Hydrophobic hydration and the anomalous partial molar volumes in ethanol-water mixtures

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The anomalous behavior in the partial molar volumes of ethanol-water mixtures at low concentrations of ethanol is studied using molecular dynamics simulations. Previous work indicates that the striking minimum in the partial molar volume of ethanol V_E as a function of ethanol mole fraction X_E is determined mainly by water-water interactions. These results were based on simulations that used one water model for the solute-water interactions but two different water models for the water-water interactions. This is confirmed here by using two more water models for the water-water interactions. Furthermore, the previous work indicates that the initial decrease is caused by association of the hydration shells of the hydrocarbon tails, and the minimum occurs at the concentration where all of the hydration shells are touching each other. Thus, the characteristics of the hydration of the tail that cause the decrease and the features of the water models that reproduce this type of hydration are also examined here. The results show that a single-site multipole water model with a charge distribution that mimics the large quadrupole and the p-orbital type electron density out of the molecular plane has “brittle” hydration with hydrogen bonds that break as the tails touch, which reproduces the deep minimum. However, water models with more typical site representations with partial charges lead to flexible hydration that tends to stay intact, which produces a shallow minimum. Thus, brittle hydration may play an essential role in hydrophobic association in water. © 2015 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4906750>]

I. INTRODUCTION

Alcohol-water mixtures have long been known to display many anomalous properties, including their partial molar volumes.¹ Since hydrophobic interactions are important in many processes such as protein folding,² alcohol-water mixtures have often been used to study hydrophobic solvation given the low solubility of pure hydrocarbons in water. The current picture of hydration of small hydrophobic units is that while the volume of configuration space available for hydrogen bonding may be reduced, rigid clathrate structures do not appear to form.³ However, this picture is too ambiguous to explain the anomalous behavior of alcohol-water mixtures. In addition, despite numerous computational studies of alcohol-water mixtures, the molecular picture of aqueous hydration of the hydrocarbon “tail” remains unclear since results from different groups are conflicting as discussed in Ref. 4, in part because of differences in the potential energy functions. Moreover, recent simulations of *t*-butanol-water mixtures⁵ in very large boxes of up to 64 000 particles indicate additional model-dependent behavior that appears only in these very large boxes at mole fractions of *t*-butanol (X_{tB}) where aggregation occurs experimentally. Namely, at $X_{tB} = 0.03$ – 0.06 , two models show qualitatively different aggregations and two models do not

even show aggregation while all four models show unphysical demixing for $X_{tB} > \sim 0.1$.

Ethanol-water mixtures show non-ideal mixing behavior.⁶ For instance, the partial molar volumes of both ethanol (V_E) and water (V_W) are not constant but instead depend on the mole fraction of ethanol (X_E). According to textbook explanations, the partial molar volume of a given molecular type in a mixture is determined by the local environment of that molecule at the composition of the mixture. Thus, at infinite dilution of ethanol, $V_E(0)$ is determined mainly by the hydration shell of an individual ethanol, while in pure ethanol, $V_E(1)$ is determined by the neighboring ethanol molecules. Strikingly, at $X_E = \sim 0.07$, V_E shows a distinctive minimum while the partial molar volume of water V_W shows a slight peak.¹ The anomalous minimum in the solute partial volume is also observed in aqueous solutions of other alcohols and ethylene glycol⁷ but not in other polar molecules such as acetone or glycerol⁸ or in hydrocarbons.^{9,10} The studies of other alcohols indicate that the minimum goes to lower concentrations and the depth of the minimum increases as the number of carbon atoms increases, indicating it is due to hydration of the hydrocarbon tail. In addition, neutron diffraction studies indicate that the general decrease at low X_E is due to the compressive effects of water.⁴ However, although the minimum has generally been ascribed to the breakdown of the hydrogen bond network, the molecular origin is not clear.

