Theory of nonionic hydrophobic solutes in mixture solvent: Solvent-mediated interaction and solute-induced phase separation

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We present a theory of nonionic solutes in a mixture solvent composed of water-like and alcohol-like species. First, we show relationship among the solvation chemical potential, the partial volumes \(v_i\), the Kirkwood-Buff integrals, the second osmotic virial coefficient, and the Gibbs transfer free energy. We examine how the solute density \(n_3\) is coupled to the solvent densities \(n_1\) and \(n_2\) in thermodynamics. In the limit of small compressibility, we show that the space-filling condition \(\sum v_i n_i = 1\) nearly holds for inhomogeneous densities \(n_i\), where the concentration fluctuations of the solvent can give rise to a large solute-solute attractive interaction. We also derive a solute spinodal density \(n_3^{\text{sp}}\) for solute-induced instability. Next, we examine gas-liquid and liquid-liquid phase transitions induced by a small amount of a solute using the Mansoori, Carnahan, Starling, and Leland model for hard-sphere mixtures [J. Chem. Phys. 54, 1523 (1971)]. Here, we assume that the solute is close to its gas-liquid coexistence and the solute interacts repulsively with the water-like species but attractively with the alcohol-like one. We calculate the binodal and spinodal curves in the phase diagrams and examine nucleation for these two phase transitions.

I. INTRODUCTION

Long-standing research has been made on the role of hydrotropes in aqueous mixtures. Short-chain alcohols (such as methanol or tertiary butyl alcohol (TBA)) are typical examples of nonionic hydrotropes, which have an amphiphilic character but form no ordered structures in water due to their small sizes.\textsuperscript{12} A hydrotrope interacts with both water and hydrophobic solutes attractively, so it can improve the solute solubility as a cosolvent. As a unique effect, microemulsion-like droplets with radii of order \(10^2 - 10^3\) nm emerge in ternary mixtures of water, alcohol, and a hydrophobic solute\textsuperscript{13} as well as macroscopic domains, depending on the solute and alcohol fractions. The former have well-defined interfaces yielding the Porod tail in the scattering amplitude\textsuperscript{6}. This phenomenon is known by the name of \textit{Ouzo effect}.\textsuperscript{5} In such phase separation, a hydrophobic solute is accompanied by alcohol (as they go out of the original liquid) and the surface tension is considerably decreased due to interfacial adsorption of alcohol\textsuperscript{14,17,19,20,21,22,23,24,25}. Furthermore, scattering experiments\textsuperscript{4,5,6,17} have indicated the presence of nanometer-sized, micelle-like aggregates\textsuperscript{5} in a wider pre-Ouzo region outside the binodal. In molecular dynamics simulation on water-ethanol-octanol mixtures\textsuperscript{6,18,19,20,21,22}, a large fraction of octanol molecules aggregate to form the cores of such nanoclusters, where a large number of ethanol molecules cover and penetrate these clusters.

In this paper, we theoretically treat a ternary mixture of a water-like solvent, an alcohol-like cosolvent, and a nonionic hydrophobic solute. We need to properly account for the steric and attractive interactions between the solute and the two solvent species at very small solute fractions. To this end, we use a continuum model of hard-sphere mixtures by Mansoori, Carnahan, Starling, and Leland (MCSL)\textsuperscript{17}, which is a generalization of the Carnahan and Starling model of one-component hard-spheres (CS)\textsuperscript{18}. For simplicity, we assume attractive interactions in the van der Waals form, so we do not treat the hydrogen bonding among constituent protons and oxygens. We also do not include a surface-active character of the cosolvent, which leads to a reduction of the surface tension. In this scheme, we can examine how the selective solvation depends on the hard-sphere diameters, the attractive interaction parameters, and the compositions.

Our model solvent is assumed to be close to its gas-liquid coexistence, which is the case for water-alcohol mixtures. We use solutes which interact with the two solvent species very differently. In this situation, we encounter solute-induced gas-liquid and liquid-liquid phase transitions. In the former, the expelled solute particles form a gas at low pressures in the absence of appreciable solute-solute attractive interaction. The latter occurs when the attractive interaction between the solute and the second species is sufficiently strong. We examine two-phase coexistence, metastability, and instability for these phase transitions. We argue that the nucleation rate for the liquid-liquid transition is much larger than that for the gas-liquid one in the bulk in mixtures of water, alcohol, and a hydrophobic solute.

As a mysterious phenomenon, long-lived mesoscopic heterogeneities (presumably phase-separated domains) have been detected at very small fractions by dynamic light scattering, which emerge with addition of a small amount of a salt, a polymer, or a hydrophobic compound in one-phase states of aqueous mixtures or polymer solutions\textsuperscript{13,14,17,19,20,21,22,23}. From their diffusion constants, their sizes were in the range \(10^2 - 10^3\) nm. Such precip-
itation occurs for various combinations of a solute and a mixture solvent, so it should generally originate from selective solvation of a solute.\textsuperscript{28,29}

As a well-known solute-induced gas-liquid transition, we mention formation of nanobubbles with dissolution of gases such as O$_2$, H$_2$, and Ar in ambient water.\textsuperscript{30-35} For example, Ohgaki et al.\textsuperscript{31} realized bubbles of such gases with radius 50 nm and volume fraction 0.01 in quasi-steady states, where bubble coalescence was suppressed by salts added. Such bulk nanobubbles are usually produced by breakup of large bubbles, while surface nonobubbles on hydrophobic walls can appear via heterogeneous nucleation. In this problem, it is crucial that ambient water is very close to its gas-liquid coexistence. Then, we can explain the bubble stability by including the Gibbs transfer free energy in the bubble free energy provided that the solute-water attractive interaction is weaker than that among the water molecules.\textsuperscript{36-37}

In the literature,\textsuperscript{38-43} much attention has also been paid to assembly of strongly hydrophobic particles in ambient water, where the proximity to gas-liquid coexistence is crucial.\textsuperscript{44,45} In our viewpoint, it can be treated as quasi-steady states, where bubble coalescence was suppressed by surface tension. OHGAKI \textit{et al.} \textsuperscript{46,47} For example, Ohgaki \textit{et al.} \textsuperscript{41} realized bubbles of such gases with radius 50 nm and volume fraction 0.01 in quasi-steady states, where bubble coalescence was suppressed by salts added. Such bulk nanobubbles are usually produced by breakup of large bubbles, while surface nonobubbles on hydrophobic walls can appear via heterogeneous nucleation. In this problem, it is crucial that ambient water is very close to its gas-liquid coexistence. Then, we can explain the bubble stability by including the Gibbs transfer free energy in the bubble free energy provided that the solute-water attractive interaction is weaker than that among the water molecules.\textsuperscript{36-37}

