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Thermodynamic and Structural Properties of Methanol-Water Solutions Using Non-Additive Interaction Models

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Abstract

We study bulk structural and thermodynamic properties of methanol-water solutions via molecular dynamics simulations using novel interaction potentials based on the charge equilibration (fluctuating charge) formalism to explicitly account for molecular polarization at the atomic level. The study uses the TIP4P-FQ potential for water-water interactions, and the CHARMM-based (Chemistry at HARvard Molecular Mechanics) fluctuating charge potential for methanol-methanol and methanol-water interactions. In terms of bulk solution properties, we discuss liquid densities, enthalpies of mixing, dielectric constants, self-diffusion constants, as well as structural properties related to local hydrogen bonding structure as manifested in radial distribution functions and cluster analysis. We further explore the electronic response of water and methanol in the differing local environments established by the interaction of each species predominantly with molecules of the other species. The current force field for the alcohol-water interaction performs reasonably well for most properties, with the greatest deviation from experiment observed for the excess mixing enthalpies, which are predicted to be too favorable. This is qualitatively consistent with the overestimation of the methanol-water gas-phase interaction energy for the lowest-energy conformer (methanol as proton donor). Hydration free energies for methanol in TIP4P-FQ water are predicted to be -5.6 ± 0.2 kcal/mole, in respectable agreement with the experimental value of -5.1 kcal/mole. With respect to solution micro-structure, the present cluster analysis suggests that the micro-scale environment for concentrations where select thermodynamic quantities reach extremal values is described by a bi-percolating network structure.

Keywords

methanol; water; aqueous solutions; polarizable force field; fluctuating charge; non-additive interactions

I. Introduction

As an industrial solvent, methanol plays a significant role in numerous chemical processing applications; its unique properties over a wide range of thermodynamic states are exploited in supercritical separations. Liquid methanol is fundamentally interesting from a chemical physics perspective as it is an exotic analogue to water in which a methyl group replaces a

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single proton. This minor substitution allows for rather significant differences between these two hydrogen-bonding liquids. For instance, in the bulk, methanol coordinates as clusters of chains or small rings as opposed to the well-known tetrahedral, network structure of bulk water¹; at its liquid-vapor interface, methanol displays surfactant-like behavior^{2,3}.

Mixtures of methanol and water are equally interesting systems, both from a practical and theoretical perspective, in part due to the rich microscopic structure and dynamics resulting from the bi-functional nature of methanol and the competitive formation of hydrogen bonds. Consequently, the investigation of these systems vigorously continues in the areas of both experiment and theory¹. For example, recent neutron diffraction data^{1,4} coupled with molecular dynamics simulation (for model fitting) indicates an extended micro-structure comprised of bi-percolating networks for *both* water and methanol within a limited range of methanol concentrations. Interestingly, these structures correspond to regimes in which various transport and thermodynamic properties reach extremal values¹. These anomalous properties are thus viewed as arising from the microstructure, or microscopic immiscibility, exhibited by methanol-water solutions.

Complementing experimental efforts, molecular simulations of methanol-water solutions have contributed much to our understanding of these systems. In terms of bulk structure, early Monte Carlo studies investigating infinitely dilute alcohol systems^{1,5-7} found support for the classic Frank and Evans model⁸ of an enhanced “ice-like” water cage surrounding the methanol methyl moiety. More recent studies using molecular dynamics simulations and differing interaction models have presented evidence suggesting that the water structure in the vicinity of alcohol hydrophobic groups is not significantly perturbed⁹⁻¹². With advancing computational resources, *ab initio* molecular dynamics studies^{13,14} have begun to shed new light on the microstructure in these systems, again indicating that the presence of methanol does not perturb the local water structure in the infinite dilution limit while also suggesting the formation of a bi-percolating network^{13,15,16}.

Until recently, molecular simulations have employed fixed-charge models to treat electrostatic interactions, generally with a mean-field approximation of the *fixed* charges to account for non-additive electronic contributions. Despite the success of these potentials, the lack of explicit treatment of electronic polarization limits the physics one can study and observe. Classical methanol force fields have only recently incorporated explicit electronic induction effects. Some of the earliest polarizable methanol models have addressed bulk and interfacial thermodynamic properties. Dang *et al.* developed a dipole polarizable force field of a six-site methanol molecule with fixed charges and a molecular polarizability placed on the oxygen atom to allow for the induction of dipoles via an iterative self-consistent procedure¹⁷. More recently, their models have been employed to study liquid-vapor phenomena and interfacial properties of methanol-water solutions¹⁸. Gao *et al.* have presented a dipole polarizable methanol force field (simultaneously parameterized with other alcohols) in much the same spirit as the Dang model¹⁹. Caldwell *et al.* contributed an additional dipole polarizable model of methanol representing accurately the density, vaporization energetics at 298K, and diffusion coefficient²⁰. Finally, Patel *et al.*^{3,21} have recently reported two new alcohol potentials for methanol and ethanol based on the charge equilibration (fluctuating charge) formalism.

Unfortunately, studies of aqueous alcohol solutions using polarizable, or non-additive potentials, are rare due to the lack of systematically developed models available. Recently, Yu *et al*²² reported a polarizable force field for methanol-water solutions; the authors discussed bulk and solution properties, emphasizing the ability of their polarizable model to reproduce the experimental concentration dependence of mixture dielectric constants. Noskov *et al*²³ have studied ethanol-water solutions using a Drude-oscillator model for ethanol and the SWM4-DP²⁴ water model. Other models such as SIBFA²⁵ and TCPE²⁶ have been introduced, but have not been extensively applied to long-time molecular dynamics simulations.

In this article, we describe thermodynamic, structural, and dynamical properties of methanol-water solutions based on molecular dynamics simulations using polarizable force fields for water-water, water-methanol, and methanol-methanol interactions. With few non-additive models in the literature parameterized to simultaneously model both pure liquids and solutions, we believe it is important to characterize the successes and deficiencies of the physics predicted by these polarizable models to both improve the models and to aid in the future development of other multi-component system models. These efforts are in the spirit of the early development of fixed-charge force fields, which have resulted in today's state-of-the-art non-polarizable force fields. The next section details the models employed as well as simulation protocols. Section III discusses results of bulk liquid solution simulations including properties such as density, excess mixing enthalpy, liquid solution structure as demonstrated by partial radial distribution functions, self-diffusion coefficients, dielectric constants, and bulk solution molecular dipole moment distributions. Section IV presents summary and conclusions.