A more detailed picture comes from recent molecular dynamics simulations.¹¹ These studies indicate that the initial fast

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decrease in V_E at very low concentrations below the minimum is due to denser packing of water around the hydrocarbon tail as the hydration shells around the tails touch each other. The mole fraction at which the minimum occurs, $X_{\min}$, is approximately the concentration where all water is in the hydration shell of an ethanol so that adding more ethanol must result in desolvation from the hydration shells. Thus, above $X_{\min}$, the subsequent fast increase in V_E up to $X_E < \sim 0.25$ is due to replacement of the water in the hydration shell of the tail with other ethanol molecules since there is no more free water, while there is a slow increase in V_E for $X_E > \sim 0.25$ as water is removed from the hydroxyl head group of the ethanol. Interestingly, both the depth of the minimum and the rate of the initial decrease in V_E appear to depend on the charge distribution of the water model, and a single-site molecular multipole model reproduces these phenomena while a three-site and a four-site model do not.

The sensitivity of the liquid structure and properties in simulations to the charge distribution of the water model used is beginning to be explored more deeply. Earlier studies indicate that several rigid nonpolarizable models of water with significantly different charge distributions are able to reproduce many bulk properties of liquid water in computer simulations reasonably well,^{12,13} and the deviations have often been attributed to a lack of electronic polarization in the model.¹² However, a recent study of thirteen nonpolarizable different models, which include three-, four-, and five-site models with partial charges as well as single-site molecular multipole models, indicates that deviations in the properties may be due to the differences in their liquid structure rather than lack of polarization.¹⁴ In particular, the results indicate that a symmetrically ordered tetrahedral hydration shell of water in the liquid phase is necessary to reproduce multiple properties of bulk water simultaneously. This type of hydration shell occurs around models that have out-of-plane charge and gives rise to a long-range tetrahedral hydrogen-bonded network in the liquid and small dipole orientation at interfaces. In addition, the results indicate that the average charge distribution of a water model should have at least a large dipole, a large quadrupole, and out-of-plane charge, so that the same multipole model that was used in the above mentioned ethanol-water studies¹¹ gives the best results in both studies. Furthermore, studies of quantum mechanical calculations indicate that the p-orbital type electron density of a water molecule in a liquid-like environment can give rise to both a large quadrupole and out-of-plane character, while “lone pairs” as represented in five-site empirical models give only a small quadrupole and out-of-plane character.¹⁵ However, the consequences of differences in the tetrahedral nature of the hydration shell of water around solutes and at interfaces are just beginning to be explored.

Here, the nature of the water structure around the hydrophobic tail that leads to the minimum in V_E is investigated in molecular dynamics simulations using water models with different charge distributions, focusing on the features of the charge distribution rather than a specific parameterization. Concentrations below potential aggregation where the ethanol molecules are still mostly hydrated are examined. To focus on the water-water interactions, the simulations here use the same water model and CHARMM22 for the ethanol to describe the solute-water interaction but the four different water models to

describe the water-water interactions. The TIP3Pm (TIP3P¹⁶ modified for use in the CHARMM force field¹⁷) model was chosen for the solute-water interactions since CHARMM22 was parameterized to be used with TIP3Pm. For the water-water interactions, the models chosen were the three-site TIP3Pm model, the four-site TIP4P-Ew¹⁸ model with a large quadrupole but no out-of-plane charge, the five-site TIP5P-E¹⁹ model with out-of-plane charge but a small quadrupole, and the single-site molecular multipole SSDQO1 (soft-sticky dipole-quadrupole-octupole)²⁰ model with both a large quadrupole and out-of-plane charge. The latter three were parameterized for use with Ewald methods and all gave better pure liquid properties than TIP3Pm.^{12,13} Thus, while the TIP3Pm and SSDQO1 simulations are the same as in the previous work,¹¹ the TIP4P-Ew simulation differs in that now the solute-water interactions are treated via TIP3Pm so that the only difference between all of the simulations here is in the water-water interactions. Since the depth of the minimum is indicative of the nature of desolvation of the hydrocarbon tail as the tails touch, the differences in the nature of the hydration between the simulations are used to elucidate what happens to the hydration shells during the initial steps of hydrophobic association. In addition to examining coordination numbers as in the previous study,¹¹ the percentages of different numbers of nearest neighbors of water molecules are examined as a function of concentration, which is so far the only quantity that shows a change at the minimum.