Before discussing phase separation, we present a statistical-mechanical theory of solvation in ternary mixtures. We relate the solvation chemical potential to various physical quantities including the partial volumes $v_i$ ($i = 1, 2, 3$). For inhomogeneous densities $n_i$, we discuss how the space-filling condition $\sum v_i n_i = 1$ is nearly satisfied at long wavelengths in the limit of small compressibility. Namely, in nearly incompressible fluid mixtures, the deviations of $\sum v_i n_i$ from 1 should be small,\textsuperscript{48,49} while the concentration fluctuations can be enhanced due to molecular clustering. This is the case for water-alcohol mixtures. Then, the solvent-mediated, solute-solute interaction arises mostly from the solute-concentration coupling for not small cosolvent fractions.

The organization of this paper is as follows. In Sec. II, we will present the theoretical background of ternary mixtures. In Sec. III, we will use the MCSL model to investigate the solvation effects. In Sec. IV, we will examine the phase separation. Additionally, we will summarize the theory of the partial volumes and the Kirkwood-Buff integrals in Appendix A, examine the solute-induced gas-liquid transition in a one-component solvent in Appendix B, and present details of the CS model in Appendix C and MCSL model in Appendix D.

II. DILUTE SOLUTE IN MIXTURE SOLVENT

We consider nonionic ternary fluid mixtures. As a mixture solvent, we consider a water-like species (called water) ($i = 1$) and a cosolvent ($i = 2$). We then add a dilute solute ($i = 3$). Their densities are written as $n_i$. The solute composition (cosolvent molar fraction) is written as $X = n_2/(n_1 + n_2)$.

The binary mixture of the solvent is assumed to be in one-phase states away from the gas-liquid criticality. The electrostatic and amphiphilic interactions are not treated explicitly. The boundary effect is beyond the scope of this paper. In all the calculations to follow, we fix the temperature $T$ at 300 K, so we do not write the $T$-dependence of the physical quantities.

A. Solvation chemical potential

The Helmholtz free energy density $f(n_1, n_2, n_3)$ is expanded with respect to $n_3$ up to second order as\textsuperscript{38,37}

$$f = f_m + k_B T \ln(n_3 \lambda_3) - 1 + n_3 + \frac{1}{2} U_{33} n_3^2,$$

where $f_m(n_1, n_2)$ is the solvent free energy density and $\lambda_3(\propto T^{-1/2})$ is the solute thermal de Broglie length. The $k_B T \nu_3(n_1, n_2)$ is the solvation chemical potential for a solute particle, which arises from the interactions with its surrounding solvent. The last term represents the (direct) solute-solute interaction defined by

$$U_{33} = \lim_{n_3 \to 0} [(\partial f / \partial n_3)_T n_1, n_2 - k_B T / n_3],$$

where $n_1$ and $n_2$ are fixed and the ideal gas part ($\propto n_3^{-1}$) is subtracted. The chemical potentials $\mu_i = \partial f / \partial n_i$ and the pressure $p = \sum_j n_j \mu_j - f$ are expanded up to first order corrections as

$$\mu_i = \mu_m + k_B T \nu_3 n_3 \quad (i = 1, 2),$$

$$\mu_3 = k_B T \ln(n_3 \lambda_3^3) + \nu_3 + U_{33} n_3,$$

$$p = p_m + k_B T (1 + \zeta_3) n_3.$$  \hspace{1cm} (3)

Here, we define $\mu_m(n_1, n_2) = \partial f_m / \partial n_1$ and $p_m(n_1, n_2) = \mu_m n_1 + \mu_m n_2 - f_m$. We also introduce

$$\nu_3 = (\partial \nu_3 / \partial n_1)_T n_2, \quad \nu_3 = (\partial \nu_3 / \partial n_2)_T n_1, \quad \zeta_3 = n_1 \nu_3 + n_2 \nu_3 = n \nu / \partial n)_T X,$$

where $n = n_1 + n_2$ is the solvent number density. In this paper, we treat nearly incompressible solvents with small compressibility $\kappa_m$ such that the inequality $nk_B T \kappa_m \ll 1$ holds for any $X$. In terms of $p_m$, $\kappa_m$ is expressed as

$$\kappa_m^{-1} = (\partial p_m / \partial n)_{T, X},$$

where $T$ and $X$ are fixed in the derivative. See Eq.(A3) in Appendix A for another definition of the compressibility in many-component fluids. For example, $\kappa_m = 4.5 \times 10^{-4}/$MPa $\sim 0.05/n_c k_B T$ for ambient liquid water with density $n_c = 33$/$\text{nm}^3$ at 300 K and 1 atm.
It is convenient to introduce the partial volumes $v_i$ for the three species in the dilute limit $n_3 \to 0$. As will be shown in Appendix A, they are expressed as

$$v_i = \kappa_m(\partial p_m/\partial n_i) \quad (i = 1, 2),$$  \hfill (10)  

$$v_3 = k_B T \kappa_m (1 + \zeta_3).$$  \hfill (11)

These volumes depend on $T$, $p$, and $X$. For not small solutes with $v_3 \gg n^{-1}$, we find $\zeta_3 \approx v_3/k_B T \kappa_m \gg 1$ in nearly incompressible fluids (see Fig.3(d)). To understand the physical meaning of $v_i$, let us prepare a reference solvent with $n_1 = n_{r1}$ and $n_2 = n_{r2}$. We then add a solute at a small density $n_3$. If $T$ and $p$ are held fixed, Eq.(A4) in Appendix A gives

$$v_1(n_1 - n_{r1}) + v_2(n_2 - n_{r2}) + v_3 n_3 \approx 0,$$  \hfill (12)

which holds in linear order in $n_3$. If $T$, $n_1$, and $n_2$ are held fixed (in a fixed volume), the pressure increases by $v_3 n_3 / \kappa_m$ from Eq.(A4).

