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A Transferable Coarse-Grained Model for Hydrogen Bonding Liquids

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Abstract

We present here a recent development of a generalized coarse-grained model for use in molecular simulations. In this model, interactions between coarse-grained particles consist of both van der Waals and explicit electrostatic components. As a result, the coarse-grained model offers the transferability that is lacked by most current effective potential based approaches. The previous center-of-mass framework¹ is generalized here to include arbitrary off-center interaction sites for both Gay-Berne and multipoles. The new model has been applied to molecular dynamic simulations of neat methanol liquid. By placing a single point multipole at the oxygen atom rather than at the center of mass of methanol, there is a significant improvement in the ability to capture hydrogen-bonding. The critical issue of transferability of the coarse-grained model is verified on methanol-water mixtures, using parameters derived from neat liquids without any modification. The mixture density and internal energy from coarse-grained molecular dynamics simulations show good agreement with experimental measurements, on a par with what has been obtained from more detailed atomic models. By mapping the dynamics trajectory from the coarse-grained simulation into the all-atom counterpart, we are able to investigate atomic level structure and interaction. Atomic radial distribution functions of neat methanol, neat water and mixtures compare favorably to experimental measurements. Furthermore, hydrogen-bonded 6- and 7-molecule chains of water and methanol observed in the mixture are in agreement with previous atomic simulations.

I. INTRODUCTION

Coarse-grained (CG) models are experiencing a renewed interest in their development and implementation from different directions.^{2, 3} Reduced models that bridge the all-atom representation and the continuum treatment of physical matter are critically needed for tackling phenomena on the spatial and temporal scale relevant to both biology and material science.⁴ Detailed discussions of different approaches in developing CG models and their applications can be found in several recent reviews.^{5–7}

Most current CG methods utilize effective potentials that ignore physical origins by lumping all interaction together and are parameterized by matching forces or fluctuations of all-atom models.⁵ Such CG models lack transferability and require constant reparameterization when the molecular composition is changed from one environment to another. Previously we published a physical-based coarse-grained model that treats both van der Waals (vdW) and electrostatic interactions explicitly.¹ The model was applied to the simulation of neat benzene, methanol and water, with reasonable success. Compared to atomic point-charge models, up to two orders of magnitude improvement in the computational efficiency has been achieved via the reduction of the number of particles and the use of a large time step. Each molecule was described as one Gay-Berne particle with a point multipole expansion including charge, dipole

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and quadrupole located at the molecular center of mass. While other Gay-Berne models that treat electrostatic interactions have been reported^{8–10}, including those with single^{11, 12} and multiple¹³ off-center multipole sites, they are limited in their use of point dipoles^{11, 13} or quadrupoles¹⁴ only and mostly have been applied to the study of liquid crystals. The novelty of our physics-based model lies in its full treatment of electrostatics and its applicability and transferability to hydrogen bonding liquids and mixtures. We report here a more generalized model with “off-center” and “multi-site” capabilities, i.e., the ability to add any number of Gay-Berne or electrostatic point multipole sites to a large, rigid-body particle, making it more flexible than the traditional Gay-Berne model where the sites are restricted to the center of mass. More importantly, the transferability of our CG model is examined on the mixture of methanol and water. All mixture properties computed are true predictions as the parameters used in mixture simulations have been derived from neat liquids only.

The methodology described in this work is rather general and can potentially be extended to other molecular systems where electrostatics plays an important role and requires explicit treatment. In addition, due to the consistent underlying physical principles, the CG model is compatible with existing atomic force fields such that its multiscale application is possible.

The present paper is organized as follows. Section II describes the multi-site model and its treatment of mixing rules, forces, torques, and the virial. Section III reports coarse-grain simulation results for neat methanol and methanol-water mixtures, comparing them with experimental results and with all-atom simulations.

