strong hydrogen bond and hydrophobic interactions leads to remarkable non-ideal physical properties, such as decreased density, longer rotational reorientation relaxation times, lower diffusion coefficients, and negative changes in molar enthalpy and volume [7–15]. Additionally, the freezing point shows strong concentration dependence. As an example, a solution of 1 mol of DMSO in 3 mol of water has a very low freezing point (−70 °C), compared to 18.6 °C for DMSO and 0 °C for water in their neat liquids [16]. The nature of the unusual physical properties of DMSO–water mixtures can typically involve the hydrogen bond interactions and the hydrophobic associations between molecules. The glass state

theories provide us a new tool to uncover the mechanism in them at low temperature or supercooled state [16,17]. Recently, more efforts have been taken to study the special dynamical and structural properties as a function of composition and temperature with the experimental and theoretical methods. Computer simulation experiments have been carried out to study the detailed properties of DMSO–water solutions extensively.

Neutron diffraction experiment [18–21] shows that the characteristic tetrahedral water structure is still preserved at concentrations $2H_2O$:1DMSO and $4H_2O$:1DMSO and the percentage of water molecules that are hydrogen bonded to themselves in this manner is substantially reduced compared to pure water. DMSO molecules destroy the extension of the tetrahedral networks in water beyond the first coordination shell. The previous simulations by Vaisman and Berkowitz [22] show a more strengthened correlation between the water–water pair at higher DMSO concentrations, as well as the existence of $2H_2O$–1DMSO hydrogen-bonded aggregates at dilute solutions of DMSO. Recent Car-Parrinello simulations [23] of a DMSO–water solution at a concentration of 0.25 mol fraction revealed the existence of transient $3H_2O$:1DMSO aggregates within a complex hydrogen-bond network. These simulations also showed that hydrogen atoms of water molecules very close to the methyl groups of

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DMSO tend to orient hydrophilically (away from the hydrogen atoms of the methyl groups), although the general orientation of water molecules in the vicinity of the methyl groups was hydrophobic [24]. Borin and Skaf [25] have recently performed a series of MD simulations across the entire DMSO composition range in SPC/E water. The results revealed that the $2H_2O$–$1DMSO$ hydrogen bond structures predominate in water-rich mixtures (DMSO mole fraction <50%). A $1H_2O$–$2DMSO$ aggregate and predominates in DMSO-rich mixtures (an association of a pair of DMSO molecules through their oxygen atoms linked by one water molecule). An NPT simulation of a $3H_2O$:$1DMSO$ mixture at ambient conditions [26] confirmed the existence of $2H_2O$–$1DMSO$ aggregates but not of $3H_2O$–$1DMSO$ aggregates. Another typical configuration was found, consisting of two DMSO and three water molecules, in which a water molecule was bridged with two DMSO molecules. Ultrasonic measurements [27], chemical reactivity measurements [28], and NMR [29] indicated even stronger bonding affinity of water molecules to DMSO than to water itself. DMSO molecules form intensive hydrogen bonds with water molecules above $x_{DMSO}=0.1$ [30]. Another experiment shows the pronounced contrast in structure of the water of hydration around DMSO, with the oxygen atom strongly hydrogen bonded, but the methyl groups surrounded by a loose, hydrogen-bonded cage of water molecules [20]. Further, dipolar interactions were not found to play a relevant role in the interaction with water [31]. The simulation results [22] suggested the existence of a hydrophobic association of DMSO molecules. A contrary conclusion was obtained by Luzar et al. [19], who reported that no evidence of hydrophobic interactions between the methyl groups of DMSO was found. This phenomenon is also proved by IR spectroscopy of the OH and OD bands [15,32] and other previous experiments [33,34]. Mancera et al. [35,36] found no evidence for a temperature-dependent hydrophobic interaction between these groups at a concentration of 0.055 mol fraction at 298, 318 and 338 K and that the hydrophilic hydration of DMSO dominates over any hydrophobic effects as the temperature is increased.