### B. Kirkwood-Buff theory

We also introduce the Kirkwood-Buff integrals $^{49-57}$.

$$G_{ij} = \int dr [g_{ij}(r) - 1],$$  \hfill (13)

where $g_{ij}(r)$ are the radial distribution functions tending to 1 at large $r$. They are related to the density correlation functions $H_{ij}(r) = \langle \delta n_i(r) \delta n_j(0) \rangle$ as

$$H_{ij}(r) = n_i n_j [g_{ij}(r) - 1] + n_i \delta_{ij} \delta(r).$$  \hfill (14)

Here, we write the microscopically defined number densities as $\hat{n}_i(r)$ and their deviations as $\delta \hat{n}_i(r) = \hat{n}_i(r) - n_i$ with care to avoid confusion with the averages $n_i$. Then,

$$I_{ij} = \int dr H_{ij}(r) = n_i n_j G_{ij} + n_i \delta_{ij},$$  \hfill (15)

which are the long-wavelength limits of the structure factors $S_{ij}(q) = \int dr \ exp[iq \cdot r] H_{ij}(r)$. Hereafter, for any space-dependent variables $\hat{A}(r)$ and $\hat{B}(r)$, we write $^{45}$

$$\langle \hat{A} : \hat{B} \rangle \equiv \int dr [\langle \hat{A}(r) \hat{B}(0) \rangle - \langle \hat{A} \rangle \langle \hat{B} \rangle],$$  \hfill (16)

Then, we have $I_{ij} = \langle \hat{n}_i : \hat{n}_j \rangle$.

The $G_{ij}$ for the solvent species $(i, j = 1, 2)$ smoothly tend to those without solute as $n_3 \to 0$. We assume that $G_{i3}$ $(i = 1, 2, 3)$ tend to well-defined dilute limits $G_{i3}^0 = \lim_{n_3 \to 0} G_{i3}$. From Eqs.(11) and (A12), we obtain

$$\zeta_3 = -(n_1 v_1 G_{13}^0 + n_2 v_2 G_{23}^0)/k_B T \kappa_m,$$  \hfill (17)  

$$v_3 = k_B T \kappa_m - (n_1 v_1 G_{13}^0 + n_2 v_2 G_{23}^0).$$  \hfill (18)

### C. Density fluctuations in binary mixtures

We here examine the fluctuations in binary solvents (with $n_3 = 0$). Using the deviations $\delta \hat{n}_1$ and $\delta \hat{n}_2$, we introduce microscopically fluctuating variables for the volume fraction and the concentration of the solvent by

$$\delta \hat{\phi}(r) = v_1 \delta \hat{n}_1 + v_2 \delta \hat{n}_2,$$  \hfill (19)  

$$\delta X(r) = n^{-2}(n_1 \delta \hat{n}_2 - n_2 \delta \hat{n}_1),$$  \hfill (20)

From results in Appendix A, we find

$$\langle \delta \hat{\phi} : \delta \hat{\phi} \rangle = k_B T \kappa_m, \quad \langle \delta X : \delta X \rangle = \chi, \quad \langle \delta \hat{\phi} : \delta X \rangle = 0.$$  \hfill (21)

The last relation indicates orthogonality between $\delta \hat{\phi}$ and $\delta X$. In terms of $G_{ij}$ for the solvent, the compressibility $\kappa_m$ and the concentration variance $\chi$ are written as

$$k_B T \kappa_m = v_1^2 n_1 + v_2^2 n_2 + \sum_{i,j=1,2} v_i n_i v_j n_j G_{ij},$$  \hfill (22)  

$$\chi = n_1 n_2 / n^3 + (n_1^2 n_2^2 / n^3) (G_{11} + G_{22} - 2G_{12})$$

+ $k_B T (\partial X / \partial \Delta)_{T,p}$,  \hfill (23)

where $G_{ij}$ are those for $n_3 = 0$ and $\Delta = \mu_2 - \mu_1$. The second line of Eq.(23) follows from Eq.(A13) $^{45}$. Here, the matrix $I_{ij}$ is diagonalized by the linear transformations in Eqs.(19) and (20), so its determinant is given by

$$I_{11} I_{22} - I_{12}^2 = n^4 k_B T \kappa_m \chi.$$  \hfill (24)

In nearly incompressible mixtures, the fluctuations of $\delta \hat{\phi}$ are small, but those of $\delta \hat{X}$ can grow due to molecular clustering $^{58-61}$ or near the consolute criticality $^{45}$.

The scattering intensity is proportional to the structure factor $I(q) = \langle |Aq|^2 \rangle$ of a linear combination $A = Z_1 \hat{n}_1 + Z_2 \hat{n}_2$, where $Z_1$ and $Z_2$ are constants. Here, $A = (Z_1 v_1 + Z_2 v_2) \delta \hat{\phi} + (Z_1 v_1 - Z_2 v_2) n^2 \delta \hat{X}$, so Eq.(21) yields the long-wavelength limit $^{51,62}$

$$I(0) = (Z_1 n_1 + Z_2 n_2)^2 k_B T \kappa_m + (Z_2 v_1 - Z_1 v_2)^2 n^4 \chi.$$  \hfill (25)

In water-alcohol mixtures, the concentration fluctuations are enhanced on nanometer scales due to the hydrogen-bonding interaction, on which a number of scattering experiments $^{63-66}$ and molecular dynamics simulations $^{58-61}$ were performed. The combination $n(G_{11} + G_{22} - 2G_{12})$ in $\chi$ in Eq.(23) exhibits a maximum as a function of the alcohol fraction, which is about 5 for methanol $^{64}$, 20 for ethanol $^{60,62,65}$, and 100 for TBA $^{52,64}$ and 1-propanol $^{52,66}$, depending on the degree of hydrophobic association of alcohol molecules $^{61}$.

For our model mixture to be explained in Sec.III, we display the mixture quantities in Fig.1 and the normalized solvation chemical potential $\nu_3$ in Eq.(2) in Fig.2 at $T = 300$ K and $p = 1$ atm. The behaviors in Fig.1 resemble those observed in water-alcohol mixtures, though we do not account for the hydrogen bonding.
Here, we neglect the cosolvent molar fraction with \( d \) between the two species. The hard-sphere diameters are in one-phase states due to a strong attractive interaction between the two species. The hard-sphere diameters are \( d_1 = 3 \) Å and \( d_2 = 1.3d_1 \). Thus, \( d_1^3 = 0.0180 \) L/mol and \( d_2^{-3} = 55.6 \) mol/L. Plotted are (a) partial volumes \( v_1 \) and \( v_2 \) divided by \( d_1^3 \) and density \( n \) multiplied by \( d_1^3 \), (b) Kirkwood-Buff integrals \( G_{ij} \), divided by \( d_1^3 \), (c) normalized compressibility \( n k_B T \kappa_m \), \( \leq 1 \), and (d) concentration variance \( \chi \) in Eq.(23) multiplied by \( n \). In (d), \( n(G_{11} + G_{22} - 2G_{12}) \) is also shown (inset), whose maximum is about 10 at \( X \sim 0.2 \). See Sec.III for details of our model.