II. METHODS

A. Off-center Potentials

The off-center model used in this paper is an extension of our previously published Gay-Berne and electric multipole (GB-EMP) model.¹ The GB part is based on an earlier generalized version of Cleaver and colleagues.¹⁵ Instead of placing both the Gay-Berne and the multipole sites invariably at the center of mass (COM) of a rigid body particle, we have expanded the GB-EMP model to accommodate the sites at any point on the particle. The resulting off-center GB-EMP model allows the placement of several multipole sites at polar regions, e.g., electron donor/acceptor atoms. It can also be applied to complex coarse-grained rigid bodies which cannot be described by a single ellipsoid shape. After a molecule or a rigid particle is placed in its inertial frame, the location of each site α relative to the COM of the molecule i in its reference frame

$$p_{i\alpha} \equiv r_{i\alpha} - R_i \quad (1)$$

is recorded for each site type along with its unit vector (in the case of Gay-Berne interaction site) or multipole tensors (for electrostatics), where r and R are the coordinates of the site and the COM in the global frame, respectively.

The potential energy due to the pairwise interaction of two sites $\phi_{i\alpha j\beta}(r_{i\alpha j\beta})$ is computed for Gay-Berne and multipole interactions as described previously.¹ The Gay-Berne sites and the multipole sites of the same particle do not interact with each other. The forces and torques on each site are computed in a pairwise fashion and then transferred to the forces and torques on the COM of the corresponding particle. The force on the particle is computed as a sum of the contribution from each site

$$F_i = \sum_j \sum_{\beta} \sum_{\alpha} f_{i\alpha j\beta} = -F_j \quad (2)$$

Where $f_{i\alpha,j\beta} = -\nabla\phi_{i\alpha,j\beta}(r_{i\alpha,j\beta})$ is the force on a single site α of particle i from site β of particle j . The torques on a particle are summed up from the torques and forces acting on its sites in a similar manner.¹⁶

$$T_i = \sum_{\alpha} \tau_{i\alpha} + \sum_{\alpha} p_{i\alpha} \times f_{i\alpha} \quad (3)$$

The total energy of the system is

$$U = \sum_i \sum_j \sum_{\alpha} \sum_{\beta} \phi_{i\alpha,j\beta}(r_{i\alpha,j\beta}) \quad (4)$$

During energy computation, the virial $V = \sum_i \sum_j R_{ij} F_{ij}$ is incremented for each site-to-site interaction¹⁷ and the final virial correction $-\sum_i \sum_{\alpha} p_{i\alpha} f_{i\alpha}$ is applied at the end of the calculation.

$$V = \sum_i \sum_j \sum_{\alpha} \sum_{\beta} r_{i\alpha,j\beta} f_{i\alpha,j\beta} - \sum_i \sum_{\alpha} p_{i\alpha} f_{i\alpha} \quad (5)$$

For a pair of heterogeneous sites, mixing rules are used to derive the interaction parameters as with the vdW potential. We considered both the canonical Lorentz-Berthelot mixing rule:

$$\varepsilon_{ij}^0 = \sqrt{\varepsilon_i^0 \varepsilon_j^0} \quad (6)$$

$$\sigma_{ij}^0 = \frac{\sigma_i^0 + \sigma_j^0}{2} = \frac{d_i + d_j}{\sqrt{2}} \quad (7)$$

as well as Halgren's mixing rule (HHG)¹⁸ for ε and quadratic mixing for σ :

$$\varepsilon_{ij}^0 = \frac{4\varepsilon_i^0 \varepsilon_j^0}{(\sqrt{\varepsilon_i^0} + \sqrt{\varepsilon_j^0})^2} \quad (8)$$

$$\sigma_{ij}^0 = \sqrt{\frac{\sigma_i^2 + \sigma_j^2}{2}} = \sqrt{d_i^2 + d_j^2} \quad (9)$$

where in both cases σ_0 reduces to $\sigma_0 = \sqrt{2}d$ for identical particles.¹⁹

B. Parameterization

Parameterization of the “coarse-grained” water model and center-of mass methanol model has been described previously.¹ The GB parameters were derived by fitting to gas-phase homodimer interactions and refined in liquid simulations after electrostatic parameters were obtained. The electrostatic parameters were calculated from average molecular multipole moments sampled from liquid simulations using polarizable atomic multipole-based force field.^{20, 21} The off-center methanol model in the current work was derived in the same fashion except the multipole expansion center is placed at the oxygen atom instead of the COM, which mainly affects the values of quadrupoles as the net charge is zero and the dipole moment is independent of the choice of origin. It is necessary to adjust the GB parameters (located at the COM) subsequently in order to accurately reproduce the experimental density and internal energy of the liquid simultaneously. The parameters for the two methanol models (the previous COM and the current off-site), including both GB and point multipoles, are compared in Table I and Table II.

