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Cite as: J. Chem. Phys. **157**, 234502 (2022); <https://doi.org/10.1063/5.0131475>

Submitted: 20 October 2022 • Accepted: 29 November 2022 • Accepted Manuscript Online: 30 November 2022 • Published Online: 15 December 2022

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Study of phase equilibria and thermodynamic properties of liquid mixtures using the integral equation theory: Application to water and alcohol mixtures

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ABSTRACT

A theoretical method for calculating the thermodynamic properties and phase equilibria of liquid–liquid mixtures using the integral equation theory is proposed. The solvation chemical potentials of the two components are evaluated by the integral equation theory and the isothermal–isobaric variation of the total density with composition is determined to satisfy the Gibbs–Duhem relation. Given the density of a pure component, the method can calculate the densities of the mixture at any composition. Furthermore, it can treat the phase equilibrium without thermodynamic inconsistency with respect to the Gibbs–Duhem relation. This method was combined with the reference interaction-site model integral equation theory and applied to mixtures of water + 1-alcohol by changing the alcohol from methanol to 1-butanol. The destabilization of the mixing Gibbs energy by increasing the hydrophobicity of the alcohol and demixing of the water–butanol mixture were reproduced. However, quantitative agreement with experiments is not satisfactory, and further improvements of the integral equation theory and the molecular models are required.

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I. INTRODUCTION

Phase equilibria and thermodynamic properties of liquid mixtures, including liquid–liquid phase separation, liquid–vapor equilibrium, and excess mixing volume, are critically important in chemical processes such as distillation and extraction.¹ These properties have been studied in many systems, and a huge amount of data has been accumulated. The use of phase-separation solvents was recently proposed for capturing carbon dioxide from flue gas or air with high energy efficiency.^{2,3} Furthermore, it has been suggested that liquid–liquid phase separation plays an important role in the biological functions in a cell.⁴

Phase equilibria are macroscopic phenomena, and their experimental observation is relatively easy. Following the accumulation of efforts to improve experimental methods and instruments, various thermodynamic properties of liquid mixtures can be determined

with high accuracy. However, it is still difficult to understand these macroscopic behaviors of liquid mixtures from the perspectives of intermolecular interaction and microscopic liquid structure.

Molecular simulation, including the molecular dynamics (MD) and Monte Carlo types, is a representative computational method to reproduce various properties of liquid systems based on their molecular structure and intermolecular interactions.⁵ When the miscibility of two liquids is quite low, a brute-force simulation could reproduce the coexistence of two liquid phases. A grand canonical simulation involving particle insertion, deletion, or exchange is also available for the simulation of phase coexistence. However, such a direct simulation is difficult when the miscibility of the two components is not that low. In addition, analysis of the microscopic driving force of the phase behavior is difficult in these simulations.

The macroscopic phase behavior under isothermal–isobaric conditions is governed by Gibbs energy, and free-energy calculation is also available for the determination of phase equilibrium by molecular simulations.^{6,7} By calculating the Gibbs energy at a given temperature and pressure as a function of composition, it can be determined whether the liquid–liquid phase separation occurs or not. Various analytical methods for free-energy calculation are available to relate the phase equilibrium and microscopic interaction. However, the free-energy calculation is computationally demanding for molecular simulation, which is a disadvantage.

The integral equation theory is another computational method for calculating the microscopic structure and macroscopic thermodynamic properties of liquids and liquid mixtures based on their intermolecular interactions.^{8,9} Based on statistical mechanics, with the introduction of some kinds of approximation, the integral equation theory gives a closed analytical relation between the intermolecular interaction and microscopic correlation functions. It also provides closed expressions for various thermodynamic properties, including the solvation free energy.¹⁰ The statistical average is taken *a priori* in the integral equation theory; therefore, it does not suffer from the poor sampling associated with the slow relaxation of long-range concentration fluctuations. The integral equation theory was originally formulated for simple liquids composed of monoatomic molecules and was extended to polyatomic molecular liquids.⁹ In this work, we propose a theoretical method to calculate the phase equilibrium and thermodynamic properties of liquid mixtures, based on the integral equation theory. In our method, the solvation free energies of the two components are calculated as functions of their compositions and the phase equilibria are analyzed, based on the chemical potentials of the components.

In numerical calculations based on the integral equation theory, the temperature and the number densities of the components are usually given as parameters that specify the thermodynamic state of the system.^{8,9} By contrast, the mixing of the two components is performed under isothermal–isobaric conditions. Therefore, we need the isobaric concentration dependence of the total density for the calculation. The densities of many liquid mixtures were measured experimentally and are available in the literature, but the experimental values for a particular system of interest are not always available, and, hence, we must determine the density of the mixture in some way. The method we propose in this work deals with the determination of the isobaric variation of the total density based on the Gibbs–Duhem relation.

The Gibbs–Duhem relation describes the relationship between the thermodynamic properties of a homogeneous system, derived from the response of thermodynamic quantities to the system size scaling. The calculation of various useful properties of the phase equilibria of liquid mixtures is based on the Gibbs–Duhem relation. Whether this relation holds or not is called “thermodynamic consistency,” which is a criterion used to validate experimental results. Thus, various thermodynamic consistency tests were proposed and applied to experiments.¹¹ Since the total density is determined to satisfy the Gibbs–Duhem relation in our method, the numerical results automatically follow the Gibbs–Duhem relation, and phase equilibria can be treated without thermodynamic inconsistency.