### D. Density fluctuations in ternary mixtures

In this subsection, we superimpose small density changes \( \delta n_i(r) \) on the homogeneous averages \( n_i \). These \( \delta n_i \) are coarse-grained variables slowly varying in space compared to the potential range. From Eq.(2) the second-order change in \( f \) is expressed as

\[
\delta f_{\text{in}} = \frac{1}{2} k_B T \sum_{i,j=1,2,3} I^{ij} \delta n_i \delta n_j,
\]

where \( k_B T I^{ij} = \partial^2 f / \partial n_i \partial n_j = \partial \mu_i / \partial n_j = \partial \mu_j / \partial n_i \). The matrix \( \{I^{ij}\} \) is equal to the inverse of the variance matrix \( \{I_{ij}\} \) in Eq.(15). For small \( n_3 \), Eq.(2) yields

\[
I^{13} = \nu_{3i} \quad (i = 1,2), \quad I^{33} = 1/n_3 + U_{33}/k_B T.
\]

Here, we neglect the \( n_3 \)-dependence of \( I^{ij} \) and \( I^{13} \) \( (i,j = 1,2) \) retaining the first diverging term \( \propto n_3^{-1} \) in \( I^{33} \), which much simplifies the following calculations.

We introduce coarse-grained deviations of the volume fraction and the concentration of the solvent by

\[
\delta \phi = v_1 \delta n_1 + v_2 \delta n_2, \quad \delta X = n^{-2}(n_1 \delta n_2 - n_2 \delta n_1),
\]

which are of the same forms as \( \delta \tilde{\phi} \) and \( \delta \tilde{X} \) in Eqs.(19) and (20). In terms of \( \delta \tilde{\phi} \) and \( \delta \tilde{X} \) the solute-solvent coupling terms in \( \delta f_{\text{in}}/k_B T \) are rewritten as

\[
(I^{13} \delta n_1 + I^{23} \delta n_2) \delta n_3 = (\zeta_3 \delta \phi + g_3 \delta X) \delta n_3,
\]

where \( \zeta_3 \) is given in Eqs.(8) and (17). We define the solute-concentration coupling constant \( g_3 \) by

\[
g_3 = n^2 (v_1 \nu_{32} + v_2 \nu_{31}) = \left( \partial \nu_3 / \partial X \right)_{T,p}.
\]

At fixed \( T \) and \( p \), Eqs.(A4) and (28) give \( v_1 \delta n_1 + v_2 \delta n_2 = 0 \) and \( n^2 \delta X = v_1^{-1} \delta n_1 = -v_2^{-1} \delta n_1 \), leading to Eq.(30). In terms of the Kirkwood-Buff integrals and the fluctuation variances, \( g_3 \) can also be expressed as

\[
g_3 = -n_1 n_2 (G_{23}^0 - G_{13}^0) = - \lim_{n_3 \to 0} \left( \delta \tilde{X} \right)_{n_3 \to 0}/\left( \delta n_3 \right)_{n_3 \to 0} /
\]

with the aid of Eqs.(21) and (A12). The difference \( G_{23}^0 - G_{13}^0 = k_B T \kappa_3^{-1} (\partial \nu_3 / \partial \mu_2)_{T,p} \) represents the preferential adsorption of a cosolvent around a solute particle. Thus, \( g_3 = (\partial \nu_3 / \partial X)_{T,p} < 0 \) for hydrophobic cosolvents.

For nonvanishing \( \zeta_3 \) and \( g_3 \), \( \delta f_{\text{in}}/k_B T \) is written as

\[
\frac{\delta f_{\text{in}}}{k_B T} = \frac{(\delta \phi_{\text{tot}})^2}{2 k_B T \kappa_m} + \frac{(\delta X + g_3 \delta n_3)^2}{2 \chi} + \frac{(\delta n_3)^2}{2 I_{33}^3}.
\]

In the first term, we define the deviation of the volume fraction including a small solute contribution as

\[
\delta \phi_{\text{tot}} = v_1 \delta n_1 + v_2 \delta n_2 + v_3^{\text{in}} \delta n_3.
\]
where we introduce a solute volume $v_{3}^{\text{in}}$ by

$$v_{3}^{\text{in}} = k_{B}T\kappa_{m}\zeta_{3} = v_{3} - k_{B}T\kappa_{m}. \quad (34)$$

From Eq.(11) $v_{3}^{\text{in}}$ is only slightly smaller than $v_{3}$ for small $\kappa_{m}$. The second term in Eq.(32) indicates that the solvent composition tends to change by $-\chi\delta n_{3}$ with the doping. In the third term, $I_{33}$ is the solute variance in Eq.(15). From Eq.(27) its inverse is expressed as

$$1/I_{33} = 1/n_{3} + U_{33}^{\text{eff}}/k_{B}T. \quad (35)$$

The $U_{33}^{\text{eff}}$ is the effective interaction parameter written as

$$U_{33}^{\text{eff}} = U_{33} - k_{B}T\sum_{i,j=1,2}I_{ij}\nu_{3i}\nu_{3j}$$

where the second line follows from Eq.(32). The second term in the second line is also written as $-(k_{B}T)^{2}\kappa_{m}\zeta_{3}^{2}$ in terms of $\zeta_{3}$. The last two terms are negative representing the solvent-mediated attractive interaction. Here, $I_{33} = (\partial\mu_{3}/\partial n_{3})_{T,\mu_{1},\mu_{2}}$ from Eq.(A7), so $U_{33}^{\text{eff}}$ is defined as

$$U_{33}^{\text{eff}} = \lim_{n_{3} \to 0} [(\partial\mu_{3}/\partial n_{3})_{T,\mu_{1},\mu_{2}} - k_{B}T/n_{3}]. \quad (37)$$

which should be compared with $U_{33}$ in Eq.(3).