C. Computational Details

Atomic force fields used in the parameterization were taken from AMOEBA polarizable model for methanol and water.^{20, 21} All-atom calculations were performed using TINKER molecular dynamic package.²² The CG simulation tools have been implemented based on TINKER including programs to handle rigid body coordinate system and the force and torque routines for the multiple site topology. CG molecular dynamics (MD) simulations were carried out for 2 ns using both NVT and NPT ensembles with rigid body integrator and 10–20 fs time step depending on the water fraction. In molecular mixtures involving water, the time step is limited to 10–15 fs due to the lower mass of the water particles (one water molecule per particle). Previously we have shown that 20 fs time step can be used with liquid benzene.¹ The larger time step is possible due to the greater mass and the elimination of high-frequency internal modes. A nominal coarse-grain water model from previous work was used in the mixture study.¹ Note that this is not a very robust coarse-grained model as each water molecule is represented by a spherical particle with one Gay-Berne and one point multipole while typically a coarse-grained water particle represents a cluster of water molecules. This “coarse-grained” water model actually resembles the atomic model TI3P with one vdW center and 3 partial charge sites. The purpose of using this water model is mainly to test the transferability of CG methanol model and the system’s hydrogen-bonding capability as methanol-water mixture is well characterized experimentally. A 12 Å cutoff for both vdW and electrostatics was applied and Berendsen thermostat²³ was used to maintain the temperature at 298K. A simulation box of 27 Å on its side was used. CG simulation trajectories were recorded with one frame every 1 ps. Each frame was later mapped back to all-atom structure utilizing the inertial frame, which is also the local reference frame for each particle. The back-mapping allows us to work with atomic coordinates in a number of formats and to compute the atomic structure and properties such as radial distribution function (RDF).

III. RESULTS AND DISCUSSION

A. Effect of improved electrostatics on liquid methanol structure

Overall, the off-center positioning of the multipole site has little effect on the computed macroscopic properties of the system, e.g., density and potential energy, comparing to the previous center-of-mass model. Both models were able to match experimental results rather well (Table III). Results from the more detailed atomic model (OPLS)²⁴ have been included as a benchmark. Compared to CG methanol, the atomic model consists of 3 vdW and 6 charge sites. The OPLS model was also extensively parameterized to match experimental liquid properties. Both the atomic and the CG models result in diffusion constant values that are too high (Table VI). Both off-center and COM coarse-grained models gave the diffusion constant of $3.8 \cdot 10^{-9} \text{ m}^2 \text{ s}^{-1}$ for pure methanol, compared to the experimental value of $2.4 \cdot 10^{-9} \text{ m}^2 \text{ s}^{-1}$,²⁵ and the all-atom simulation result of $3.2 \cdot 10^{-9} \text{ m}^2 \text{ s}^{-1}$.²⁴

A set of local frames have been defined for each coarse-grained particle based on the inertia frames computed from the atomic structure (Fig. 1). This allows us to map the configurations from the coarse-grained dynamics simulation into atomic trajectories by aligning the atomic inertia frames to the local frames of each CG particle and to investigate structure and dynamics at the atomic level.