II. MODEL AND METHODS

A. Water and Methanol Force Fields

The water model adopted for this work is the TIP4P-FQ model developed by Rick *et al*. The methanol model is the charge equilibration model developed by Patel and Brooks³. Both pure liquid force fields are based on the charge equilibration formalism to include explicit electronic polarization, as will be briefly discussed next.

The charge equilibration model has been applied to various systems over the last decade^{3,21,27–32}. The method derives from the density functional theory of atoms in molecules as formulated by Yang and Parr³³. More fundamentally, the method is founded on Sanderson's idea of electronegativity equalization^{34,35}. In a molecule, this translates to the redistribution of charge among constituent atoms so as to equalize the electronegativity (chemical potential) at each point. The reader is referred to the literature for more detailed discussions^{30,31,33,36–40}.

In the charge equilibration formalism, the electrostatic energy of an N -atom molecule in vacuum is:

$$E_{electrostatic} = \sum_{i=1}^N \chi_i^0 Q_i + \frac{1}{2} \sum_{i=1}^N \sum_{j=1}^N \eta_{ij} Q_i Q_j + \sum_{i=1}^N \Phi_i Q_i \quad 1$$

The χ 's are atom electronegativities (formally the Mulliken electronegativities) related to the chemical potential of an electron gas surrounding a nucleus by,

$$\mu_i = \frac{\partial E}{\partial N} = -\chi_i^0 = -e \frac{\partial E}{\partial q_i} \quad 2$$

The η 's are the atom hardnesses. These values represent a 'resistance' to electron flow to/from an atom. The last term in equation 1 represents contributions from an external potential.

Homogeneous hardness values, η_{ii} , are taken from the work of Patel and Brooks³. Heterogeneous elements, η_{ij} , are derived from the homogeneous values based on the combining rule:

$$\eta_{ij}(R_{ij}, \eta_i, \eta_j) = \frac{\frac{1}{2}(\eta_i + \eta_j)}{\sqrt{1.0 + \frac{1}{4}(\eta_i + \eta_j)^2 R_{ij}^2}} \quad 3$$

where R_{ij} is the separation between atoms (or more generally *sites*) i and j . This local screened coulomb potential has the correct $1/r$ limiting behavior for separations greater than about 2.5 Å. This interaction is computed for 1–2, 1–3, and 1–4 sites (sites included in bonds, angles, and dihedrals); sites separated by 5 or more sites interact via a standard Coulomb interaction. In the case of interacting molecules, the interaction between sites on different molecules is also of the Coulomb form. Finally, any external potential is included in the ϕ term of equation 2. With respect to charge dynamics, an extended Lagrangian formalism is used to propagate the charges in time with the constraint that the total charge on a molecule is conserved. The fictitious charge dynamics, analogous to wavefunction dynamics in Car-Parrinello (CP) type methods⁴¹, is determined by a charge 'mass' (adiabaticity parameter in CP dynamics). The units for this mass are (energy time² / charge²). The charges are propagated based on forces arising from the difference between the average electronegativity of the molecule and the instantaneous electronegativity at an atomic site.

The non-bond interaction is of the Lennard-Jones type (standard in the CHARMM⁴² implementation):

$$E(R) = \sum_{ij} \epsilon_{ij} \left(\frac{R_{min,ij}^{12}}{r_{ij}^{12}} - 2 \frac{R_{min,ij}^6}{r_{ij}^6} \right) \quad 4$$

where the summation runs over all non-bonded atom pairs. The water-water Lennard-Jones interactions are treated using the TIP4P-FQ water model as developed by Rick *et al*³². The methanol-methanol Lennard-Jones interactions are modeled using the charge equilibration model developed by Patel and Brooks³. Lennard-Jones *cross interactions* between water and

methanol are obtained via the Lorentz-Berthelot combination rule, applied here in order to maintain consistency with the CHARMM force field. We also permit the methanol to interact with water hydrogen atoms as in the original CHARMM fluctuating charge force field as developed by Patel and Brooks²⁷ in order to maintain consistency in terms of the global development of a CHARMM polarizable force field for biomacromolecules. Intra-molecular interaction potentials (bond stretching, angle bending, dihedral rotation) are retained from the non-polarizable CHARMM27 (C27) force field. Table 1 shows the electrostatic and van der Waals parameters for the current models.

B. Simulation Details

Bulk solution simulations were performed using systems of varying numbers of water and methanol molecules in cubic simulation cells; systems were generated from pre-equilibrated pure liquid systems. System sizes varied with the concentration modeled; Table 3 lists the molecule numbers used for each concentration. A Verlet leapfrog integrator with timestep of 0.0005 picoseconds (0.5 femtoseconds) generated the trajectories in the constant pressure-temperature ensemble (NPT). Constant pressure was maintained via a Langevin piston method⁴³ and a constant temperature of 298K was maintained with a Hoover thermostat⁴⁴. Non-bonded interactions were switched to zero via a switching function from 9 to 10 Å. Conditionally convergent long-range electrostatic interactions were treated using the Smooth Particle Mesh Ewald⁴⁵ method with 24 grid points in each dimension and screening parameter of $\kappa=0.35$. Charge degrees of freedom were maintained at 1 K using a single Nose-Hoover bath. Methanol and water charge degrees of freedom were assigned masses of 0.00007 and 0.000069 (kcal mol⁻¹ ps²)/e², respectively. Charge normalization was maintained over individual molecules with no intermolecular charge transfer; the size of the molecular units is of adequate spatial extent to limit molecular polarization to that dictated by Pauli exclusion in the condensed phase⁴⁶. To generate starting solution configurations, two equilibrated boxes of pure water and pure methanol were combined into a single simulation cell. An equilibration simulation for 1 nanosecond under constant temperature and pressure at 298K and 1 bar was performed on the combined system.