The integral equation theory used in this work is the reference interaction-site model (RISM) theory.⁹ RISM theory is an integral

equation theory for molecular liquids, in which a polyatomic molecule is described as a collection of interaction sites. RISM theory and its extension to the three-dimensional description of the solute, 3D-RISM theory,¹² have been applied to many systems of chemical and biological interest. Perry and Sing employed the polymer version of RISM theory (PRISM theory) to model the phase equilibrium of polymer coacervate.¹³ An advantage of RISM theory is that the calculation of the solvation free energy of a solute can be performed quickly, because it is given in a closed analytical form when RISM theory is combined with the hypernetted-chain (HNC) or the Kovalenko–Hirata (KH) closures. The original expression of the solvation free energy proposed by Singer and Chandler¹⁰ overestimates the solvation free energy associated with cavity formation. However, various correction methods have been proposed, and it is now possible to evaluate the solvation free energy of a solute quantitatively.^{14–18}

We applied our method to a model system for the mixtures of water and 1-alcohol. Due to their chemical and biological importance, they have been studied intensively using experiments, theories, and computer simulations.^{7,19–22} In particular, the mixing Gibbs energy of the water–methanol mixture was calculated in the pioneering work of Kvamme using RISM theory.²² The mixing Gibbs energies of water with various alcohols were evaluated recently by means of MD simulation.⁷ The hydrophobicity of 1-alcohols increases when increasing the size of the alkyl group. The mixtures are miscible at any composition up to 1-propanol, and the liquid–liquid phase separation occurs in cases of 1-butanol and larger alcohols.

Section II presents our theoretical method, together with the description of the theories on which our method is based. The details of the model systems are also shown. The numerical results on the mixing thermodynamics and phase behavior are presented in Sec. III. The effects of various approximations are also examined and discussed. Finally, the work is summarized in Sec. IV.

II. THEORETICAL METHODS

A. Thermodynamics

The system we consider is the liquid mixture composed of two components: water (W) and alcohol (A). Their number densities are denoted as ρ_W and ρ_A , respectively. The total number density is defined as $\rho_T \equiv \rho_W + \rho_A$, and the molar fraction of A is denoted as $x_A \equiv \rho_A/\rho_T$. Although we use the subscripts “W” and “A” here, the theoretical formulation below applies to arbitrary binary liquid mixtures.

The solvation free energy is the minimum work required to transfer a molecule from ideal gas to liquid. Once the solvation free energies of the two components, denoted as μ_W^{SFE} and μ_A^{SFE} , are calculated, their chemical potentials are given by

$$\mu_i = \mu_i^0 + k_B T \ln \left(\frac{\rho_i}{\rho_0} \right) + \mu_i^{SFE}, \quad (1)$$

where $i \in \{W, A\}$ is an index of the components, and k_B and T stand for the Boltzmann constant and the absolute temperature, respectively. The standard chemical potential in the gas phase is denoted as μ_i^0 , and ρ_0 refers to the number density of the standard state. The

constant values of μ_i^0 and ρ_0 can be taken arbitrarily, as long as they do not depend on any thermodynamic conditions.

Under the isothermal condition, the Gibbs–Duhem relation is given by

$$dP = \rho_W d\mu_W + \rho_A d\mu_A, \quad (2)$$

where P stands for pressure. Therefore, the right-hand side of Eq. (2) must be zero when x_A is varied under isothermal–isobaric conditions as

$$\rho_W d\mu_W + \rho_A d\mu_A = 0. \quad (3)$$

In this work, we used Eq. (3) as the relation that gives ρ_T as a function of x_A . Substitution of Eq. (1) into Eq. (3) yields

$$\frac{1}{\rho_T} d\rho_T + \frac{1}{k_B T} \{x_W d\mu_W^{SFE} + x_A d\mu_A^{SFE}\} = 0, \quad (4)$$

which describes the variation of ρ_T in response to a change in x_A . The molar fraction of W, $x_W \equiv 1 - x_A$, is defined here. To determine the absolute value of ρ_T , the density of neat W, $\rho_T(x_A = 0) = \rho_W^0$, is fixed as the experimental value. The use of Eq. (4) for the determination of ρ_T is the essential point of this work, which guarantees the thermodynamic consistency of chemical potentials, Eq. (3). As will be shown in Sec. III, the density of the mixture must be determined according to the set of molecular models and the approximations for free-energy calculation, to obtain the thermodynamically consistent mixing Gibbs energy.