II. METHODS

Molecular dynamics simulations were performed with the molecular mechanics package CHARMM²¹ version 36 using the CHARMM22¹⁷ all-atom nonpolarizable potential energy parameter sets for ethanol. As mentioned above, the water-water interactions are described by four different models: TIP3Pm, TIP4P-Ew, TIP5P-E, and SSDQO1 (see Table I for summary of models; for more information see Ref. 13) while the solute-water interactions used CHARMM22 ethanol and TIP3Pm water regardless of the water model used for the water-water interactions. The simulations in which a different water model was used for the water-water interactions than the solute-water interactions were performed using MSCELE²² and an ONIOM²³-type method in which one subsystem contained ethanol and TIP3Pm water, and the other contained TIP4P-Ew, TIP5P-E, or SSDQO1 water.

The simulations utilized the leapfrog Verlet algorithm with cubic periodic boundary conditions and were maintained at 300 K and 1 atm using the Nosé-Hoover algorithm for the thermostat and barostat.^{24,25} Each system was prepared by assigning velocities according to a Gaussian distribution every 200 fs for 50 ps and then scaling velocities every 1 ps if the temperature exceeded $300 \text{ K} \pm 5 \text{ K}$ for 250 ps. The system was then allowed to run unrestrained for 7.5 ns; all quantities were calculated from the last 6 ns of data. The electrostatic interactions were calculated using particle mesh Ewald,²⁶ and SHAKE²⁷ was used to constrain covalent bonds involving hydrogen atoms. The initial cubic box length was 27.6 Å, varying from 700 water molecules for pure water to 216 ethanol molecules for pure ethanol at approximately $X_E = 0.0, 0.0014, 0.006, 0.01, 0.021, 0.03, 0.04, 0.05, 0.075, 0.1, 0.15, 0.2, 0.3,$

TABLE I. Summary of characteristics of water models and ethanol, with multipoles defined with the oxygen at the origin.^a

Model	q_H (e)	q_O (e)	d_{OM} (Å)	d_{OL} (Å)	μ_0 (D)	Θ_0 (D-Å)	Θ_2 (D-Å ²)	Ω_0 (D-Å ²)	Ω_2 (D-Å ²)
TIP3Pm	0.417	-0.834	0	0	2.35	0.23	1.72	-1.21	1.68
TIP4P-Ew	0.524	0	0.125	0	2.32	0.21	2.16	-1.53	2.11
TIP5P-E	0.241	0	0	0.7	2.29	0.13	1.56	-1.01	0.59
SSDQO1	NA	NA	NA	NA	2.12	0.00	2.13	-1.34	1.15
Ethanol	0.43	-0.66	0	0	2.15 ^b	-0.24	2.61	-2.15	2.23

^aAll water models use the same nuclear geometry with OH bond length of 0.9572 Å and HOH angle of 104.52°. The TIPnP models have sites on the oxygen and hydrogen atoms and possibly additional massless sites. The M site with charge equal to $-2q_H$ is located on the dipole vector toward the hydrogen atoms, and the two L particles with charge equal to $-q_H$ are located perpendicular to the molecular plane with an LOL angle of 109.47°. The SSDQO1 model has multipole moments located on a single site at the oxygen. For ethanol, the multipole moments of CH₂OH, which is neutral in the CHARMM22 parameters, is given, with the coordinate system such that the z-axis bisects the COH angle and the yz-plane is defined by C, O, and H, with the H in the positive y direction. The charge on the methyl carbon is -0.27 e and on the methylene hydrogens is 0.09 e.

^b $\mu_x = -0.37$, $\mu_y = -0.04$.

0.4, 0.6, and 1.0. For SSDQO1, additional simulations were run at $X_E = 0.024, 0.026, 0.027$ to resolve the minimum better; for TIP3Pm, the simulation at $X_E = 0.026$ was the only one between 0.01 and 0.05 since the densities were very close to ideal mixing values. Small boxes were used for the MSCALE simulations because they are very computationally intensive, and the same size boxes were used for TIP3Pm for consistency. However, the size dependence was examined in simulations of TIP4P-Ew and TIP5P-E that just used simple combining rules for solute-solvent interactions so that larger boxes could be run; comparisons of initial cubic boxes of length 27.6 Å and 36.8 Å (1664 water molecules for pure water) at $X_E = 0.006, 0.01, 0.021, 0.026, 0.03, 0.04, 0.05$ indicate that the results were not box size dependent. However, although there is less evidence for aggregation in water mixtures with the lower alcohols such as ethanol, the effects of aggregation, which require much larger simulation box sizes, should be investigated.