III. RESULTS AND DISCUSSION

IIIA. Gas-Phase Cluster Structure and Energetics

To provide a context for the interpretation of condensed phase results, we first consider the structure and energetics of gas-phase water-methanol clusters and compare to available *ab initio* calculations; we consider the cases with methanol as proton donor (PD) and proton acceptor (PA). For the dimer with methanol as proton donor (PD), we obtain an absolute water-methanol interaction energy of 4.64 kcal/mole and an oxygen-oxygen distance of 2.86 Å. With methanol as proton acceptor (PA), the dimer energy is 5.97 kcal/mole with an oxygen-oxygen distance of 2.76 Å. The dimer energies are within the range of reported values based on higher level *ab initio* calculations, though we find bond lengths are roughly 0.1–0.2 Å shorter than the *ab initio* values. For comparison, TABLE 2 shows results of the current model along with literature values for a variety of *ab initio* calculations. Aside from the systematic shift in the bond lengths to smaller values, the current polarizable force field appears to reasonably capture the gas-phase dimer energetics, particularly in light of the fact

that the cross interactions have not been built into the parameterization of either force field individually. Moreover, the relative gas-phase energetics of the two isomers (methanol as proton acceptor versus methanol as proton donor) is consistent with rotation-tunneling spectra⁴⁷ as well as in qualitative agreement with recent high-level *ab initio* calculations on methanol-water dimers⁴⁸.

IIIB. Bulk Solution Thermodynamic Properties

IIIB.1 Densities and Excess Mixing Enthalpies—We first consider bulk solution densities and excess enthalpies of mixing. Table 3 and Figures 1A and 1B show the computed densities and excess mixing enthalpies as well as experimental measurements and statistical uncertainties based on the current calculations. The excess mixing enthalpies are computed as²²:

$$\Delta H_{mix} = \frac{U_s - N_w U_w - N_m U_m + P(V_s - N_w V_w - N_m V_m)}{N_w + N_m} \quad 5$$

The U_a 's correspond to potential energies (including intramolecular contributions) of the relevant *pure* fluid, P is the pressure, the V_a 's are the total system volumes, the X 's are mole fractions and N 's are the numbers of molecules specifically used in the simulation. It is clear from Figure 1B that the current force field overestimates the enthalpic contribution to the water-methanol interaction relative to experimental values⁴⁹. This behavior is consistent with the energetics of the gas-phase PA dimer for which the binding is approximately 0.9 kcal/mol stronger than a value of 5.02 kcal/mol reported for recent high-level CCSD(T) calculations⁴⁸ (Table 3). A study of methanol-water solutions using the Charge on Spring (COS) polarizable force field²², interestingly, obtains mixing enthalpies that are *slightly less* favorable than experiment (though still in accord with experiment within the statistical uncertainty reported). This is somewhat counterintuitive as one would expect that condensed-phase many-body effects would dominate the interaction, leading to somewhat more attractive forces in the bulk. As for the predicted densities from this work shown in Figure 1A, we observe that, consistent with the overestimation of vacuum dimer interaction energies, solution densities are also higher than experiment⁴⁹ over the concentration range studied. The maximum density deviation from experiment occurs for $X_{MeOH}=0.5$.

IIIB.2 Free Energy of Hydration—To further assess the water-methanol interaction model, hydration free energies for the current methanol model in TIP4P-FQ water have been independently calculated using 1). standard umbrella sampling molecular dynamics simulations, and 2). thermodynamic integration. This serves to further characterize the CHARMM charge equilibration force field in terms of phase-transfer free energetics neglected in the original parameterization scheme^{3,27}. For the umbrella sampling calculations, a single methanol molecule was harmonically restrained at various positions along the z -axis of a cubic box of 216 TIP4P-FQ water molecules centered within a larger rectangular box; this geometry effectively simulates a bulk liquid in equilibrium with its vapor. Applying the Weighted Histogram Analysis Method (WHAM)⁵⁰ to the biased probability distribution of finding methanol at a given z -position in the system, we computed the equilibrium potential of mean force (PMF). Our protocol involved umbrella potentials

with harmonic force constant of $2 \text{ kcal mol}^{-1} \text{ \AA}^{-2}$ fixed at $0.5 \text{ \AA}$ increments beginning at the center of a box of 216 TIP4P-FQ water molecules. Each window was sampled for 2.5 nanoseconds; the statistical uncertainty in the local free energy estimate is obtained via a Monte Carlo bootstrapping procedure as discussed in Grossfield *et al.*⁵¹.

As an independent check, we have also computed the hydration free energy of a single methanol molecule using thermodynamic integration (TI). For this calculation, we use a two-step path in which we first electrostatically decouple the methanol molecule from the solvent before decoupling the van der Waals interactions. Double wide sampling is employed over 40 windows (20 for the electrostatic decoupling and 20 for the van der Waals decoupling) each representing 60 ps total time (20 ps of equilibration and 40 ps of sampling) as we decouple a single methanol molecule from a cubic unit cell containing 512 TIP4P-FQ water molecules. Equilibrium charge distributions on each molecule are reversibly sampled as we electrostatically decouple the solute. The separation shifted scaling method of Zacharais *et al.*⁵² is employed to ensure more uniform sampling along the van der Waals decoupling path.

For the current models, we obtain a TI hydration free energy of $-5.6 \pm 0.2 \text{ kcal/mol}$, slightly more negative than our PMF result of $-5.3 \pm 0.04 \text{ kcal/mole}$ and the experimental value of -5.1 kcal/mol . Again, the slightly more favorable solvation free energies are consistent with the enhanced interactions observed in the gas-phase dimer energies. That the total free energy of hydration is not egregiously in error with respect to experiment suggests that there is an entropic deficit upon mixing which effectively helps cancel the enthalpic contribution to the overall solvation thermodynamics. This idea can be connected to the formation of micro-scale structure to be addressed below in relation to a cluster analysis of these mixtures.

We finally note that the current model is competitive with published methanol models based on alternate formalisms for treating polarization. The Charge on Spring model of Yu *et al.*²² underestimates the hydration free energy for transfer into the COS/G2 water model, predicting a value of -4.7 kcal/mol ; this underestimation for the COS/M polarizable methanol model is consistent with the model's underestimation of the excess mixing enthalpies which are less favorable relative to experiment across the entire concentration range studied. The authors attribute this effect to a relatively low molecular polarizability leading to a lower effective dipole moment in the condensed phase and thus a concomitant reduction in methanol-water dipole-dipole contributions to the hydration free energy. Analogously, the enhancement of methanol dipole moments in solution (to be discussed below) leads to a more favorable hydration free energy.