Based on the Gibbs–Duhem relation, the Gibbs energy of the system is given by

$$\frac{1}{V} G = \rho_W \mu_W + \rho_A \mu_A, \quad (5)$$

where V denotes the volume of the system, and the mixing Gibbs energy is defined as

$$\Delta G_{mix}(x_A) \equiv G(x_A) - [x_W G(x_A = 0) + x_A G(x_A = 1)]. \quad (6)$$

The combination of Eqs. (1), (5), and (6) gives

$$\begin{aligned} \frac{1}{\rho_T V} \Delta G_{mix}(x_A) &= k_B T [x_W \ln x_W + x_A \ln x_A] \\ &+ k_B T [\ln \rho_T - x_W \ln \rho_W^0 - x_A \ln \rho_A^0] \\ &+ [x_W (\mu_W^{SFE} - \mu_W^{SFE,0}) + x_A (\mu_A^{SFE} - \mu_A^{SFE,0})], \quad (7) \end{aligned}$$

where ρ_A^0 stands for the number density of neat A, and $\mu_i^{SFE,0}$ denotes the solvation free energy of the component i in its neat liquid. The first term of the right-hand side is usually referred to as the “ideal” term. The ideal term originates from the increase in the translational entropy of both components upon mixing, which is included in the second term of Eq. (1). The number densities of both components, ρ_A and ρ_W , decrease upon mixing, which leads to the stabilization of their chemical potentials. The third term of Eq. (7) describes the contribution of the solvation free energies of both components. The second term, the contribution of the number density, can further be transformed as

$$\begin{aligned} &k_B T [\ln \rho_T - x_W \ln \rho_W^0 - x_A \ln \rho_A^0] \\ &= k_B T \ln \frac{\rho_T}{\rho_T^{id}} + k_B T \ln \frac{\rho_T^{id}}{(\rho_W^0)^{x_W} (\rho_A^0)^{x_A}}, \quad (8) \end{aligned}$$

$$\frac{1}{\rho_T^{id}} \equiv \frac{x_W}{\rho_W^0} + \frac{x_A}{\rho_A^0}. \quad (9)$$

The ideal value of the total number density, ρ_T^{id} , defined by Eq. (9), is the total number density in the absence of the excess mixing volume. Thus, the first term of the right-hand side of Eq. (8) refers to the contribution of the excess mixing volume. The decrease in total volume upon mixing decreases the translational entropy of all the molecules, resulting in the increase in the Gibbs energy. The second term is nonpositive, and it is equal to 0 when $\rho_W^0 = \rho_A^0$. Therefore, the second term can be interpreted as the contribution of the difference in the molecular sizes of W and A.

B. RISM integral equation theory

In the interaction-site description of molecular liquids, a molecule is described as a collection of interaction sites that correspond to an atom or a united atom in the molecule. In RISM theory, the intramolecular geometry of the molecule is given by the intramolecular correlation function, $\omega_{\alpha\gamma}(\mathbf{r})$, where α and γ indicate the interaction sites within a molecule. For a rigid molecule, $\omega_{\alpha\gamma}(\mathbf{r})$ is explicitly given by

$$\omega_{\alpha\gamma}(\mathbf{r}) = \frac{1}{4\pi l_{\alpha\gamma}^2} \delta(r - l_{\alpha\gamma}), \quad (10)$$

where $l_{\alpha\gamma}$ stands for the distance between sites α and γ , and the ensemble average of the right-hand side should be taken for a flexible molecule. The intermolecular interaction is described as the sum of the site–site interactions, $u_{\alpha\gamma}(r)$, which are assumed to be isotropic.

RISM theory comprises two equations: the site–site Ornstein–Zernike (SSOZ) and the closure equations.⁹ The former defines the site–site direct correlation function $c_{\alpha\gamma}(\mathbf{r})$ as

$$\tilde{c}(q) = [\boldsymbol{\rho} \cdot \tilde{\omega}(q)]^{-1} - \tilde{\chi}^{-1}(q), \quad (11)$$

where bold symbols denote the matrices that possess the indices of the interaction sites, and the dot represents the matrix product. The tilde stands for the Fourier-transformed function in the reciprocal space, and $\boldsymbol{\rho}$ is a diagonal matrix, whose diagonal component is the number density of the site. The site–site partial structure factor $\tilde{\chi}(q)$ is defined as

$$\tilde{\chi}(q) \equiv \boldsymbol{\rho} \cdot \tilde{\omega}(q) + \boldsymbol{\rho} \cdot \tilde{h}(q) \cdot \boldsymbol{\rho}, \quad (12)$$

and the total correlation function, $h_{\alpha\gamma}(r)$, is related to the site–site radial distribution function $g_{\alpha\gamma}(r)$ as

$$h_{\alpha\gamma}(r) \equiv g_{\alpha\gamma}(r) - 1. \quad (13)$$

The closure equation is another relation between $c_{\alpha\gamma}(\mathbf{r})$ and $h_{\alpha\gamma}(r)$, which is coupled to the SSOZ equation, Eq. (11), to obtain these correlation functions. In this work, we used the KH closure as⁹

$$\xi_{\alpha\gamma}(\mathbf{r}) \equiv -\frac{u_{\alpha\gamma}(r)}{k_B T} + h_{\alpha\gamma}(r) - c_{\alpha\gamma}(\mathbf{r}), \quad (14)$$

$$g_{\alpha\gamma}(r) = \begin{cases} \exp \xi_{\alpha\gamma}(r) & (\xi_{\alpha\gamma}(r) \leq 0), \\ 1 + \xi_{\alpha\gamma}(r) & (\xi_{\alpha\gamma}(r) \geq 0). \end{cases} \quad (15)$$