As in experimental studies of alcohol-water mixtures,⁷ the partial molar volumes are calculated according to

$$V_i = M_i \left[(1/\rho_{ij}) + (1 - w_i) \frac{\partial(1/\rho_{ij})}{\partial w_i} \right], \quad (1)$$

where i, j are alcohol or water, ρ_{ij} is the density of the solution of i and j , and w_i and M_i are the weight fraction and molar mass, respectively, of i , which satisfies the condition of holding the number of moles of j fixed. The derivative in Eq. (1) was calculated in two ways from the excess $1/\rho_{Ej}(w_E)$, where the ideal inverse density is $1/\rho_{ij}^* = w_i/\rho_i + w_j/\rho_j$. First, the derivative was estimated as the difference between the excess $1/\rho_{Ej}(w_E)$ at the next higher w_E and the preceding value at approximately the same interval; i.e., at intervals of 0.01 for $0 < X_E \leq 0.04$, 0.025 for $0.04 < X_E \leq 0.075$, 0.05 for $0.075 < X_E \leq 0.15$, and 0.1 for $0.15 < X_E$. The error in V_E was mostly due to the estimation of the derivative in Eq. (1). The apparent errors in the inverse densities were 0.0002-0.0004 g/cm³, or less than ~0.04%, as calculated by dividing the trajectory into four intervals. Thus, the error in this approach was estimated as ~0.6 cm³/mol for $X_E = 0.006$, ~0.3 cm³/mol for $0.006 < X_E < 0.04$, and successively smaller as the concentration increases. Second, the derivative was calculated from a least-squares fit of the excess $1/\rho_{Ej}(w_E)$ to a third order polynomial in w_E between $0 < X_E \leq 0.075$ since the experimental excess

volume has an inflection point at $X_E < 0.1$;²⁸ this was used to interpolate V_E at $X_E = 0$ and $X_{\min}$, the concentration of the minimum for a specific model. The R^2 of the fits of the excess $1/\rho_{Ej}(w_E)$ was greater than 0.999; although there were fewer concentrations for the TIP3Pm simulations, the excess $1/\rho_{Ej}$ was very small. Since the root-mean square deviation of the simulated $1/\rho_{Ej}(w_E)$ from the fit values was ~0.0001, the error in V_E calculated by this approach was estimated as 0.02 cm³/mol.

The coordination numbers for each simulation were calculated by integrating the calculated radial distribution functions to the same distances regardless of the models used. For each type of coordination number, the distance was chosen as the first minimum in the relevant radial distribution function of the neutron diffraction data for pure water²⁹ and ethanol in water.³⁰ Thus, the distance for coordination numbers of water around a water molecule n_{WW} was 3.36 Å, around the methyl carbon n_{CW} was 4.5 Å, and around the hydroxyl oxygen n_{OW} was 3.36 Å.

III. RESULTS AND DISCUSSION

The effects of the charge distribution on hydrophobic hydration were studied here using four models of water: TIP3Pm, TIP4P-Ew, TIP5P-E, and SSDQO1. The partial molar volumes of ethanol V_E as a function of mole fraction of ethanol X_E were calculated using the four models of water (Figure 1, Table II) and compared to those from experimental densities.²⁸ In addition, the coordination numbers around the methyl carbon, the hydroxyl, and other water molecules, n_{CW} , n_{OW} , and n_{WW} , respectively, as a function of X_E were also calculated (Figure 2 and Table III) and compared to neutron diffraction data.^{29,30} Overall, SSDQO1 gives the best agreement with the experimental partial molar volumes and coordination numbers, indicating that SSDQO1 gives good ethanol-water structure. The differences between the simulated results are now discussed in more detail. In this discussion, the simulations at $X_E = 0.0014$ are referred to as “infinite dilution” because only a single ethanol is in the simulation box and the concentration is less than half of that when the experimental V_E becomes constant as $X_E \rightarrow 0$.