IIIB.3. Dynamics—The diffusion coefficient of methanol and water is determined from the time dependence of the mean squared displacement at long times via the Einstein relationship⁴³:

$$D_{self} = \lim_{t \rightarrow \infty} \frac{1}{6t} \langle (r(t) - r(0))^2 \rangle \quad 6$$

where the average is taken over all molecules over the dynamics trajectory. Results from the current work are shown in Figure 1C (methanol) and Figure 1D (water). For pure methanol and water, the fluctuating charge force field predicts liquid diffusivities of $2.39 \times 10^{-5} \pm 0.07$ cm²/sec and 1.93×10^{-5} cm²/sec³⁷, respectively. The value for pure methanol is competitive with existing force fields and in good agreement with the experimental value of 2.42×10^{-5} cm²/sec⁵³. The pure TIP4P-FQ water self-diffusion constant is widely known to be lower than the experimental value of 2.30×10^{-5} cm²/sec, though it is slightly closer to experiment than most fixed-charge water models. For all concentrations studied, methanol diffusion is underestimated relative to experiment and there is a systematic shift at each concentration. Water self-diffusion is also underestimated at all concentrations, but deviations from experiment appear to diminish at higher methanol mole fractions. Greatest deviations for both systems occur in the concentration range between 0.2 and 0.4 mole fraction methanol, consistent with the extremal values in mixing enthalpies. That we observe further reduction of dynamics upon mixing is appears to be consistent with the increased interaction between methanol and water. These qualitative trends are similar to those observed for water-ethanol systems using Drude oscillator models²³.

IIIC. Bulk Solution Electrostatics

IIIC.1. Condensed Phase Dipole Moments—Polarizable force fields allow for the development of a richer condensed phase electrostatic environment relative to their fixed-charge counterparts. In particular, redistribution of molecular charge leads to differing molecular multipole moment distributions under different conditions (in this case, varying methanol concentrations). In Figures 2A and 2B we consider the behavior of the most probable molecular dipole moment, μ_{Max} , for water and methanol over the concentration range studied. Values of μ_{Max} are determined by a Gaussian fit over the full width at half max region to reduce any bias arising from the slightly skewed tails of the dipole distribution. Figure 2A shows the behavior of μ_{Max} for methanol molecules hydrogen bonded to water (oxygen-hydrogen distance less than 2.33 Å) and other methanol molecules. Figure 2B shows the concentration dependence of μ_{Max} for water associated with methanol and other water molecules. First, there is clearly a dependence on concentration, with the methanol dipole moment distribution shifting to lower values at higher methanol concentrations. At lower concentrations, where the electrostatics are largely defined by water, we note a non-trivial increase in the average methanol molecular dipole moment; within an almost bulk water-like environment, where individual water molecules have relatively large condensed phase dipole moments, methanol molecules hydrogen bonded to these water molecules are strongly polarized. Complementary to this picture are the trends in the water molecular dipole moment distributions shown in Figure 2B. For water, we observe that as methanol is added, the electrostatic environment becomes less polar relative to pure bulk water; this leads to a concomitant shift towards lower water dipole moments for water molecules that are hydrogen bonded to methanol molecules. Likewise, for water associated with other water molecules, a weaker dipole-dipole interaction is observed at high methanol mole fractions where the environment is less polar and resembles that of bulk methanol. Across the concentration range studied, the overall shift in mean water dipole moment is roughly 0.1 D compared to roughly a 0.6 D shift for methanol. This is also consistent with the difference in molecular polarizabilities, with methanol having a larger response to

perturbations in electric field ($2.8 \text{ \AA}^3$) relative to the TIP4P-FQ water model ($1.1 \text{ \AA}^3$). For dilute methanol solutions, the present results indicate that the methanol molecules are *more* polarized in the electrostatic environment defined by water and on average display a shift toward higher induced dipoles.

IIIC.2. Dielectric Constants—A second metric of the microscopic electrostatic environment is the dielectric constant computed via the Kirkwood dipole fluctuation relation:

$$\epsilon = \epsilon_{\infty} + \frac{4\pi}{3k_B T \langle V \rangle} \left(\langle M^2 \rangle - \langle M \rangle^2 \right) \quad 7$$

where M is the total dipole moment of the main simulation cell. The infinite frequency dielectric ϵ_{∞} is related to the Clausius-Mossotti relation,

$$\frac{\epsilon_{\infty} - 1}{\epsilon_{\infty} - 2} = \frac{4\pi\alpha}{3v} \quad 8$$

where v is the molecular volume and α is the molecular polarizability. Figure 3 shows the variation of the computed and experimental bulk dielectric constant with concentration. The simulation results are in qualitative agreement with experiment; furthermore, the observed concentration dependence of the methanol-water dielectric response is very similar to the trend reported for dielectric constants of ethanol and water²³ computed via molecular dynamics simulations using Drude oscillator models. Near the end-points, the solution dielectric environment is essentially fully determined by the dielectric of the more concentrated species and is consistent for both species. Near the middle of the concentration range, $X=0.2$ to $X=0.5$, corresponding to the extrema in the excess mixing enthalpy profile, there is greater drift from experiment relative to the endpoints. We note that the solution dielectric constants demonstrate an accuracy similar to the Drude model for ethanol-water interactions.²³

IIID. Bulk Liquid Microstructure: Distribution Functions, Networks, and Cluster Analysis

There has been much study of the microstructure in methanol and its aqueous solutions using both experiment and theory; this is motivated by the observation of greater deviation of dynamic and excess thermodynamic properties from ideal mixing behavior at low to mid ranges of methanol concentration^{54–57}. This anomalous behavior is linked to the formation of some unique microstructure (enhanced water structure around alcohol methyl groups; molecular-scale immiscibility leading to a micro-emulsion environment, particularly at high alcohol concentrations). Extensive neutron diffraction experiments¹ coupled with atomistic simulations of aqueous methanol solutions have recently shed light on the bi-percolating network structure of methanol-water solutions over extended concentration ranges. A recent investigation of ethanol-water solutions using polarizable Drude oscillator-based interaction potentials reported a percolating network for water at low ethanol concentrations; however, at no concentration is there observed any ethanol network structure²³. We note, that though perhaps conjectural at this point, a bi-percolating microstructure is consistent with anomalous (relative to that expected from ideal mixing) behavior; higher viscosity, lower

excess entropy, and lower diffusion coefficients are consistent with molecular-scale heterogeneity. In this regard, detailed analysis of such microstructure is warranted, with particular attention on the *interactions* underlying the evolution of this structure.