In the second line of Eq.(36), the second term much exceeds $-k_{B}T\zeta_{3}$ for small solute particles in nearly incompressible solvents. This contribution is already known for one-component solvent. In Sec.III, we shall see that the third term can even be larger than the second term. Thus, the right hand side of Eq.(35) vanishes when $n_{3}$ is equal to a spinodal density given by

$$n_{3}^{\text{spi}} = -k_{B}T/U_{33}^{\text{eff}}. \quad (38)$$

We then have $I_{33} = n_{3}((1-n_{3}/n_{3}^{\text{spi}})$ and

$$G_{33} = 1/(n_{3}^{\text{spi}} - n_{3}), \quad (39)$$

at small nonvanishing $n_{3}$. Its dilute limit is given by

$$G_{33}^{0} = 1/n_{3}^{\text{spi}} = -U_{33}^{\text{eff}}/k_{B}T. \quad (40)$$

Here, $G_{33} > 0$ for $n_{3} < n_{3}^{\text{spi}}$, while $G_{33} < 0$ for $n_{3}^{\text{spi}} < 0$. If $G_{33} > 0$, the interaction among the solute particles is attractive on the average, which can occur even if the direct interaction is repulsive ($U_{33}$ > 0). With further increasing $n_{3}$, we eventually encounter the unstable regime $n_{3} > n_{3}^{\text{spi}} > 0$, leading to spinodal decomposition of gas-liquid or liquid-liquid phase transition. Similarly, Roij and Mulders calculated demixing spinodal for binary hard-rod mixtures using the second virial expansion of the Helmholz free energy density as in Eq.(26).

We also notice that the density fluctuations are enhanced as $n_{3} \to n_{3}^{\text{spi}}$ in one-phase states. From Eq.(32), the concentration variance $\chi_{R} = \langle \hat{X} - \bar{X} \rangle$ increases as

$$\chi_{R} = \chi + g_{3}^{2}\chi^{2}n_{3}/(1 - n_{3}/n_{3}^{\text{spi}}). \quad (41)$$

where no phase-separated droplets are assumed and $\chi$ is defined in Eqs.(21) and (23). The second term can be significant compared to the background $g_{3}^{2}\chi n > 1$ even for small $n_{3}$ (see Fig.3(e) and Eq.(65)).

E. Space-filling condition

Because $v_{3}^{\text{in}} \approx v_{3}$ for small $\kappa_{m} \ll (nk_{B}T)^{-1}$, the combination $\delta\phi_{\text{tot}}$ in Eq.(33) represents the deviation of the total volume fraction from 1. The space integral of the first term in Eq.(32) yields the steric free energy,

$$F_{\text{steric}} = \int dr\frac{1}{2\kappa_{m}}[\sum_{j=1,2,3}v_{j}\delta n_{j}]^{2}, \quad (42)$$

where $\delta n_{i}$ can vary slowly in space. This free energy serves to realize the space-filling $\sum_{j}v_{j}n_{j} = 1$ even for inhomogeneous densities in the limit of small $\kappa_{m}$. See Eqs.(12) and (46) where this condition holds for homogeneous density changes. Previously, the steric free energy in the same form was assumed for polymer mixtures.

If the composition-dependence of $v_{i}$ is weak at given $T$ and $p$, the space-filling holds at any compositions with common $v_{i}$ (depending on $T$ and $p$). In our case, this is roughly the case in Fig.1(a) and Fig.3(b). It is worth noting that the Flory-Huggins theory for polymer mixtures and the Bragg-Williams theory of binary alloys are based on the space-filling assumption, where the volumes of constituent particles (monomers for polymers) are equal to the cell volume of an incompressible lattice.

F. Osmotic pressure

For mixture solvents, the osmotic pressure $\Pi$ is the pressure difference $\Pi = p(n_{1}, n_{2}, n_{3}) - p(n_{1}, n_{2}, 0)$ at fixed chemical potentials $\mu_{i}(n_{1}, n_{2}, n_{3}) = \mu_{i}(n_{1}, n_{2}, 0)$ ($i = 1, 2$), where $n_{1}$ and $n_{2}$ are the solvent densities in a reference state with $n_{3} = 0$. In the virial expansion $\Pi = k_{B}T(n_{3} + B_{2}n_{3}^{2} + \cdots)$, McMillan and Mayer found the relation $B_{2} = -G_{33}^{0}/2$ for one-component solvents. Large negative $B_{2}$ eventually leads to solute aggregation. At fixed $T$, $\mu_{1}$, and $\mu_{2}$, we have $d\Pi = n_{3}d\mu_{3} = k_{B}Tn_{3}I_{33}^{-1}dn_{3}$ from Eq.(A8). Then,

$$\left(\frac{\partial \Pi}{\partial n_{3}}\right)_{T,\mu_{1},\mu_{2}} = k_{B}T/(1 + n_{3}G_{33})$$

$$= k_{B}T(1 - n_{3}/n_{3}^{\text{spi}}) \quad (43)$$

where use is made of Eq.(39) in the second line. Thus,

$$B_{2} = -1/2n_{3}^{\text{spi}} = -G_{33}^{0}/2 = U_{33}^{\text{eff}}/2k_{B}T. \quad (44)$$

From Eq.(A8) we also find

$$\left(\frac{\partial n_{i}}{\partial n_{3}}\right)_{T,\mu_{1},\mu_{2}} = \frac{n_{i}G_{33}}{1 + n_{3}G_{33}} \quad (i = 1, 2). \quad (45)$$
This is integrated to give \( n_i - n_{ri} \cong n_i G_{ri} n_3 \), for small \( n_3 \) at fixed \( T, \mu_1, \) and \( \mu_2 \). Therefore, from Eqs. (18) and (34), we find another form of the space-filling condition,

\[
v_1(n_1 - n_{r1}) + v_2(n_2 - n_{r2}) + v_3^n n_3 \cong 0, \tag{46}
\]

where \( v_3 \) in Eq. (12) is replaced by \( v_3^n \).

For nonionic solutes in water, \( B_3 \) has been examined in experiments\(^88\) and simulations\(^89\). For charged colloidal particles in a mixture solvent, \( B_2 \) changed from positive to negative on approaching the consolute critical point before their near-critical aggregation\(^25\).\(^76\).