FIG. 1. The partial molar volumes of ethanol, V_E , as a function of ethanol mole fraction X_E , where all solute-water interactions use TIP3Pm and the ethanol was described by CHARMM22 parameters. The water-water interactions use TIP3Pm (brown), TIP4P-Ew (green), TIP5P-E (blue), SSDQO1 (red), and experiment (black). The derivatives were estimated by a difference (filled circles connected by a dotted line) and by a polynomial fit at low concentrations (solid line); see methods for more details including errors. $X_E = 0.05$ and 0.25 are also indicated.

V_E from the simulations were compared for all four models (Figure 1, Table II). Since the CHARMM22 parameters were used for ethanol in all of these simulations, the V_E converge to $59.9 \text{ cm}^3/\text{mol}$ as $X_E \rightarrow 1$ (pure ethanol) in the simulations, which is a slight overestimate of experimental value of $58.6 \text{ cm}^3/\text{mol}$.¹¹ Since the only difference between these simulations is the water model for the water-water interactions, most of the decrease in V_E relative to $V_E(1)$ as water is added to pure ethanol and the decrease in V_E relative to $V_E(0)$ as ethanol is added to pure water must be determined in large part by the water structure. At infinite dilution, the decrease in V_E with respect to pure ethanol, i.e., $V_E(1) - V_E(0)$, was too small compared to experiment in the TIP3Pm simulation, which indicates the water density in the first hydration shell is too low, while it is better in the TIP4P-Ew, TIP5P-E, and SSDQO1 simulations, indicating that water models with more tetrahedrally ordered hydration shells of water molecules in the pure liquid (i.e., the latter models)¹⁴ also better represent water in hydration shells around ethanol molecules. However, since $V_E(1) - V_E(0)$ is actually now too large in TIP4P-Ew, TIP5P-E, and SSDQO1, too much water may be in the first hydration shell. Also, $X_{\min}$ is too high in TIP3Pm and too low in the other models, which is consistent with $X_{\min}$ being the point where all water is in the hydration shells of ethanol since the more water that is involved in hydration, the lower the concentration where no free water is available. In addition,

TABLE II. Selected quantities for the partial molar volumes of ethanol in ethanol-water mixtures. $V_E(1) = 59.9 \text{ cm}^3/\text{mol}$ in simulation, $58.6 \text{ cm}^3/\text{mol}$ in experiment. Experimental values are from Ref. 28.

Simulation	$V_E(1) - V_E(0)$ (cm^3/mol)	$X_{\min}$	$V_E(0) - V_E(X_{\min})$ (cm^3/mol)
TIP3Pm	1.6	0.075	0.5
TIP4P-Ew	6.4	0.020	0.3
TIP5P-E	5.8	0.020	0.5
SSDQO1	6.9	0.025	1.6
Experiment	3.9	0.065	1.83

FIG. 2. The coordination numbers of water molecules around the ethanol methyl carbon n_{CW} (solid), water molecules around the ethanol hydroxyl n_{OW} (dotted), and water molecules around water n_{WW} (dash) for TIP3Pm (brown), TIP4P-Ew (green), TIP5P-E (blue), and SSDQO1 (red). The neutron diffraction data are also shown for n_{CW} (solid circles), n_{OW} (open circles), and n_{WW} (crosses). $X_E = 0.05$ and 0.25 are also indicated.

since the large decrease in V_E at $X_{\min}$ with respect to infinite dilution, $V_E(0) - V_E(X_{\min})$, observed experimentally is seen only in the SSDQO1 simulations, SSDQO1 water must be behaving differently. Furthermore, these effects must be mainly due to the water-water interactions around the hydrocarbon tail since water interacts strongly with the hydroxyl head via hydrogen bond interactions, which are treated using TIP3Pm in all of the simulations, while water around the hydrocarbon tail interacts only weakly with the carbons.

Interestingly, the coordination numbers show different behaviors for the different water models. At infinite dilution (Table III), the value of $V_E(0)$ is roughly anti-correlated with n_{CW} since the distorted hydrogen bonds allowed by the TIP3Pm and TIP4P-Ew models give rise to a lower density of the hydration of the tail, as seen in the smaller n_{CW} , while the more tetrahedral TIP5P-E and SSDQO1 have higher density hydration, consistent with previous results.¹¹ As X_E increases (Figure 2), the coordination numbers of the two models with out-of-plane charge, SSDQO1 and TIP5P-E, show similar rate of decrease, although the n_{CW} and n_{OW} are slightly greater and thus the n_{WW} are slightly smaller for SSDQO1. However, for $0.05 < X_E < 0.25$, TIP4P-Ew shows a greater rate of decrease of n_{CW} and n_{OW} , and a slower rate of decrease of n_{WW} . Presumably, this is because in TIP4P-Ew, water is able to form distorted hydrogen bonds with other water molecules, which leads to a slower increase in V_E since hydrogen bonded water

TABLE III. Coordination numbers and number of neighbors in pure water* and coordination numbers at infinite dilution;** the latter is at $X_E = 0.014$ for the simulation and extrapolated for experimental value. Experimental values are from Refs. 29 and 30.