To investigate structural aspects of the methanol solutions considered in this study, we first examine radial distribution functions (RDF) for various atom-type pairs. Figure 4 shows RDF's for methanol oxygen to water hydrogen (panels a1 and a2) and water oxygen to methanol hydrogen (panels b1 and b2) at various methanol concentrations. Figure 5 shows RDF's for water oxygen to water oxygen (panel a), methanol oxygen to methanol oxygen (panel b), and methanol carbon to methanol carbon, (panel c). The $O_{\text{Water}}-O_{\text{Water}}$ RDF displays an increase in the first peak height at roughly the same location with increasing methanol mole fraction; this is consistent with the simulation and experimental results of Dougan *et al*¹. The methyl carbon RDF is also qualitatively in agreement with the EPSR results of Dougan *et al*¹. At low methanol concentrations, the location of the peak in the carbon-carbon RDF is reduced compared to that at higher concentrations. This behavior is suggestive of a micro-clustering structure at lower concentrations with small clusters of methanol molecules in close contact with neighboring hydrophobic methyl groups and reminiscent of micellar structure. One can then envisage these small clusters as nucleation centers for larger network formation (as separate clusters “fuse”) at higher concentrations; cluster distributions will be discussed below. Finally, we note that the RDF's presented in Figures 4 and 5 are qualitatively in accord with the results of the COS/M model of Yu *et al*²².

We finally discuss more correlated structure in the form of a network/cluster analysis that provides a more refined picture of micro-environment in the simulated solutions and facilitates comparison with experimental results. In the present study, a cluster analysis is performed to determine the fraction of total molecules of a given species associated in clusters of various sizes. The algorithm employed is based upon the pair list scheme adopted from Geiger *et al*⁵⁸. For water, two water molecules are considered to be hydrogen bonding if their oxygen-to-oxygen atom distance is less than 3.2Å. Though several earlier studies include an H-O-H angle criterion, we only consider the oxygen–oxygen distance for the present purposes. For methanol, motivated by a recent study by Noskov and coworkers²³ which only considers the hydrogen-bonding definition for isolating ethanol clusters in the condensed phase, we consider two definitions to identify methanol clusters in order to investigate the sensitivity of this definition on the microscopic picture obtained. First, we consider a hydrogen-bonding criterion based on oxygen-oxygen intermolecular distances; we consider two methanol molecules as hydrogen bonding if the oxygen-oxygen distance is less than 3.2Å. This particular distance is chosen as the separation of the first minimum in the oxygen-oxygen radial distribution function for methanol. We emphasize that this definition is a stringent criterion on the *type of interaction* giving rise to methanol self-association, namely, hydrogen bonding. A second and widely used criterion for clustering is to define clusters based on the carbon-carbon distance. Dougan *et al*¹ have used such a criterion and suggest that this definition is more representative of methanol clustering instead of a hydrogen bonding criterion. This criterion, as will be discussed below, combines

the effects of hydrophobic and hydrogen bonding interactions in order to yield a more structured picture of the methanol microstructure.

Figures 6A and 6B show the cluster size distribution curves for water and methanol, respectively; the hydrogen-bonding definition is used for analysis of water clustering, and the carbon-carbon distance for methanol clustering. Also shown are the predicted cluster size distributions at the percolation threshold (dashed lines) based on a power law relation^{1,59}, $n_s \approx s^{-2.2}$, for random percolation on a three-dimensional cubic lattice. The signature of percolation at a given mole fraction is the emergence of a single cluster size to which effectively all molecules belong, i.e., a vertical line; hence, there is a network of connections between all like molecules. Over the concentration range studied, methanol forms hydrogen-bonded clusters of varying sizes, with the largest clusters forming at the higher concentration ranges. Large methanol clusters incorporating most of the total methanol molecules in the mixture begin to form when $X_{\text{MeOH}} = 0.2$ (Figure 6B), in agreement with the experimental conclusion that methanol percolates for mole fractions larger than 0.27¹. The C-C distance criterion suggests that both the hydrogen bonding network and the hydrophobic packing network contribute to percolation. Water percolation appears to emerge between $X=0.4$ and $X=0.5$, with smaller clusters dominating the methanol-rich concentration regime. This transition concentration coincides with methanol concentration ranges exhibiting anomalous solution properties¹. Thus, the concentration range from 0.2 to 0.5 corresponds to a regime where the water and methanol form a bi-percolating network structure, exactly in keeping with previous experimental and theoretical results¹. Finally, Table 4 shows the fraction of total water molecules associated with a cluster of any given size. At high methanol concentrations, roughly 22.4% of all water molecules are associated with a water-only cluster. The majority of water molecules are essentially isolated, and water dimers account for 20% of the cluster-associated molecules. At 0.1 mole fraction methanol, 97.6% of all water molecules are associated with water-only clusters, and specifically, the water hydrogen bonded network.

Interestingly, at no concentration does methanol form a percolating network structure based on a hydrogen-bonding criterion for cluster definition as demonstrated in Figure 7. The form of these curves is reminiscent of the behavior observed for ethanol in ethanol-water mixtures studied using molecular dynamics simulations with Drude oscillator electrostatic interaction models. The significantly different distributions of cluster sizes predicted by the two criteria imply the importance of hydrophobic interactions in methanol–water mixtures. From Figure 8, the clustering methanol fraction increases nearly *linearly* with the concentration based on the hydrogen bond criterion compared with an *exponential*-like behavior observed for the carbon-carbon criterion. The hydrogen bonding interaction between methanol molecules seems to depend more strongly on concentration than the hydrophobic interaction in the mixtures because methanol can also be hydrogen bonded to water. It is noticeable that even for very low concentrations ($X_{\text{MeOH}} = 0.1$), 74.9% of methanol molecules form clusters based on the C-C distance criterion compared to only 11.5% of methanol molecules for the hydrogen-bonding criterion. At low concentrations, the methanol network appears to be mainly based on hydrophobic interactions. As the mole fraction of methanol is increased, the

difference in clustering fractions between the two criteria decreases and the hydrogen-bonding interaction plays a more significant role in the clustering process.

From Figure 8, we observe that water clusters percolate throughout the mixture at low concentrations of methanol ($X_{\text{MeOH}} = 0.3$). As the concentration of methanol increases, the water clusters become more isolated and incorporate fewer water molecules relative to the total number available in the mixture until the percolating water network is destroyed ($X_{\text{MeOH}} = 0.5$). This observation predicts a critical fraction of $0.4 < X_{\text{MeOH}} < 0.5$ for water percolating in methanol–water mixtures close to EPSR and MD results¹ ($X_{\text{MeOH}} \approx 0.54$) and consistent with ethanol–water mixtures' critical fraction (slightly less than $X_{\text{MeOH}} = 0.5$)²³.