The KH closure was originally derived as a partial linearization of the HNC closure, and the analytical expression of the solvation free energy for the HNC closure derived by Singer and Chandler¹⁰ was also extended to the KH closure. When a solute molecule, X, is dissolved in a mixture solvent, S, the solvation free energy of X is described as⁹

$$\frac{\mu_X^{SFE}}{k_B T} = \sum_{\alpha \in X} \sum_{\gamma \in S} \rho_\gamma \int_0^\infty 4\pi r^2 \left[h_{\alpha\gamma}^2(r) \Theta(-h_{\alpha\gamma}(r)) - c_{\alpha\gamma}(r) - \frac{1}{2} h_{\alpha\gamma}(r) c_{\alpha\gamma}(r) \right] dr, \quad (16)$$

where $\Theta(x)$ stands for the Heaviside step function. In the case of a liquid mixture of A and W, either one of the components is regarded as the solute X dissolved in the mixture solvent composed of A and W. The solvation free energy obtained from Eq. (16) is referred to as the Singer–Chandler (SC) solvation free energy in this work.

In addition to $\mu_i^{SFE,SC}$, the Gaussian-fluctuation (GF) expression of the solvation free energy²³

$$\frac{\mu_X^{SFE,GF}}{k_B T} = \sum_{\alpha \in X} \sum_{\gamma \in S} \rho_\gamma \int_0^\infty 4\pi r^2 \left[-c_{\alpha\gamma}(r) - \frac{1}{2} h_{\alpha\gamma}(r) c_{\alpha\gamma}(r) \right] dr \quad (17)$$

was also tested because Tanimoto *et al.* demonstrated that GF describes the hydration free energies of various solutes better than SC, despite its simpler mathematical expression.¹⁸

C. Model systems and numerical method

The systems we considered in this work were the liquid mixtures of water and 1-alcohols, where we varied the alcohols between methanol, ethanol, 1-propanol, and 1-butanol. The temperature and the pressure were 298.15 K and 1 bar, if not stated otherwise. Water and alcohols were modeled by the extended simple point charge (SPC/E)²⁴ and transferable potentials for phase equilibria-united atom (TraPPE-UA)²⁵ models, respectively. In the TraPPE-UA model, the methyl and the methylene groups are treated as united atoms. These molecular models are slightly modified by placing a Lennard-Jones (LJ) core of 0.1 nm diameter on the hydroxyl hydrogen atoms of both molecules.²⁶ All the intramolecular degrees are fixed to the stable geometry. In particular, the dihedral angles of alcohols are 180° (all-trans conformation).

In changing x_A from 0 to 1 under the isothermal–isobaric condition, the calculation was performed with the interval $\Delta x = 0.01$. Suppose that the total number density and the solvation free energies of both components are determined at $x_A = x - \Delta x$. Then, Eq. (4) is discretized as

$$\begin{aligned} & \frac{2(\rho_T(x) - \rho_T(x - \Delta x))}{\rho_T(x) + \rho_T(x - \Delta x)} + \frac{1 - x + \frac{\Delta x}{2}}{k_B T} \\ & \times [\mu_W^{SFE}(\rho_T(x), x) - \mu_W^{SFE}(\rho_T(x - \Delta x), x - \Delta x)] \\ & + \frac{x - \frac{\Delta x}{2}}{k_B T} \cdot [\mu_A^{SFE}(\rho_T(x), x) - \mu_A^{SFE}(\rho_T(x - \Delta x), x - \Delta x)] = 0, \end{aligned} \quad (18)$$

and the total density at $x_A = x$ was determined by solving Eq. (18) in an iterative way. The total number density at $x_A = 0$ (neat water) was set to be the experimental value, and the solvation free energy of the alcohol was calculated therein in the infinite dilution limit.

III. RESULTS AND DISCUSSION

A. Mixing Gibbs energy and liquid–liquid phase separation

The mixing Gibbs energies of four mixtures are shown in Fig. 1 as functions of the molar fraction of alcohol, x_A . The results of SC and GF are presented in Figs. 1(a) and 1(b), respectively. In both cases, the mixing Gibbs energies of all the mixtures are larger than the ideal one defined by the first term of the right-hand-side of Eq. (7), and their value increases with increasing the alkyl chain length of the alcohol, reflecting that the mixing of water with more hydrophobic alcohol is thermodynamically less favorable. The mixing Gibbs energies of the aqueous mixtures of methanol are a convex function of x_A using both expressions of the solvation free energy, corresponding to the fact that these mixtures are miscible at any composition. The mixing Gibbs energy of the butanol mixture exhibits a concave region at intermediate x_A , which is consistent with the liquid–liquid phase separation of the mixture in the real system. In the case of propanol, however, concave behavior is found in the theoretical mixing Gibbs energies of both SC and GF, although