To characterize the atomic interactions between methanol molecules, we have computed the radial distribution functions for methanol oxygen and hydrogen atoms. Previously, the center-of-mass GB-EMP was shown to produce hydrogen-bonding that was too weak, as evident by a low first peak in the O···H RDF in comparison with experiment (COM CG in Fig. 2a).¹ In the current study, the placing of the multipole site on the hydroxyl oxygen while leaving the GB center at the center-of-mass seems to have greatly improved the treatment of hydrogen

bonding (Fig. 2a). The resulting multi-site (MS) O $\cdots$ H RDF plot (hydroxyl hydrogens only) shows a sharp first peak at ~ 2 Å, consistent with experimentally derived RDF.²⁶ The first peak is pushed only slightly to the right compared to experiment; this is expected as the coarse-grained methanol molecule is effectively larger in size in order to correctly reproduce the system's density and internal energy simultaneously. The same is observed for the O $\cdots$ O RDF (Fig. 2b); compared to experiment²⁷ the first peak is lower and is shifted to the right. A first shell coordination number of two has been computed by integrating the O $\cdots$ O RDF to its first minimum, indicating two hydrogen bonds formed per methanol molecule. This result is consistent with other simulations and experimental work.^{27, 28}

B. Methanol-water mixture

To test the transferability of our model from a neat liquid to a heterogeneous system, we have performed MD simulations for methanol-water bulk system at various molar ratios using NPT ensembles. The results, summarized in Table IV, Table V and Table VI, and Fig. 4 and Fig. 5, are true "predictions" as all parameters were derived independently from neat liquids and kept fixed in the mixture study.

The density of mixture from the multi-site CG model, atomic simulation using OPLS, and experiment has been plotted in Fig. 5. Compared to the experimental data with its nearly linear plot, the density plot of the CG model displays greater curvature. Nevertheless, the density from the CG model shows a reasonable correlation with experiment, as shown in Table IV. The average error is 0.0126 g cm^{-3} over the whole mixture range, with a maximum error of 0.0203 g cm^{-3} . The agreement between the CG model and experiment is no worse than that given by atomic OPLS model (Fig. 5).

When mixing different types of Gay-Berne particles, a mixing rule is used to compute the heterogeneous pair interaction. The above results were derived using the canonical Lorentz-Berthelot averaging rules for Gay-Berne, i.e., arithmetic for σ and geometric for ϵ . We have also carried out otherwise identical simulations using the quadratic mixing rule for the range parameter σ and Halgren's HHG rule¹⁸ for the strength parameter ϵ . The results show significant similarity for selected mixtures and are virtually identical to Lorentz-Berthelot averaging as shown in Table IV. The insensitivity to the choice of a mixing rule is due to small differences in σ and ϵ values for coarse-grained methanol and water particles (Table I), compared to typical atomic values where the differences are much more pronounced. For example, the σ and ϵ OPLS parameters for H are 2.5 and 0.03, while for O they are 3.7 and 0.25, respectively.

The internal potential energy values of the mixture predicted by the CG model are in good agreement with those given by the atomic model (Table V). A more sensitive quantity than the potential energy is the enthalpy of mixing, for which experimental measurements are available. The mixing enthalpy for the methanol and water mixture has been computed from our simulations as:

$$\Delta H_{\text{mix}} = U_{\text{mix}} - \chi_{\text{MeOH}} U_{\text{MeOH}} - (1 - \chi_{\text{MeOH}}) U_{\text{Wat}} \quad (10)$$

where χ_{MeOH} is methanol molar fraction; U_{mix} , U_{MeOH} and U_{Wat} are the internal (or intermolecular) potential energies of the mixture, pure methanol and pure water, respectively. In Fig. 4 it shows clearly that that our CG model reproduces experimental mixing enthalpy results²⁹ within $0.1 \text{ kcal mol}^{-1}$ accuracy, which is in fact a better agreement than what is achieved by the all-atom model.²⁴

A comparison of diffusion constant values as the function of methanol molar fraction to experimental and all-atom results produced mixed results.^{24, 30} The CG data (Table VI) clearly overestimates the diffusion constant over the whole range when compared to both

experimental and all-atom data, by up to a factor of 2 when using 10 fs time step. Especially the dependence of methanol diffusion constant on the methanol concentration is considerably less pronounced than experimentally observed. It is in general difficult for molecular mechanical model to predict the diffusion rate accurately.³¹ For example, common all-atom (3-site) water models TIP3P and SPCE give diffusion constants of 5.06 and $3.85 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, respectively,³² compared with the experimental value of $2.4 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$. In addition, there is evidence that reduced models display intrinsically faster kinetics than experimental observation or the all-atom counterparts suggest.³³ It is interesting to note, however, that when 10 fs time step is used for high-water concentration mixture, the diffusion is about twice as fast than by using 2 fs time step. The latter is erroneously in better agreement with experiment. Thus the kinetics from the CG model appears to be rather sensitive to time step, unlike the thermodynamic properties. It is likely that the large time step is not applicable to the mixture at higher water concentrations as the system becomes less coarse-grained.