Simulation	n_{WW}^*	% $\leq 3\text{-neighbor}^*$	% 4-neighbor^*	n_{CW}^{**}	n_{OW}^{**}
TIP3Pm	4.8	9.7	30.5	10.7	3.1
TIP4P-Ew	4.5	9.9	44.5	10.9	3.0
TIP5P-E	4.6	10.1	41.1	11.1	3.2
SSDQO1	4.4	12.5	45.3	11.3	3.3
Experiment	4.3	NA	NA	11.6	2.7

should pack against the tail less densely than water molecules without hydrogen bonds. Furthermore, all four models show a decrease in n_{OW} with increasing X_E unlike experiment, which has a constant value of about 2.7 water molecules. The large value of n_{OW} at infinite dilution appears to be why the TIP4P-Ew, TIP5P-E, and SSDQO1 models all overestimate $V_E(1) - V_E(0)$. Also, this decrease in n_{OW} with X_E in all of these water models indicates that the hydration of the ethanol hydroxyl may not be described correctly, although this may be in structure or affinity, since the polar hydroxyl interacts strongly with the water unlike the nonpolar carbons. This suggests the need for new hydroxyl-water parameters.

To understand how the water-water structure differs between the models as a function of concentration, the percentages of water molecules with different numbers of nearest neighbor water molecules were also examined. In this discussion, water molecules are referred to as 5-, 4-, and ≤ 3 -neighbor water, according to the number of nearest-neighbor water molecules (i.e., within 3.36 Å) around the water. Of course, this is not meant to imply that the types of water molecules are long-lived species, since the neighbors are continually exchanging with “bulk” water so that the identity of the neighbors as well as the number of neighbors is not constant for a given water molecule. Since $n_{WW} = 4.3$ for the pure liquid according to neutron diffraction experiments,²⁹ presumably real pure water is composed mostly of 4- and 5-neighbor water, with a smaller fraction of ≤ 3 -neighbor water. This holds for the relative composition of the neighbors for all of the water models at $X_E = 0$, although the exact proportions differ (Table III). The percentage of 5-neighbor water in pure TIP3Pm water is probably too high since its $n_{WW} = 4.8$, while the ratios in the rest are probably more reasonable since their n_{WW} approach the experimental value (Table III), with the percentage of 5-neighbor water decreasing with n_{WW} .

As X_E increases (Figure 3), the number of 5-neighbor water decreases, as expected since less water is available to hydrate a given water molecule. In SSDQO1, the percentage of 4-neighbor water remains almost constant with increasing ethanol concentration up to X_{min} , the concentration where all water molecules are in hydration shells, while in TIP3Pm, TIP4P-Ew, and TIP5P-E, it increases slightly. Instead, the

FIG. 3. The percentage of water molecules in the mixtures with different numbers of nearest neighbor water molecule: five neighbors (dot dash), four neighbors (solid), and one to three neighbors (dash) for TIP3Pm (brown), TIP4P-Ew (green), TIP5P-E (blue), and SSDQO1 (red).