G. Ostwald coefficient, Gibbs transfer free energy \( \Delta G \), and Henry’s constant \( k_H \)

The solvation chemical potential \( k_B T n_3 \) is measurable in two-phase coexistence. Let phase \( \alpha \) be a a solute-poor liquid and phase \( \gamma \) be a solute-rich gas or liquid. The densities are \( n_{i\alpha} \) in phase \( \alpha \) and \( n_{i\gamma} \) in phase \( \gamma \) (\( i = 1, 2, 3 \)). The Ostwald coefficient is defined by \( L = n_{i\gamma}^2 / n_{i\alpha}^2 \) for the solute in equilibrium. Its dilute limit is written as\(^29\)

\[
L_0 = \lim_{n_3 \to 0} L = \exp[-(\Delta G)_3/k_B T], \tag{47}
\]

where \((\Delta G)_3 \) is the Gibbs transfer free energy (from \( \gamma \) to \( \alpha \) phase) for a solute particle. Since \( \mu_2 \) in Eq. (5) assumes the same value in the two phases, we find

\[
(\Delta G)_3/k_B T = \nu_3(n_{1\gamma}^2, n_{2\gamma}^2) - \nu_3(n_{1\alpha}^2, n_{2\alpha}^2). \tag{48}
\]

If the \( \gamma \) phase is a gas far below the criticality, we obtain \((\Delta G)_3/k_B T \cong \nu_3(n_{1\gamma}^2, n_{2\gamma}^2)\), since \( \nu_3 \) is small in gas. For example, \((\Delta G)/k_B T \cong 3.4 \) for \( \text{O}_2 \) in water at \( T = 300 \text{ K} \).

Henry’s constant is defined in gas-liquid coexistence. Its usual definition is \( k_H = f_3/x_{3\gamma}^w \), where

\[
f_3 = k_B T \alpha_3^3 \exp(\mu_2/k_B T) \cong k_B T n_{3\gamma}^w v_3 \tag{49}
\]

is the solute fugacity and \( x_{3\gamma}^w = n_{3\gamma}^w / \sum_j n_{j\gamma}^w \) is the solute molar fraction in liquid\(^80\). As \( n_3 \to 0 \) we have

\[
k_H^w = \lim_{n_3 \to 0} k_H = k_B T n_\ell \exp(\nu_3(n_{1\gamma}^2, n_{2\gamma}^2)), \tag{50}
\]

where \( n_\ell = n_{1\gamma}^2 + n_{2\gamma}^2 \) is the liquid density. Thus, \( k_H^w \cong k_B T n_\ell / L_0 \) far from the criticality.

Tucker and Christian\(^80\) furthermore obtained the correction \( k_H/k_H^w - 1 = -8\chi_{13}^3 \) at small \( x_{3\gamma}^w \) for benzene in water at \( 308 \text{ K} \), which is weakly hydrophilic with \( L_0 = 3.6 \). In Appendix B, \( k_H/k_H^w - 1 \) will be calculated to linear order in \( n_{1\gamma}^2 \) or \( n_{2\gamma}^2 \) for one-component solvents as

\[
k_H/k_H^w - 1 = (2B_3^w + 1/n_{1\gamma}^2 - 2v_{3\gamma}^w) n_{1\gamma}^2 + k_B T \kappa_{n3} n_{1\gamma}^2
\]

\[
+ v_{3\gamma}^w (n_{1\gamma}^2 - n_{1\alpha}^2)^{-1}(n_{1\gamma}^2 n_{2\gamma}^2 - n_{1\alpha}^2 n_{3\alpha}^2), \tag{51}
\]

where \( \kappa_{n3}, v_{3\gamma}^w, \) and \( B_3^w \) are the liquid values of \( \kappa, v_3, \) and \( B_2 \). For benzene, we have \( n_1 B_2^w \sim -50 \) and \( n_{1\gamma} v_{3\gamma}^w \sim 10 \), so the first term is dominant in Eq. (51) and can well explain the observed correction\(^80\), as was shown by Rossky and Friedman\(^28\). However, for hydrophilic solutes with \( L_0 \ll 1 \), we have \( k_H/k_H^w - 1 \cong v_{3\gamma}^w n_{1\gamma}^2 \). See Appendix B for the correction \( L/L_0 - 1 \) of the Ostwald coefficient.

III. NUMERICAL RESULTS ON SOLVATION

In the density functional theory\(^\text{82-84}\), use has been made of the Carnahan-Starling (CS) model for pure fluids\(^18\) and the Mansoori-Carnahan-Starling-Leland (MCSL) model for mixtures\(^24\) (see Appendices C and D). These models provide the equation of state for hard spheres in agreement with simulations\(^12\). In our previous paper\(^27\), we used the MCSL model for water-oxygen mixtures. In this paper, we use it for ternary mixtures.

A. MCSL model and van der Waals model

For the coarse-grained smooth densities \( n_i \), we write the Helmholtz free energy density as

\[
f = \sum_{i=1,2,3} k_B T n_i [\ln(n_i \lambda_i^3) - 1] + f_h + f_a, \tag{52}
\]

where \( f_h \) is the hard-sphere part and \( f_a \) is the attractive part. The potential from the boundary walls\(^82\) is not written. Each species has a hard-sphere diameter \( d_i \). We write the diameter ratios as

\[
\alpha_2 = d_2/d_1, \quad \alpha_3 = d_3/d_1. \tag{53}
\]

In the literature\(^28\), \( f_a \) has the pairwise form with Lennard-Jones potentials \( \phi_{ij}(r) \) for \( r > d_{ij} = (d_i + d_j)/2 \). In this paper, we use the simple van der Waals form\(^45\)

\[
f_a = -\frac{1}{2} \sum_{i,j=1,2,3} w_{ij} n_i n_j. \tag{54}
\]

The coefficients \( w_{ij} \) are related to the hard-sphere diameters and the Lennard-Jones energies \( \epsilon_{ij} \) by\(^3\)\(^4\)

\[
w_{ij} = -\int_{r>d_{ij}} dr \phi_{ij}(r) = \frac{4}{9} \sqrt{2} \epsilon_{ij}(d_i + d_j)^3. \tag{55}
\]

In our scheme, the chemical potentials are written as

\[
\mu_i = k_B T \ln(n_i \lambda_i^3) + \mu_{hi} - \sum_j w_{ij} n_j. \tag{56}
\]

See Eq. (D3) for the hard-sphere part \( \mu_{hi} = \partial f_h / \partial n_i \). As \( n_3 \to 0 \), we calculate \( \nu_3 \) and \( U_{33} \) in Eq. (2) as

\[
\nu_3(n_1, n_2) = \lim_{n_3 \to 0} \mu_{hi} - w_{13} n_1 - w_{23} n_2 / k_B T, \tag{57}
\]

\[
U_{33}(n_1, n_2) = \lim_{n_3 \to 0} (\partial \mu_{hi} / \partial n_3) - w_{33}. \tag{58}
\]