The methanol $\text{O}\cdots\text{O}$ RDF in the 7:3 methanol-water mixture predicted by the coarse-grained model is again a reasonable match to the experimental result (Fig. 2c), similar to what is observed in the neat methanol simulation. The $\text{O}\cdots\text{O}$ RDF by the coarse-grained model shows a strong first peak at around $2.9 \text{ \AA}$, shifted to the right from the $2.8 \text{ \AA}$ of neutron-scattering RDF.²⁷ The decrease in the peak height when going from pure methanol (Fig. 2b) to the mixture (Fig. 2c) is also evident.

We also evaluated water-water and water-methanol correlation even though the water model is not truly “coarse-grained” as mentioned before. It is however of interest to examine water structure in the presence of coarse-grained methanol, especially because water-water RDF from neutron-scattering experiment has been reported for the exact same mixture.²⁷ The $\text{O}\cdots\text{O}_w$ RDF for the methanol-water mixture (Fig. 3c) is of similar quality to the methanol $\text{O}\cdots\text{O}$ RDF (Fig. 2c), in comparison with the experiment. For the $\text{O}_w\cdots\text{O}_w$ RDF, the overall upward trend in the first peak height going from pure water (Fig. 3a) to methanol-water 7:3 mixture (Fig. 3b) is in good qualitative agreement with the experiment, which has been proposed as evidence for incomplete mixing and molecular segregation in water-methanol solution. Quantitatively, the nearest-neighbor $\text{O}_w\cdots\text{O}_w$ coordination number drops from 4.8 in pure water to 1.5 in 7:3 mixture according to our simulations, whereas Dixit *et al.* reported a decrease from 5.0 ± 0.2 to 1.2 ± 0.2 .²⁷ Note that our 7:3 mixture density is slightly lower than the experimental value (Fig. 5), which may be the cause of the slightly broader first peak in the $\text{O}_w\cdots\text{O}_w$ RDF in the mixture.

We also investigated detailed molecular structure of 7:3 methanol-water mixture from the coarse-grained dynamics trajectory by back-mapping to atomic structures using the unique local frames. We have found that GB-EMP methanol forms 5- and 6-molecule chains hydrogen-bonded molecules in neat methanol. When water is present, we observe longer 7- and 8-molecule chains and rings that include water molecules in the methanol-water mixture (Fig. 6). The hydrogen-bond stabilized chain structures are consistent with the observed formation of 6- and 8-molecule methanol chains and rings in the methanol-water mixture at higher ($>70\%$) methanol concentrations, reported in the literature.^{34, 35} The long chains appear to be less frequent than predicted by the atomic model, possibly due to the internal rigidity of the coarse-grained particle. Internal degrees of freedom, including bond stretching, angle bending or rotation around the $\text{C}\cdots\text{O}$ bond, are not represented in the reduced model, which has a limiting effect on the potential hydrogen-bonded configurations.

IV. CONCLUSION

We have demonstrated that our generalized GB-EMP model for polar liquids is capable of reproducing thermodynamic properties such as density and enthalpy. The agreement with experimental measurement is on a par with that achieved by the more detailed atomic model.

Formation of hydrogen bonds is clearly demonstrated by a sharp peak in the intermolecular O $\cdots$ H RDF of neat methanol, and is significantly improved over the previous model where the point multipole is placed at the center-of-mass. The O $\cdots$ O RDF of neat methanol is also in close agreement with experiment, and the first shell coordination number clearly indicates two hydrogen bonds per methanol molecule. We attribute these improvements to the better representation of electrostatics by off-center multipoles.