FIG. 4. Water molecules (red for oxygen and white for hydrogen) involved in the association of the hydration shells of two ethanol molecules (large red sphere for the hydroxyl and large cyan spheres for the carbons) in (a) TIP4P-Ew and (b) SSDQO1 water. Only water molecules in the first hydration shell of either methyl carbon are shown (ball-and-stick except the two waters at the interface of the hydration shells, which are in wire). Hydrogen bonds to other first shell water molecules are indicated as green dotted lines; hydrogen bonds to the second shell are not shown. In TIP4P-Ew, the interface water molecules have a total of four hydrogen bonds while in SSDQO1, only the one on the right in SSDQO1 has four hydrogen bonds while the other has only three.

number of ≤ 3 -neighbor water is higher in SSDQO1 than in the other three. Since the concentration range $0 < X < X_{min}$ corresponds to increasing numbers of hydration shells that are touching, this behavior appears to be associated with the water molecules at the interface between two tails, which must choose between distorting and breaking hydrogen bonds in order to satisfy the constraints of the hydrogen bonding of the two hydration shells (Figure 4). This implies that in SSDQO1 the hydration shell is composed of more ≤ 3 -neighbor water molecules than the other models because the out-of-plane charge does not allow distorted hydrogen bonds in the lone pair directions and instead prefers broken hydrogen bonds. On the other hand, in the TIPnP models, the hydration shell has more 4-neighbor water molecules because the lack of out-of-plane charge (or in the case of TIP5P, weak out-of-plane charge, Table I) apparently allows the formation of distorted hydrogen bonds.¹¹

This behavior should affect V_E because the number of neighbors of a water molecule affects its packing against the hydrocarbon tail. In the pure liquid, 4-neighbor water molecules in the hydration shell around a water molecule correspond to tetrahedral hydration with low-density packing, while 5-neighbor water molecules have higher density packing. While the 5-neighbor water molecules can also be expected to pack densely around the hydrocarbon tail, 4-neighbor water molecules pack differently. In previous results for an ethanol molecule at infinite dilution,¹¹ a preference for strongly tetrahedral order in SSDQO1 leads to “corrugated” high density hydration of the hydrocarbon tail

while the distortion from tetrahedral allowed in TIP4P-Ew leads to a “stretched” low density hydration shell. In addition, while the ≤ 3 -neighbor water molecules have even lower density packing than 4-neighbor water in the pure liquid, they can pack more tightly against the hydrocarbon tail since they do not form hydrogen bonds to it. Thus, at infinite dilution, SSDQO1 has the smallest $V_E(0)$. As X_E increases and the hydration shells of the hydrocarbon tail begin to touch, the water molecules at the interface between two or more tails have a choice between forming either ordered hydrogen bonds, which is hard to do when the water is near two or more tails, or breaking them, resulting in more ≤ 3 -neighbor water molecules. Thus, the faster the percentage of ≤ 3 -neighbor water molecules increases, the faster V_E decreases. In SSDQO1, the tendency is to break bonds so V_E decreases rapidly. On the other hand, in the TIPnP models, the tendency is to form distorted hydrogen bonds so that V_E does not decrease as quickly.

These results indicate that the hydration shells of the ethanol tails are “brittle” in SSDQO1 because hydrogen bonds break when they touch each other, while they are flexible and form distorted hydrogen bonds in the TIPnP models upon touching. The lack of brittle behavior in TIP5P-E is somewhat surprising since it forms symmetric hydration shells in the pure liquid,¹⁴ so brittleness must not only be a function of the symmetry of the hydration shell formed but also of the strength of the hydrogen bonding interaction. This implies that intact hydration shells around hydrophobes are too favorable in TIPnP type models, which would affect hydrophobic association in simulations using them. More fundamentally, this implies that the brittleness of the hydration shell around hydrophobes is an important factor in hydrophobic association.

IV. CONCLUSIONS

This study of the effects of the charge distribution of a water molecule in simulations of ethanol-water mixtures elucidates several points about the nature of aqueous solvation of ethanol. The water-water interactions appear to give rise to the unusual behavior of the partial molar volumes of ethanol-water mixtures because they determine the structure of water around the hydrocarbon tail of ethanol. In particular, the symmetric, ordered tetrahedral hydration shells predicted by a charge distribution with a large quadrupole with out-of-plane charge give an initial sharp decrease in the partial molar volume of ethanol as ethanol is added to water, which is seen in experiment. By examining the simulations, this occurs as the hydration shells of the ethanol molecules begin to touch and break hydrogen bonds. Furthermore, this “brittle” behavior may play an important role in hydrophobic association. Finally, since the details in the behavior of the partial molar volumes such as concentration of the minimum may involve a balance of the water-water and solute-water interactions, studies with new solute parameters that have carefully balanced hydroxyl-water interactions are necessary to fully quantitate the behavior.

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