Here, \( \nu_3 \) and \( U_{33} \) are complicated functions of \( \eta = \pi(n_1 d_1^3 + n_2 d_2^3) / 6, X, \alpha_2, \) and \( \alpha_3 \) (see Appendix D). They increase steeply with increasing \( \eta \geq 0.5 \) and behave as \( \alpha_2^2 \propto \eta_3 \) and \( \alpha_3^2 \propto \eta_3^2 \), respectively, for \( \alpha_3 > 1 \). In particular, for one-component solvents (\( n_2 = 0 \)) we obtain\(^28\)

\[
\nu_3(n_1, 0) = (3\alpha_3 + 6\alpha_3^2 - \alpha_3^3) u_1 + 3\alpha_3^2 u_1^2 + \alpha_3^3 u_1^3 (4 + 2u_1)
\]

\[-(\alpha_3 - 1)^2 (2\alpha_3 + 1) \ln(1 - \eta_1) - w_{13} n_1 / k_B T, \tag{59}
\]

where \( \eta_1 = (\pi d_1^3 / 6) n_1 \) and \( u_1 = \eta_1 / (1 - \eta_1) \).
existence as a reference state of the first species, we set

\[ n_r = 1.0049d_1^{-3}, \quad n_\ell = n_r - 1.5 \times 10^{-5}n_r, \]

\[ n_g = p_{\text{ex}}^0/k_BT = 2.1 \times 10^{-5}n_r. \]  

(61)

The hard-sphere volume fraction is \( \eta_1 = \pi n_r d_1^3/6 = 0.526 \) for this \( n_r \). The \( n_\ell \) here is larger than the corresponding density of real water by 10%. The compressibility is \( 1.71 \times 10^{-4}/\text{MPa} = 0.023/n_r k_BT \) in the reference state, while the experimental one is \( 4.5 \times 10^{-4}/\text{MPa} \).

We choose the parameters of the second species such that the mixture solvent remains in one-phase states at any \( X \) in ambient conditions. We thus set

\[ d_2 = 3.9 \, \text{Å}, \quad \epsilon_{12}/k_B = 550 \, \text{K}, \quad \epsilon_{22}/k_B = 500 \, \text{K}, \quad (62) \]

for which \( w_{12}/\epsilon_{11} d_1^3 = 22.44 \) and \( w_{22}/\epsilon_{11} d_1^3 = 29.47 \). Here, \( \epsilon_{12} \) and \( \epsilon_{22} \) are close to \( \epsilon_{11} \). In Fig.1, we have displayed the mixture properties. We further make remarks. (i) As \( n_2 \to 0 \), the second species has the Gibbs transfer free energy \( (\Delta G)_{12} \approx -7.8 k_B T \) at \( T = 300 \, \text{K} \), so it is hydrophilic. (ii) At \( T = 300 \, \text{K} \), the gas-liquid coexistence pressure \( p_{\text{ex}}^0 \) without solute is calculated as 0.031, 0.075, 0.089, 0.10, 0.11, and 0.13 in units of atm, where the molar fraction \( X^\alpha \) of the second species in liquid is 0, 0.2, 0.4, 0.6, 0.8, and 1.0, respectively. These low pressures stem from the strong hydrophilicity of the second species (see Eq.(B3) and sentences below it). Note that the coexistence pressure of real water-alcohol mixtures is very low at room temperatures.

We then add a small amount of a hydrophobic solute. In most cases to follow, we set \( \epsilon_{13} = \epsilon_{33} = 0 \) and \( \epsilon_{23} = 300 \, \text{K} \), for which the solute interacts with the two solvent species differently, resulting in a large solute-concentration coupling. In Fig.2, we have shown the overall behaviors of \( \nu_3 \) in the \( X-\eta \) plane at fixed \( \epsilon_3 \) and \( \nu_3/\alpha_3^2 \) in the \( \epsilon_3-\eta \) plane at fixed \( X \). The \( \nu_3 \) increases steeply with increasing \( \eta \) for \( \eta \gtrsim 0.5 \), decreases with increasing \( X \), and behaves as \( \alpha_3^2 \) for \( \alpha_3 \gtrsim 1 \) (see Appendix D for analytic results). The asymptotic relation \( \nu_3 \sim \alpha_3^2 \) is natural. The same result follows from the simple van der Waals model of fluid mixtures, where the steric free energy density is given by \( -k_B T (\sum_i n_i) \ln(1 - \sum_i \epsilon_{i0}^0 n_i) \), with \( \epsilon_{i0}^0 \) being hard-sphere volumes.

In Fig.3, we plot quantities related to \( \nu_3 \) vs \( X \). Displayed are (a) \( \nu_3 \), (b) \( \nu_3^3 \) in Fig.(11) and \( \nu_3^0 \) in Eq.(34), (c) \( \nu_31 \) and \( \nu_32 \) in Eq.(7), (d) \( \chi_3 \) in Eq.(8), (e) \( g_3 \) in Eq.(30), and (f) \( G_30 = G_{13}^0 \) appearing in Eq.(31). As the result follows from the simple van der Waals model, where the steric free energy density is given by

\[ d_3 = \alpha_{12} = 3 \, \text{Å}, \quad \epsilon_{11}/k_B = 588.76 \, \text{K}, \]  

(60)

where \( w_{11}/\epsilon_{11} d_1^3 = 15.80 \) from Eq.(55). We choose \( \epsilon_{11} \) such that the coexistence (saturated vapor) pressure at \( T = 300 \, \text{K} \) is equal to its experimental one \( p_{\text{ex}}^0 = 0.031 \, \text{atm} \) (see Appendix C). The density in the reference state

\[ n_r \] and the coexisting liquid and gas water densities, \( n_\ell \) and \( n_g \), at \( T = 300 \, \text{K} \) are calculated as

\[ n_r = 1.0049d_1^{-3}, \quad n_\ell = n_r - 1.5 \times 10^{-5}n_r, \]

\[ n_g = p_{\text{ex}}^0/k_BT = 2.1 \times 10^{-5}n_r. \]  

We then add a small amount of a hydrophobic solute. In most cases to follow, we set \( \epsilon_{13} = \epsilon_{33} = 0 \) and \( \epsilon_{23} = 300 \, \text{K} \), for which the solute interacts with the two solvent species differently, resulting in a large solute-concentration coupling. In Fig.2, we have shown the overall behaviors of \( \nu_3 \) in the \( X-\eta \) plane at fixed \( \epsilon_3 \) and \( \nu_3/\alpha_3^2 \) in the \( \epsilon_3-\eta \) plane at fixed \( X \). The \( \nu_3 \) increases steeply with increasing \( \eta \) for \( \eta \gtrsim 0.5 \), decreases with increasing \( X \), and behaves as \( \alpha_3^2 \) for \( \alpha_3 \gtrsim 1 \) (see Appendix D for analytic results). The asymptotic relation \( \nu_3 \sim \alpha_3^2 \) is natural. The same result follows from the simple van der Waals model of fluid mixtures, where the steric free energy density is given by \( -k_B T (\sum_i n_i) \ln(1 - \sum_i \epsilon_{i0}^0 n_i) \), with \( \epsilon_{i0}^0 \) being hard-sphere volumes.