In addition, the coarse-grained model performed well when applied to methanol-water mixture, where both the methanol and the water parameters had been derived from neat liquids.¹ The predicted mixture density and enthalpy of mixing predicted by the CG model are in satisfactory agreement with experiment. The error is less than or similar to that obtained from all-atom force field. Microscopic methanol-water structures stabilized by the hydrogen-bonding chain have been observed in the CG simulation, in accordance with previous atomic simulation. On the other hand, the coarse-grained model overestimates the kinetics of molecular diffusion, likely a feature of a reduced model. We have also verified that the mixing rules are adequate for heterogeneous molecular liquids tested in this study.

Atomic pair correlation functions, or radial distribution functions, obtained from CG simulation are in good agreement with those derived from neutron-scattering experiment for the methanol-water mixture. The off-center GB-EMP model is indeed capable of capturing the important features of polar molecules in neat liquids as well as in mixtures, especially hydrogen bonding and molecular segregation in water-methanol solution. There is increasing evidence that specific molecular interactions, such as directional hydrogen bonds, could be essential in describing the physics behind phase separation and hydrophobic effect at the coarse-grain level. Recent simulations of micellar self-assembly using coarse-grained models lacking hydrogen-bonding have suggested enthalpy-driven micellization, in contrast to the more conventional entropy-driven explanation.^{36, 37} Physical models that incorporate hydrogen bonding at CG level, such as the one presented in this work, would be able to provide valuable insight into such phenomena.

It is especially encouraging that the current model is shown to be transferable from neat liquid to mixtures without re-parameterization. We attributed the transferability to the explicit treatment of vdW and electrostatic interactions in the model. Therefore, we have presented here a transferable and general coarse-grain methodology based on physical principles of molecular interactions.

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List of abbreviations

CG, coarse-grained; COM, center of mass; GB-EMP, generalized coarse-grained model with Gay-Berne and electric multipole potentials; MD, molecular dynamics; MS, multi-site; RDF, radial distribution function; vdW, van der Waals.

FIG. 1. Multi-site model of methanol. The Gay-Berne site (#) defining the uniaxial anisotropic shape of the molecule is placed at the center of mass, while the multipole site (*) is placed at the oxygen in order to capture hydrogen bonding.

FIG. 2.

Methanol RDFs from GB-EMP model and experiment. The new multi-site GB-EMP model (solid line) is a clear improvement over the previous COM GB-EMP methanol model (circles) in comparison with experimental results (dotted line). a) Neat methanol O...H RDF; b) Neat methanol O...O RDF; c) Mixture (7:3) O...O RDF

FIG. 3. Water and methanol RDFs from GB-EMP model (solid line) and experiment (dotted line). a) Neat water $O_w \cdots O_w$ RDF; b) Mixture (7:3) $O_w \cdots O_w$ RDF; c) Mixture (7:3) $O \cdots O_w$ RDF.

FIG. 4. Mixing enthalpy as a function of the molar fraction of methanol. GB-EMP model (solid line) shows close agreement with experimental data (data points) compared to all-atom OPLS-TIP4P mixture (dash line). Mixing enthalpy computed with Eq. 10. Experimental values are from Ref. 29 and all-atom data from Ref.24.

FIG. 5. Density plot for water-methanol mixture at different molar fractions. Multi-site GB-EMP model displays greater curvature than experimental values but generally agrees with all-atom data.

FIG. 6.

Structure of methanol-water clusters. The structure was produced by back-mapping of coarse-grain coordinates to atomic representation. The image represents hydrogen-bonded ring structure found in methanol-water mixture (water molar fraction 30%). The hydrogen bonds were defined with 3.0 Å distance cutoff and 30° angle cutoff.

Table I

Gay-Berne parameters for center-of-mass (COM) methanol, multi-site (MS) methanol, and water GB-EMP models.