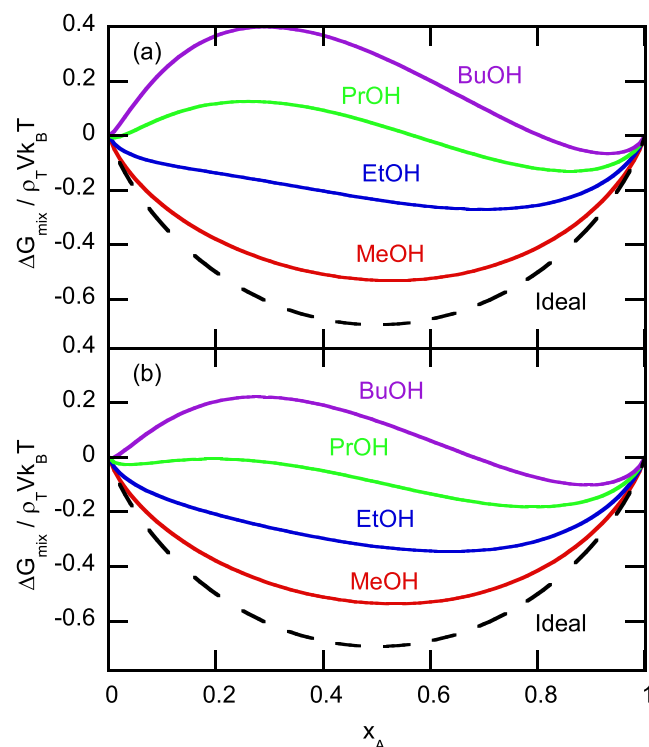


FIG. 1. Mixing Gibbs energies of the mixtures of water with methanol (red), ethanol (blue), 1-propanol (green), and 1-butanol (purple). The results of SC and GF are shown in panels (a) and (b), respectively, and the black dashed curves indicate the ideal mixing Gibbs energy defined by the first term of the right-hand-side of Eq. (7).

a real water + 1-propanol mixture is miscible at any composition. In addition, a weak concave region is found in the mixing Gibbs energy of water + ethanol mixture using the SC expression.

There are two possible reasons for the disagreement in the phase behavior of water + 1-propanol mixture. One is the systematic error associated with the approximations introduced in RISM theory, and the other is the insufficiency of the molecular model. Idrissi and Jedlovsky calculated the mixing Helmholtz energies of the mixtures of water with various alcohols.⁷ The results were dependent on the molecular models of both water and alcohols, and the mixing Helmholtz energy was sometimes positive in the case of 1-propanol. Therefore, we cannot judge, at present, which of the two reasons are mainly responsible for the liquid–liquid phase separation of the water + 1-propanol mixture in Fig. 1, and we consider that our theoretical method works qualitatively well, because it can describe the demixing trend with increasing the alkyl chain length of the alcohols.

The obtained mass densities of the four mixtures are shown as a function of x_A in Fig. 2. The results using the SC and GF expressions of the solvation free energy are presented in Figs. 2(a) and 2(b), respectively, and the experimental values are also plotted together in the two panels for comparison.^{27–30} The theoretical densities are larger than the experimental ones for all the mixtures. Because the

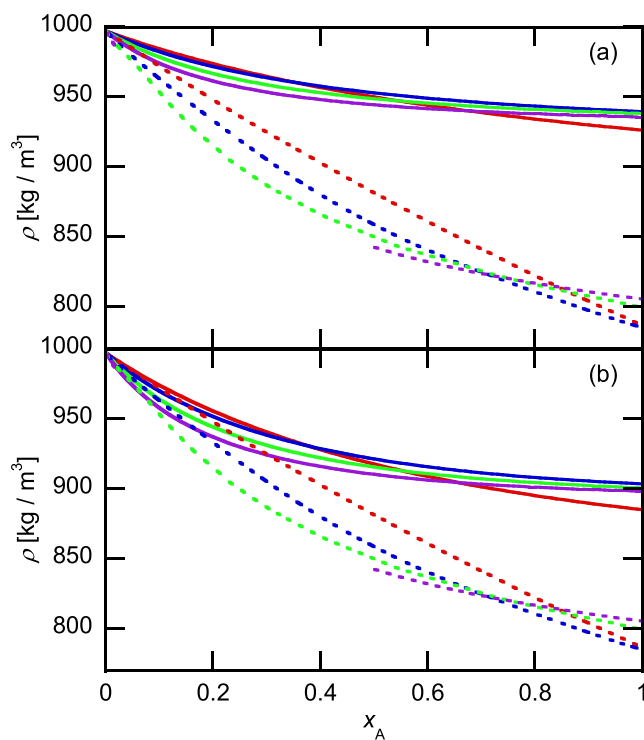


FIG. 2. Mass densities of the mixtures of water with methanol (red), ethanol (blue), 1-propanol (green), and 1-butanol (purple). The results using SC and GF expressions of the solvation free energy are shown in panels a and b, respectively. The theoretical and the experimental values are plotted with solid and dotted curves, respectively. The experimental value of the water + 1-butanol mixture is missing at $0.1 < x_A < 0.5$ due to the phase separation.

density is calculated by the integral from neat water, the error accumulates with increasing x_A , and the deviation from the experiment amounts to 15%–20% for neat alcohols. These mass density values are within the acceptable range of liquid density, but the deviation is quantitatively unsatisfactory. Although we could not find any MD simulation works on the densities of the alcohol + water mixtures using TraPPE-UA and SPC/E models, to the best of our knowledge, it has been reported that these models reproduce the experimental densities of the neat liquids at the ambient temperature and pressure well. The deviation is as small as 0.2% for the SPC/E model of water,³¹ while the simulation densities of methanol and ethanol are about 2%–3% lower than the experimental ones.^{32,33} Therefore, the deviation is caused fully by the error in the solvation free energy of the integral equation theory, and an improvement in the RISM integral equation theory would be required for future work.