IV. CONCLUSIONS

We present an analysis of thermodynamic and structural properties of methanol-water solutions for methanol concentrations from 0.1 to 0.9 mole fraction using molecular dynamics and non-additive interaction potentials for all species interactions. Specifically, we consider the ramifications of an electrostatic interaction model that allows polarization according to the charge equilibration formalism. Gas-phase interaction energies for water-methanol dimers fall within the range of values based on *ab initio* calculations, though the current model slightly overestimates the gas-phase interaction with methanol as proton acceptor (5.97 kcal/mole) and underestimates the interaction with methanol as proton donor (4.64 kcal/mole) relative to the canonical hydrogen bond energy of 5 kcal/mole. Both models are constructed with gas-phase (single molecule) molecular polarizabilities lowered relative to *ab initio* values. With respect to bulk thermodynamics, the current calculations predict a solvation free energy for methanol in TIP4P-FQ water of -5.6 ± 0.2 kcal/mole and -5.3 ± 0.04 kcal/mole based on thermodynamic integration and potential of mean force calculations, respectively. These values are roughly within 0.4 kcal/mole of experimental estimates of -5.1 kcal/mole. In this respect, the methanol-water interaction model appears to afford a robust description of these interactions despite the fact that there was no specific parameterization to optimize the interactions (self-interactions were developed independently). Excess mixing enthalpies exhibit the greatest deviation from experiment across the low to mid range of methanol concentrations. This is a consequence of the enhanced dipole-dipole interactions realized by the shift in methanol molecular dipole moment in water-rich environments. Interestingly, water appears to define the condensed phase electrostatics in this regard as the methanol responds significantly to the electrostatic environment of the water. Also influencing this is the difference in molecular polarizabilities of the methanol and water. Water molecular polarizability is $1.1 \text{ \AA}^3$ (compared to the value of 1.4 for the experimental gas-phase polarizability); the methanol molecular polarizability is $2.8 \text{ \AA}^3$. Solution dielectric constants are generally in good agreement with available experimental data and predicted values are comparable to those based on current force fields (polarizable and non-polarizable). On the micro-scale, the current potential model reinforces the standard view of methanol-water mixtures being bi-percolating mixtures of two independent networks. We find that for water, percolation onset begins at a methanol mole fraction of $X=0.4$, while that for methanol begins at $X=0.2$. Interestingly, we observe that the characterization of microstructure is quite sensitive to the definition used to identify

molecular-scale connectivity; that is, using an oxygen-oxygen distance (effectively a hydrogen bonding definition) versus a carbon-carbon distance (inclusive of hydrophobic effects) leads to drastically different pictures of the microstructure. Thus, any discussion of microstructure necessarily must include a definition that captures both forces in these types of systems. In the final analysis, the current results suggest a bi-percolating network for methanol-water mixtures in the intermediate concentration range where observed extrema in select thermodynamic properties occur.

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References

1. Dougan L, Bates SP, Hargreaves R, Fox JP, Crain J, Finney JL, Reat V, Soper AK. *J Chem Phys.* 2004; 121(13):6456–6462. [PubMed: 15446945]
2. Matsumoto M, Kataoka Y. *J Chem Phys.* 1988; 90(4):2398–2407.
3. Patel S, Brooks CL III. *J Chem Phys.* 2005; 122
4. Dixit S, Crain J, Poon WCK, Finney JL, Soper AK. *Nature.* 2002; 416:829–832. [PubMed: 11976678]
5. Jorgensen WL, Madura JD. *J Am Chem Soc.* 1983; 105(6):1407–1413.
6. Bolis G, Corongui C, Clementi E. *Chem Phys Lett.* 1982; 86:299.
7. Okazaki S, Touhara H, Nakanishi K. *J Chem Phys.* 1984; 81:890.
8. Frank H, Evans M. *J Chem Phys.* 1945; 13:507.
9. Meng E, Kollman P. *J Phys Chem.* 1996; 100:11460.
10. Laaksonen A, Kusalik P, Svishchev IM. *J Phys Chem A.* 1997; 101:5910.
11. Marcus Y. *Phys Chem Chem Phys.* 1999; 1:2975.
12. Allison SK, Fox JP, Hargreaves R, Bates SP. *Phys Rev B.* 2005; 71:04201–04201.
13. Erp, TSv; Meijer, EJ. *Chem Phys Lett.* 2001; 333:290–296.
14. Erp, TSv; Meijer, EJ. *J Chem Phys.* 2003; 118:8831–8840.
15. Morrone JA, Tuckerman ME. *J Chem Phys.* 2002; 117(9):4403–4413.
16. Morrone JA, Haslinger KE, Tuckerman ME. *J Phys Chem B.* 2006; 110:3712–3720. [PubMed: 16494428]
17. Dang LX, Chang T-M. *J Chem Phys.* 2003; 119(18):9851–9857.
18. Chang T-M, Dang LX. *J Phys Chem B.* 2005; 109:5759–5765. [PubMed: 16851625]
19. Gao J, Habibollahzadeh D, Shao L. *J Phys Chem.* 1995; 99:16460–16467.
20. Caldwell JW, Kollman PA. *J Phys Chem.* 1995; 99:6208–6219.
21. Patel S, Brooks CL III. *J Chem Phys.* 2005; 123:164502. [PubMed: 16268707]
22. Yu H, Geerke DP, Liu H, Gunsteren Wv. *Journal of Computational Chemistry.* 2006; 27:1494–1504w. [PubMed: 16838298]
23. Noskov SY, Lamoureux G, Roux B. *J Phys Chem B.* 2005
24. Lamoureux G, MacKerell AD, Roux B. *J Chem Phys.* 2003; 119(10):5185–5197.
25. Gresh N, Garmer DR. *J Comp Chem.* 1996; 17:1481–1495.
26. Masella M, Flament J-P. *Molecular Physics.* 1998; 95(1):97–106.
27. Patel S, Brooks CL III. *J Comp Chem.* 2004; 25:1–15. [PubMed: 14634989]
28. Patel S, MacKerell AD Jr, Brooks CL III. *J Comp Chem.* 2004; 25:1504–1514. [PubMed: 15224394]
29. Patel S, Charles L, Brooks I. *Molecular Simulation.* 2006; 32:3–4.