	COM Methanol	MS Methanol	Water
d_w	1.0	1.0	1.0
l (Å)	3.18	3.20	2.27
d (Å)	2.55	2.52	2.27
ε_o (kcal/mol)	0.542	0.43	0.14
$\varepsilon_E/\varepsilon_S$	1.03	1.0	1.0

Table II
Multipole parameters for center-of-mass (COM) methanol, multi-site (MS) methanol, and water GB-EMP models

	COM Methanol			MS Methanol			Water		
Charge (e)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Dipole (Debye)	1.152	2.07	0.0	1.205	2.035	0.0	-2.180	0.0	0.0
	-0.453	-4.10	0.0	1.190	-1.537	0.0	0.8	0.0	0.0
Quadrupole (Debye e)	-4.10	1.536	0.0	-1.537	1.112	0.0	-0.220	0.8	0.0
	0.0	0.0	-1.083	0.0	0.0	-2.302	0.0	0.0	-2.380
Inertia (g/mol Å ²)	4.056	20.258	20.999	4.056	20.258	20.999	1.196	0.581	1.777

Table III

MD simulation results comparison for neat methanol

	GB-EMP Model ^a		All-atom OPLS ^b	Experiment
	COM	MS		
Potential energy (kcal/mol)	-8.45	-8.29	-7.933	-8.36 ^c
Density (NPT) (g cm ⁻³)	0.809	0.794	0.773	0.787 ^d
Self-diffusion constant (10 ⁻⁹ cm ² s ⁻¹)	3.8	3.8	3.2	2.4 ^e

^aUsing 20 fs time step^bFrom Ref. 24^cFrom the enthalpy of vaporization in Ref. 38^dFrom Ref. 39^eFrom Ref. 25

Table IVDensity values for methanol-water mixture (g cm^{-3}).

Methanol Mole Fraction	GB-EMP Model		All-atom OPLS ^a	Experiment ^b
	L-B ^c	Q-H		
1.0	0.794±0.004		0.773	0.787
0.9	0.805±0.004		0.793	0.803
0.8	0.817±0.004	0.818±0.004	0.809	0.822
0.7	0.833±0.005		0.827	0.841
0.6	0.852±0.005		0.845	0.861
0.5	0.873±0.005	0.873±0.005	0.864	0.881
0.4	0.899±0.005		0.884	0.903
0.3	0.928±0.005		0.907	0.925
0.2	0.959±0.005	0.958±0.005	0.932	0.948
0.1	0.994±0.005		0.961	0.970
0.0	1.011±0.003		0.993	0.997

^aFrom Ref. 24 by cubic spline^bFrom Ref. 39^cL-B and Q-H refer to Lorentz-Berthelot and Quadratic-HHG mixing, respectively

Table V

Intermolecular energy values for methanol-water mixture (kcal/mole)

Methanol Mole Fraction	GB-EMP Model		All-atom OPLS ^b
	L-B ^a	Q-H ^a	
1.0	-8.26±0.05		-7.933
0.9	-8.37±0.05		-8.239
0.8	-8.50±0.05	-8.53±0.05	-8.515
0.7	-8.64±0.05		-8.761
0.6	-8.80±0.05		-8.982
0.5	-8.97±0.05	-8.99±0.05	-9.178
0.4	-9.15±0.05		-9.354
0.3	-9.34±0.05		-9.51
0.2	-9.52±0.05	-9.52±0.05	-9.65
0.1	-9.70±0.06		-9.775
0.0	-10.00±0.04		-9.888

^aL-B and Q-H refer to Lorentz-Berthelot and Quadratic-HHG mixing, respectively^bFrom Ref. 24 by cubic spline

Table VISelf-diffusion coefficient D values for methanol ($10^{-9} \text{ m}^2 \text{ s}^{-1}$)

Methanol Mole Fraction	GB-EMP Model	Expt ^a
1.0	3.792	2.369
0.9	3.913	2.049
0.8	3.723	1.718
0.7	3.577	1.517
0.6	3.599	1.369
0.5	3.833	1.225
0.4	3.724	1.129
0.3	3.782	1.068
0.2	3.527	1.078
0.1	3.513	1.205

^aFrom Ref. 30