Comparing the results of SC and GF, the densities of GF are closer to the experimental values than those of SC. In addition, GF properly shows that water + ethanol mixture is miscible at any composition, whereas SC wrongly predicts phase separation. Therefore, GF showed better performance than SC with respect to agreement with the experiments, which also agrees with the work of Tanimoto *et al.* that GF describes the hydration free energies of various solutes better than SC.¹⁸ Further analyses are thus performed hereafter based on the GF results.

Figure 3 shows the division of the mixing Gibbs energy due to various contributions. According to Eq. (7), the mixing Gibbs energy is described by the sum of three terms, named ideal, density, and solvation terms, and the numerical result of the division is plotted in Fig. 3(a). The ideal term is common to all the mixtures and is always negative. The solvation terms of all the mixtures are positive, and their absolute value increases with increasing the alcohol hydrophobicity. The variation of the mixing Gibbs energy with alcohol (Fig. 1) is ascribed to the solvation term. The absolute value of the density term was smaller than those of other two terms, but its contribution was not negligible. The density term works to stabilize the mixture, and the stabilization becomes stronger as the size of the alcohol increases.

The density term is further divided into the contributions of the excess mixing volume and the size difference [Eq. (8)]. These terms are plotted in Fig. 3(b) as a function of x_A . The excess volume contribution was almost zero, much smaller than that of the size difference. The increase in stabilization due to the density term from methanol to 1-butanol is thus ascribed to the increase in the molar volume of neat liquid.

Because the density term depends solely on the densities of the mixture and the neat liquids, it can be calculated from the experimental density, and the numerical results are shown in Fig. 3(c). The absolute value of the excess volume term from the experimental density was larger than the theoretical one, because the decrease in volume upon mixing was underestimated in the theoretical calculation. However, the size contribution dominated the density term in all the mixtures, and the neglect of the excess volume term worked well as a first approximation. The magnitude of the size contribution from the theoretical density [Fig. 3(b)] was a little smaller than that from the experimental density [Fig. 3(c)], which was attributed to the overestimation of the densities of neat alcohols (Fig. 2).

Given the mixing Gibbs energy (Fig. 1), the compositions of the phase boundary are determined by the two contact points of the

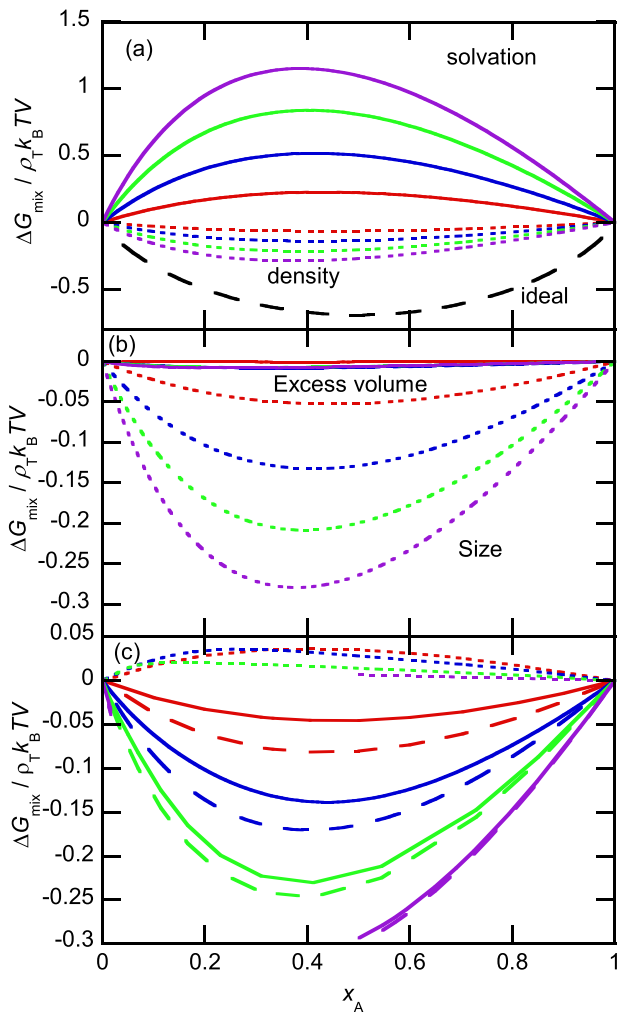


FIG. 3. Divisions of the mixing Gibbs energies of the mixtures of water with methanol (red), ethanol (blue), 1-propanol (green), and 1-butanol (purple). In (a), the ideal term, which is common to all the mixtures, is plotted with a black dashed line, whereas the solvation and the density terms are drawn assolid and dotted lines, respectively. In (b), the density term is further divided into the excess volume (solid) and size (dotted) terms. In (c), the density (solid), excess volume (dotted), and size (dashed) terms are calculated using the experimental densities.

common tangential line, as is described in thermodynamics textbooks. However, one may find difficulty in drawing the common tangential line for the water + 1-butanol mixture, because the convex behavior is not observed around $x_A = 0$ at the scale of Fig. 1. Mathematically speaking, $k_B T x_A \ln x_A$ in the first term of Eq. (7) should dominate the mixing Gibbs energy in the limit of $x_A \rightarrow 0$, because all the other terms are analytically around $x_A = 0$, and the convex region of the mixing Gibbs energy must be present in the very close vicinity of $x_A = 0$. In addition, it would also be difficult to determine the common tangential line for the water + ethanol mixture in Fig. 1(a), because the concave behavior is very weak. Therefore, we shall show an alternative graphical method to determine the phase boundary.³⁴