30. Rick, SW.; Stuart, SJ. Reviews in Computational Chemistry. Lipkowitz, KB.; Boyd, DB., editors. John Wiley and Sons, Inc.; 2002. p. 89
31. Rick SW, Stuart SJ, Bader JS, Berne BJ. Journal of Molecular Liquids. 1995; 65/66:31–40.
32. Rick SW, Stuart SJ, Berne BJ. J Chem Phys. 1994; 101(7):6141–6156.
33. Parr, RG.; Yang, W. Density-Functional Theory of Atoms and Molecules. Oxford University Press; Oxford: 1989.
34. Sanderson RT. Science. 1951; 114:670. [PubMed: 17770191]
35. Sanderson, RT. Chemical Bonds and Bond Energy. Academic; New York: 1976.
36. Rick SW, Berne BJ. J Am Chem Soc. 1996; 118:672–679.
37. Rick SW. J Chem Phys. 2001; 114(5):2276.
38. Sprik M, Klein ML. J Chem Phys. 1988; 89(12):7556–7560.
39. Mortier WJ, Ghosh SK, Shankar S. J Am Chem Soc. 1986; 108:4315–4320.
40. Mortier WJ, Genechten KV, Gasteiger J. J Am Chem Soc. 1985; 107:829–835.
41. Car R, Parrinello M. Phys Rev Lett. 1985; 55:2471. [PubMed: 10032153]
42. Brooks BR, Bruccoleri RE, Olafson BD, States DJ, Swaminathan S, Karplus M. J Comp Chem. 1983; 4:187–217.
43. Allen, MP.; Tildesley, DJ. Computer Simulation of Liquids. Clarendon Press; Oxford: 1987.
44. Nose S. Mol Phys. 1984; 52:255.
45. Darden T, York D, Pederson L. J Chem Phys. 1993; 98:10089.
46. Lamoureux, GaR; B. J Phys Chem B. 2006; 110(7):3308–3322. [PubMed: 16494345]
47. Stockman PA, Blake GA, Lovas FJ, Suenram RD. J Chem Phys. 1997; 107(10):3782.
48. Fileti EE, Canuto S. International Journal of Quantum Chemistry. 2005; 104:808–815.
49. Mikhail SZ, Kimel WR. J Chem Eng Data. 1961; 6:533.
50. Kumar S, Rosenberg JM, Bouzida D, Swendsen RH, Kollman PA. Journal of Computational Chemistry. 2004; 13(8):1011–1021.
51. Grossfield A, Ren P, Ponder JW. J Am Chem Soc. 2003; 125:15671–15682. [PubMed: 14664617]
52. Zacharias M, Straatsma TP, McCammon JA. J Chem Phys. 1994; 100(12):9025–9031.
53. Ivash EV, Dennison DM. J Chem Phys. 1953; 21:1804.
54. Gibson R. J Chem Phys. 1935; 57:1551.
55. Lama R, Lu BC-Y. J Chem Eng Data. 1965; 10:216.
56. Schott H. J Chem Eng Data. 1969; 14:236.
57. Yergovich T, Swift G, Kurata F. J Chem Eng Data. 1971; 16:222.
58. Geiger A, Stillinger FH, Rahman A. J Chem Phys. 1979; 70(9):4185.
59. Jan N. Physica A. 1999; 266(72)
60. Bene JED. J Chem Phys. 1971; 55(9):4633.
61. Tse Y-C, Newton MD, Allen LC. Chem Phys Lett. 1980; 75:350.
62. Bakkas N, Bouteiller Y, Loutellier A, Perchard JP, Racine S. J Chem Phys. 1993; 99(5):3335.
63. Kim S, Jhon MS, Scheraga HA. J Phys Chem. 1988; 92:7216–7223.
64. Beggerow, G. New Series of Landolt-Bornstein. Springer-Verlag; Berlin, Germany: 1976.
65. Wensink EJ, Hoffmann AC, Maaren PJv, Spoel Dvd. J Chem Phys. 2003; 119(14):7308–7317.
66. Derlacki ZJ, Eastal AJ, Edge AVJ, Woolf LA, Roksandic Z. J Phys Chem. 1985; 89:5318–5322.
67. Akerlof G. J Am Chem Soc. 1932; 54(11):4125–4139.
68. Tsuzuki S, Uchimaru T, Matsumura K, Mikami M, Tanabe K. J Chem Phys. 1999; 110:11906.

Figure 1.

Simulated (solid lines with symbols) and experimental (dashed lines) density (panel A), excess mixing enthalpy (panel B), methanol self-diffusion constant (panel C), and water self-diffusion constant (panel D) as a function of methanol mole fraction. Dashed lines are experimental data: density from Reference⁴⁹, mixing enthalpy from Reference⁶⁴, methanol self-diffusion constant from Reference 57, and water self-diffusion constant from Reference 58.

Figure 2. Most probable molecular dipole moment, μ_{Max} , as a function of methanol mole fraction. Panel A shows the variation of μ_{Max} for methanol molecules associating with other methanol molecules (circles) and with water molecules (squares). Panel B shows the variation of μ_{Max} for water molecules associating with methanol molecules (circles) and with other water molecules (squares).

Figure 3. Dielectric constants as a function of concentration. Solid line with circles represents experimental data⁶⁷ and dashed line represent results of current work.

Figure 4.

Comparison of $O_{\text{Water}}-H_{\text{MeOH}}$ radial distribution functions of aqueous methanol solutions at different concentrations. The curves in each panel are shifted appropriately for clarity.

Panels a1 and a2 show the series of curves for methanol as proton acceptor; panels b1 and b2 show curves for the case of methanol as proton donor. Labels for curves: *i*: $X_{\text{MeOH}} = 0.1$, *ii*: $X_{\text{MeOH}} = 0.2$, *iii*: $X_{\text{MeOH}} = 0.3$, *iv*: $X_{\text{MeOH}} = 0.4$, *v*: $X_{\text{MeOH}} = 0.5$, *vi*: $X_{\text{MeOH}} = 0.6$, *vii*: $X_{\text{MeOH}} = 0.7$, *viii*: $X_{\text{MeOH}} = 0.8$, *ix*: $X_{\text{MeOH}} = 0.9$.

Figure 5. Radial distribution functions (RDF's) for water and methanol self-correlations. Top panel shows RDF's for water oxygen-oxygen pairs, middle panel for methanol oxygen-oxygen pairs, and bottom panel for methanol carbon-carbon pairs. Dashed lines indicate methanol mole fraction of $X_{\text{MeOH}} = 0.9$ and solid lines indicate methanol mole fraction of $X_{\text{MeOH}} = 0.1$.