Both the translational and rotational motions, evaluated by NMR [37–40] and dielectric relaxation [41], showed a considerably slower dynamics compared to the motions of pure liquids with a minimum at the composition $2H_2O$:$1DMSO$. The hydrogen bond lifetimes of DMSO–water are longer than water–water hydrogen bonds, which in turn are alive longer than those in pure water [18,19]. At ambient conditions, the proton motions associated with H-bond lifetimes point to dynamics that are 5 to 10 times slower for water–water and water–DMSO hydrogen bond in the mixture, compared to pure water, respectively, which is due to the reduced likelihood of the presence of free hydrogen bonding sites [42]. In the mixture at the composition $2H_2O$:$1DMSO$, the proton librational motion is no longer be the determining mechanism for the H-bond breaking [21]. The previous simulations [23,25,43,44] show that the mobility of the DMSO and water molecules is lower in the mixtures than in the pure liquid. The calculated diffusive reorientation of the DMSO and water molecules slows down in going from the pure liquids to the mixtures and subsequently speeds up at higher mole fractions. Too longer relaxation times for the water and DMSO molecules at intermediate and high concentrations of DMSO were presented [25,43]. The observed minima in mixing heats, mixing volumes and diffusion coefficients and maxima in the rotational correlation time and viscosity are shifted from $x_{DMSO}=0.33$ in the experiments to about $x_{DMSO}=0.50$ composition in their simulations [44]. In the simulations of DMSO–water mixtures using the P2-SPC/E model by Borin and Skaf [25], the non-ideal minima of reorientation correlation times locates at $x_{DMSO}=0.35$ for the DMSO molecules and $x_{DMSO}=0.5$ for the water molecules. From simulations using the P2-SPC, P2-SPC/E, and P2-TIPS2 models, Chalaris and Samios [23] also reported trends in the self-diffusion of DMSO and water. For P2-SPC, the observed mobility of the DMSO molecules agreed nicely with experiment. As a whole, the previous simulations, to a higher or lesser degree, yield reasonable descriptions of DMSO–water solutions.

The previous quantum chemistry study [46] shows that the minimum energy or optimized structures of the DMSO–water clusters were biased by the united atom force field (the methyl carbon and hydrogen atoms of DMSO molecule looked as one group) in the order of about 5 kJ mol^{-1}. In addition, the authors also pointed out that the assumption of pairwise additivity and the united-atom ansatz were not suitable to describe the interactions between the molecules in the DMSO–water clusters and there is a strong connection between methyl group favored structures and many body effects. The many-body effects amount to 40 kJ mol^{-1}. They think that most MD simulations are not able to account for all other $1DMSO$–$3H_2O$ clusters, because pairwise additivity is assumed. Car-Parrinello molecular dynamics simulations [47] show that a large increase of the local dipole moment of DMSO from 3.97 to 7.39 D was observed. The methyl water interaction became more important upon solvation. The methyl groups played an important role in determining the properties of DMSO–water mixtures [48]. Too low static dielectric permittivity of DMSO–water mixtures obtained from the standard force fields also meant that the additivity model could not reasonably describe the dielectric environment of solutions [25,43,49]. For the previous additive models (RS model [50], P2 (P1) models [19], VG model [51], OPLS potential [2], GROMOS96 model [43], and the flexible CHARMM model [52]), none of them could accurately reproduce the radial distribution function between heavy atoms at the media range from the neutron scattering experiments [19]. In order to improve the reasonability of model, a polarizable all-atom model is recommended to be developed for the simulation of DMSO–water mixtures.

The polarizable dipole (multipole) model [53–55], fluctuating charge model [56–59], and drude shell (dispersion oscillator) model [60] have been developed to treat the polarizable effects. In this paper, a flexible polarizable force field for DMSO was developed and applied to the small molecule cluster and the bulk liquids. The fluctuating charge model proposed by Rick et al. [56] was adopted to incorporate polarizable effects. This fluctuating charge model derived from the electronegativity equalization approach on the basis of the DFT theory [61]. The charge-related parameters in this work were fully extracted from *ab initio* calculations, which could avoid the problem of the insufficient experimental data. The TIP4P-FQ water model has been shown to represent liquid water at 298 K and 1 atm well, giving fairly accurate values for the energy, pressure, diffusion constant, the dielectric constant and the pair correlation function [56]. The model was found to reproduce the experimental neutron scattering data on pure water [62]. The potential has been successfully applied to many systems [63–71], but there were no publications about DMSO systems under it. In order to be consistent with the well-defined TIP4P-FQ water force field, the average TIP4P-FQ water dipole in pure liquid (at 298 K and 1 atm) used as the external perturbation field, are positioned at different distances and orientation of gas-phase DMSO molecule. This is a little different from the previous procedure [60]. Fluctuating charge model is a unique field- and conformation-dependent method. It can reflect the field-induced redistribution of electrons that results in instantaneous changes to atomic charges and to the potential energy surface that defines intramolecular motion. This is very important for the strong hydrogen bond dynamics with the flexible model. The consistent FQ model was employed to explore the physical properties and the polarized effects of pure DMSO liquid and DMSO–water mixtures.

The paper is organized as follows. Sections 2 and 3 outline the methods and parameterization procedure we have used to arrive at the polarizable and flexible model and necessary parameters for DMSO. Section 4 analyzes the solution structures, thermodynamic, and dynamic properties, concluding remarks are given in Section 5.

2. The fluctuating charge model for DMSO

The fluctuating charge (FQ) model has been discussed in detail elsewhere [56–59,61]. In this section, we briefly introduce the FQ