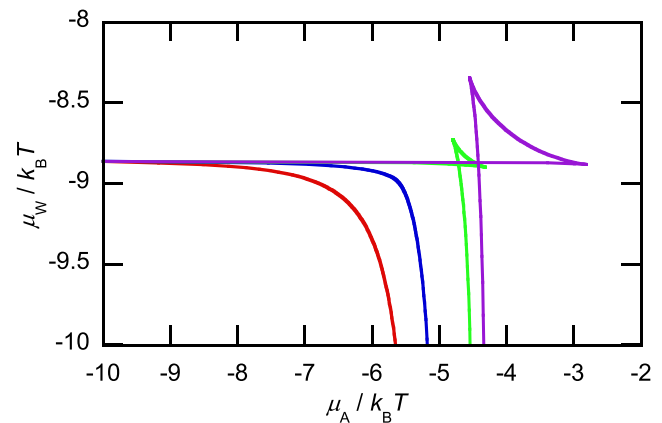


FIG. 4. The relation between chemical potentials of water and alcohols, μ_W and μ_A , respectively, for the mixtures of water with methanol (red), ethanol (blue), 1-propanol (green), and 1-butanol (purple). The alcohol concentration increases from the upper left corner to the lower right.

Figure 4 shows the relationship between μ_W and μ_A for all four mixtures. For the plot of the absolute values of these chemical potentials, we set $\mu_W^0 = \mu_A^0 = 0$ and $\rho_0 = 1 \text{ nm}^{-3}$. The upper left and lower right regions correspond to the water- and alcohol-rich regions, respectively. The thermodynamic stability condition requires that μ_W decreases and μ_A increases monotonically with increasing x_A . Therefore, a smooth variation of the chemical potentials is observed for the methanol and ethanol cases, where the liquid–liquid phase separation does not occur. By contrast, a knot is observed in cases of 1-propanol and 1-butanol. The phase boundary is then determined by the crossing point of the knots, because the chemical potentials of each component in both phases are equal there.

The thermodynamic consistency based on the requirement of the Gibbs–Duhem relation does not include the consistency between the thermodynamic quantities calculated from the solvation free energy and those from the low-wavenumber limit of the structure factor. The partial molar volume of each component can be obtained based on Kirkwood–Buff theory, which describes the long-wavelength limit of fluctuation in terms of thermodynamic quantities,^{35,36} but its consistency with the derivative of the total density (determined in the way described in Sec. II A) with respect to composition is not guaranteed. Similarly, the concentration fluctuation in the long-wavelength limit does not correspond to the second derivative of the Gibbs energy calculated from the solvation free energy. A converged solution of the RISM equation was obtained by our numerical calculation in the composition region of phase instability in which the long-range concentration fluctuations should diverge. In a theoretical work of Wilson and Lee, the integral equation theory was applied to the binary mixture of a LJ fluid, and the gas–liquid phase equilibrium was examined.³⁷ By optimizing the adjustable parameters in a bridge function, they succeeded in satisfying the relation between the long-wavelength density fluctuations and the derivatives of both pressure and chemical potentials. We consider that the extension of their theory to molecular liquids, if possible, could be an improvement of our RISM treatment of the liquid–liquid phase equilibrium.

B. Thermodynamic inconsistency without the Gibbs-Duhem relation

One of the novelties of our present work is the method for determining the mixture density according to the Gibbs–Duhem relation. If available, a simpler alternative would be to use the experimental density of the mixture. Although the Gibbs–Duhem relation must be satisfied by the theoretical calculation, free from approximations using experimental density, the Gibbs–Duhem relation does not hold, in general, due to the errors in the integral equation theory and the molecular model. Here, we demonstrate how the breakdown of the Gibbs–Duhem relation affects the theoretical treatment of the phase equilibrium by performing a calculation using the experimental density using the water + ethanol mixture as an example.

The chemical potentials of both components, μ_A and μ_W , are plotted in Fig. 5(a). Both values are smaller than the corresponding ones calculated using the density from the Gibbs–Duhem relation, particularly in the alcohol-rich region. The density determined using the Gibbs–Duhem relation is larger than the experimental one (see Fig. 2). Therefore, the smaller chemical potentials of both components using experimental density can be ascribed to the smaller packing fraction.

The Gibbs energy of the mixture was calculated using Eq. (5) in both calculations. The Gibbs energy using the experimental density shows a clear convex behavior around $x_A \approx 0.2$, suggesting a liquid–liquid phase separation. From the common tangent, the compositions of the phase separation are roughly estimated to be $x_A \approx 0.01$ and 0.8. According to Fig. 5(a), however, the chemical potentials μ_A and μ_W are not equal at these two compositions, and the chemical equilibrium does not hold between these two compositions. The apparent contradiction is because the Gibbs–Duhem relation is not satisfied in the calculation using the experimental density. In other words, based on Eq. (2), the pressure in the RISM calculation varies along the experimental density of isobaric mixing.