Figure 6. Water (Panel A) and methanol (Panel B) cluster size distribution in terms of molecular fraction at different concentrations. Water analysis based on hydrogen-bonding distance criterion; methanol cluster sorting based on carbon-carbon distance criterion. The dashed line is the predicted distribution at the percolation threshold based on a 3-dimensional lattice model⁵⁹.

Figure 7.

Methanol cluster size distribution in terms of molecular fraction at different concentrations using the hydrogen bonding criterion for cluster sorting. The top panel shows curves for $X_{\text{MeOH}} = 0.1 - 0.5$, and the lower panel for $X_{\text{MeOH}} = 0.6 - 0.9$. The dashed line is the predicted distribution at the percolation limit based on a 3-dimensional lattice model⁵⁹.

Figure 8.

Concentration dependence of cluster occupation. Circles represent percentages based on the methanol oxygen to oxygen atom distance. Squares represent percentages based on methanol carbon to carbon atom distance. Diamonds represent percentage of water molecules involved in clusters based on water oxygen to oxygen atom distance.

Table 1

Electrostatic and non-bond parameters for methanol and TIP4P-FQ water. Parameters for TIP4P-FQ are taken from Rick *et al.*³² (cross terms are not shown, and the reader is referred to the work of Rick *et al.*³² for further details). Methanol parameters taken from Patel and Brooks³.

Molecule	Atom Type	ϵ_i (kcal/mol)	$R_{\text{min}}/2$ (Å)	χ (kcal/mol)/e	η (kcal/mol)/e ²
Methanol	CT3	0.073	2.0	54.1403	117.769
	OH1	0.1601	1.73	101.776	150.625
	H	0.046	0.2245	0.0	253.4605
	HA3	0.026	1.2345	49.7344	245.697
TIP4P-FQ	OT	0.2862	1.7729	0.0	0.0
	OM	0.0	0.0	68.49	371.6
	HT	0.0	0.0	0.0	353.0

Gas-phase water-methanol dimer energies and oxygen-oxygen distances. Data is shown for methanol as proton acceptor (PA) and proton donor (PD).

Table 2

Dimer	Property	Current Work	¹ _{Masella}	² _{Del Bene}	³ _{Tse}	⁴ _{Bakkas}	⁵ _{Kim}	⁶ _{Canuto}	⁷ _{Tsuzuki}
MeOH (PA)	Energy (kcal/mol)	5.97	6.08	5.22	5.73	5.433	7.78	5.02	–
	R _{O,O} (Å)	2.76	2.91	2.77	–	2.96	2.8	2.844	–
MeOH (PD)	Energy (kcal/mol)	4.64	5.51	6.26	5.55	5.517	6.74	4.45	4.90
	R _{O,O} (Å)	2.86	2.86	2.71	–	2.97	2.82	2.912	2.859

¹ Reference:²⁶ MP2(FC) using a 6-311+G(2df,2p) basis at the optimized MP2(FC)/6-311+G(d,p) geometry

² Reference:⁶⁰ LCAO-SCF using a STO-3G basis

³ Reference:⁶¹ STO-3G basis

⁴ Reference:⁶² SCF using a 6-31G** basis

⁵ Reference:⁶³ SCF using a 6-31G basis

⁶ Reference:⁴⁸ BSSE corrected CCSD(T) energy using an aug-cc-pVDZ basis at the optimized MP2/aug-cc-pVDZ geometry

⁷ Reference:⁶⁸ BSSE corrected CCSD(T) energy extrapolated to the aug-cc-pVXZ CBS limit using the optimized MP2/aug-cc-pVDZ geometry

Table 3

Densities, enthalpies of mixing, dielectric constants and self-diffusion coefficients of methanol and water in the mixtures, computed from simulations of 5 ns. Experimental data: density from Reference⁴⁹ and mixing enthalpy from Reference⁶⁴; Water and methanol diffusion constants from References⁶⁵ and⁶⁶.

X_{MeOH}	ρ (g/L)	H_{mix} (kcal/mol)	ϵ	D_w ($10^{-5}\text{cm}^2/\text{sec}$)	D_{MeOH} ($10^{-5}\text{cm}^2/\text{sec}$)	Number Methanol Molecules	Number Water Molecules
0.1	989.83 (6.74)	-0.3391 (0.1432)	75.62 (0.55)	1.37 (0.01)	0.882 (0.007)	24	216
0.2	978.18 (7.56)	-0.5156 (0.1338)	72.80 (0.65)	1.05 (0.01)	0.735 (0.003)	54	216
0.3	963.83 (7.12)	-0.6028 (0.1198)	63.63 (0.248)	0.988 (0.004)	0.713 (0.004)	93	216
0.4	947.54 (6.97)	-0.6201 (0.1104)	63.44 (0.27)	0.987 (0.003)	0.761 (0.001)	144	216
0.5	927.67 (7.42)	-0.5810 (0.1075)	55.25 (0.21)	1.08 (0.002)	0.883 (0.002)	216	216
0.6	904.70 (6.56)	-0.5012 (0.1118)	49.68 (0.37)	1.26 (0.005)	1.04 (0.003)	277	185
0.7	880.25 (7.24)	-0.4008 (0.1190)	43.70 (0.79)	1.42 (0.006)	1.23 (0.004)	277	119
0.8	854.98 (9.26)	-0.2858 (0.1288)	40.94 (0.66)	1.64 (0.007)	1.41 (0.01)	277	69
0.9	827.65 (10.66)	-0.1453 (0.1425)	31.20 (0.80)	1.86 (0.016)	1.68 (0.01)	277	31

Percent of molecules involved in a cluster based on various schemes for defining association— carbon-carbon versus oxygen-oxygen atom distance for methanol networks. Methanol concentrations are shown in increments of 0.1 beginning at 0.1. Under each column are percentage of total molecules of a species present that are associated for: **(A)** methanol (based on an oxygen to oxygen atom criterion for association), **(B)** methanol (based on a carbon to carbon atom criterion for association), and **(C)** water (based on water oxygen to oxygen atom criterion).

Table 4

		Methanol Mole Fraction, X_{MeOH}									
		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	
Methanol											
Percent Associated (A) (oxygen-oxygen criterion)	11.5	22.98	33.75	42.88	54.64	63.99	72.3	79.13	84.79		
Percent Associated (B) (carbon-carbon criterion)	74.85	93.68	98.3	99.51	99.83	99.94	99.96	99.98	99.99		
Water											
Percent Associated (C) (oxygen-oxygen criterion)	97.62	96	93.57	89.34	83.1	73.16	60.14	42.61	22.43		