Another demonstration of the breakdown of the Gibbs–Duhem relation is the derivative of the Gibbs energy of the mixture with respect to composition. According to the Gibbs–Duhem relation, the derivative is related to the difference in the chemical potentials of the two components as

$$\frac{1}{\rho_T V} \cdot \frac{\partial G}{\partial x_A} = \mu_A - \mu_W. \quad (19)$$

Both sides of Eq. (19) are compared in Fig. 5(c). The relation is numerically confirmed when the density is determined based on the Gibbs–Duhem relation, and it is not confirmed when the experimental density is used in the calculation.

The numerical results shown in Fig. 5 emphasize the importance of the Gibbs–Duhem relation in discussing phase equilibria based on the Gibbs energy obtained from the solvation free energy of each component. The condition applies to methods based on the solvation free energy, including those using molecular simulations—not only to those based on integral equation theories. In order to satisfy the Gibbs–Duhem relation, the density of the mixture must be determined in a consistent way, with the combination of the molecular model and the approximations for the free-energy calculation, rather than using the experimental density.

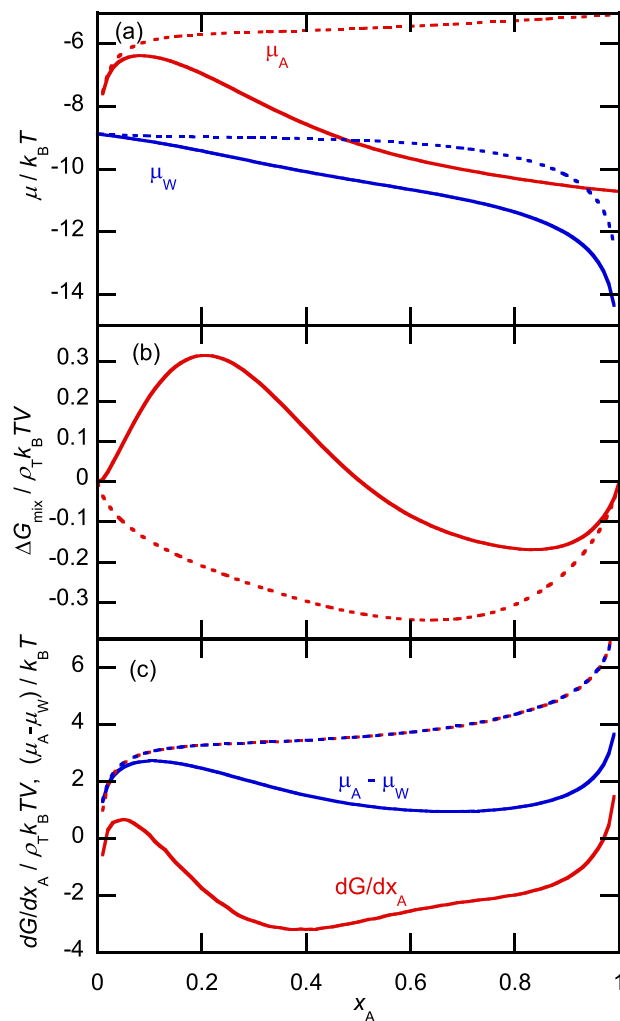


FIG. 5. The results of calculations using experimental density (solid) and the density determined by the Gibbs–Duhem relation (dotted). (a) Chemical potentials of water (blue) and ethanol (red). (b) Mixing Gibbs energy. (c) $\frac{1}{\rho_T V} \cdot \frac{\partial G}{\partial x_A}$ (red) and $\mu_A - \mu_B$ (blue). In panel (c), the two dotted curves overlap.

IV. SUMMARY

A theoretical method is proposed for determining the thermodynamic quantities and phase equilibria of liquid mixtures from the solvation free energy of each component obtained using the integral equation theory. The composition of the mixture was varied at constant pressure, and the density could also be determined based on the Gibbs–Duhem relation. The theoretical method was then applied to mixtures of water + 1-alcohols, and we succeeded in reproducing the destabilization of the mixture by increasing the hydrophobicity of the alcohols from methanol to 1-butanol. By contrast, the theoretical calculation overestimates the density in the alcohol-rich region, and the spurious liquid–liquid phase separation is also observed in the water + 1-propanol mixture. Therefore, we consider that improvement of the RISM theory would be necessary, together with

examination of the molecular models, to improve the agreement between the calculated and measured values.

ACKNOWLEDGMENTS

The idea for the analysis using Fig. 4 was originally proposed by Professor M. Ohba (Meijo University), and T.Y. is indebted to him for the valuable discussions. T.Y. and N.Y. were financially supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI (Grant Nos. 19H02677 and 22H05089). Numerical calculations were partially conducted at the Research Center for Computational Science, Institute for Molecular Science, National Institutes of Natural Sciences (Project No. 22-IMS-C076), and using the MCRP-S at the Center for Computational Science, University of Tsukuba.

AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

Tsuyoshi Yamaguchi: Data curation (lead); Methodology (lead); Resources (equal); Software (lead); Visualization (lead); Writing – original draft (lead); Writing – review & editing (equal). **Song-Ho Chong:** Conceptualization (equal); Writing – review & editing (equal). **Norio Yoshida:** Conceptualization (equal); Funding acquisition (lead); Resources (equal); Validation (lead); Writing – review & editing (equal).

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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