In Fig.3, we plot quantities related to \( \nu_3 \) vs \( X \). Displayed are (a) \( \nu_3 \), (b) \( \nu_3^3 \) in Fig.(11) and \( \nu_3^0 \) in Eq.(34), (c) \( \nu_31 \) and \( \nu_32 \) in Eq.(7), (d) \( \chi_3 \) in Eq.(8), (e) \( g_3 \) in Eq.(30), and (f) \( G_30 = G_{13}^0 \). These quantities increase as \( \alpha_3^2 \) with increasing \( \alpha_3 \). In the insets in (d) and (e), \( \chi_3(nk_BT\kappa_m)^{1/2} \) and \( g_3(n)^{1/2} \) indicate large sizes of \( \alpha_3^2 \phi \) and \( g_3X \) in Eq.(29). In (d) and (e), the solute-solvent coupling coefficients \( \chi_3 \) and \( g_3 \) are both large. In (f), \( G_3^0 = G_{13}^0 \) is peaked at \( X \sim 0.2 \). Previously, Booth et al. found a maximum of \( G_3^0 \) as a function of the hydro trope density \( n_g \) for various solutes (drugs) in water-hydrotrope mixture solvents.

We should have \( |g_3| \gg 1 \) and \( g_3^2 n_X \gg 1 \) for relatively large hydrophobic solutes in water-hydrotrope solvents, especially in the presence of pre-Ouzo aggregates.
as thermal fluctuations. For water(1)-ethanol(2)-octanol(3), results of molecular dynamics simulation lead to rough estimations, \(n(G_{33}^0 - G_{33}^{spi}) = 100 - 300\), \(-g_3 = 20 - 60\), and \(g_3^2/\kappa = 300 - 3000\), at \(X = 0.2\). For smaller (less hydrophobic) methane at \(X \sim 0.2\), \(g_3\) was numerically about \(-5\) in water-methanol and about \(-15\) in water-TBA.

C. \(n_{3}^{spi}, G_{33}^0,\) and \(B_2\) for mixture solvent

The spinodal solute density \(n_{3}^{spi}\), the Kirkwood-Buff integral \(G_{33}^0\), and the second osmotic virial coefficient \(B_2\) are related as \(G_{33}^0 = -2B_2 = 1/n_{3}^{spi}\) in Eqs. (40) and (44). In Fig.4, we plot (a) \(n_{3}^{spi}\) and (b) \(G_{33}^0\) vs \(X\), where the former (latter) decreases (increases) with increasing \(\alpha_3\). The minimum of \(n_{3}^{spi}\) is small, which is \(2.82 \times 10^{-3}\) at \(X = 0.236\) and is \(6.63 \times 10^{-4}\) at \(X = 0.234\) for \(\alpha_3 = 1.3\). In (c) and (d), we decompose \(U_{33}/k_BT = -G_{33}^0\) into \(U_{33}/k_BT\), \(-n_{3}^{spi}/k_BT\kappa_n\), and \(-g_3^2\chi\) from Eq.(36) and compare them for \(\alpha_3 = 0.9\) and 1.3. For these examples, the concentration part dominates for not very small \(X \gtrsim 0.05\) and the sum of the first two terms nearly vanishes for \(X \gtrsim 0.8\). Thus, for \(g_3^2n\chi \gg 1\) and \(X \gg 0.05\), we find

\[
n_{3}^{spi} = 1/G_{33}^0 \cong (g_3^2\chi)^{-1}.
\]  

D. \(n_{3}^{spi}, G_{33}^0,\) and \(B_2\) for one component solvent

In nearly incompressible, one-component solvents (\(X = 0\)), there is no concentration part in Eq.(36), but the direct interaction \(U_{33}\) and the solvent-mediated one \(-U/\kappa_m\) are still large in magnitude (\(\sim k_BT/\mu_1\)) for not small solutes. They largely cancel but their difference can give large positive \(G_{33}^0\). The resultant attractive interaction leads to the well-known assembly of hydrophobic particles in ambient water.

Furthermore, for \(n_3 > n_3^{spi} = 1/G_{33}^0\), spinodal decomposition of gas-liquid phase transition occurs. Previously, these two contributions to \(U_{33}^{eff}\) (or to \(B_2\)) have been calculated separately for one-component solvents, but there has been no analysis of their dependences on the solute size and the solute-solvent attractive interaction.

In Fig.5, we plot \(n_{3}^{spi}, G_{33}, G_{33}^0,\) and \((v_3^{in})^2/\kappa_m U_{33}\) vs \(\alpha_3\) at \(X = 0\), where \(\epsilon_3/k_B = 0.250, 400\) K. In these cases, \(n_{3}^{spi}\) rapidly decreases to very small values with increasing \(\alpha_3\).

IV. PHASE SEPARATION WITH A SOLUTE

We now examine gas-liquid and liquid-liquid coexistence induced by a hydrophobic solute in our mixture solvent characterized by Eqs.(60) and (62) at \(T = 300 K\). We require that the chemical potentials \(\mu_i\) and the pressure \(p\) assume common values in coexisting two phases, so we treat macroscopic phase separation. The resultant densities are written as \(n_i^0\) in the solute-poor liquid phase and \(n_i^\gamma\) in the solute-rich phase. The surface tension is included in Sec.IV in discussions of nucleation.

A. Solute-induced gas-liquid phase separation

In our gas-liquid transition, the solute is squeezed out of the liquid, while \(n_i^0\) and \(n_i^\gamma\) remain small. In Fig.6, we show the densities in gas-liquid coexistence by varying the molar fraction \(X = n_i^\gamma/(n_i^0 + n_i^\gamma)\) at fixed pressure \(p = p_{cx} = 1\) atm with \(\alpha_3 = 1.1\). Gas-liquid coexistence in ternary mixtures is uniquely determined for each given \(T, p,\) and \(X\). For our parameter choice, \((\Delta G_3)/k_BT\) in Eq.(48) decreases with increasing \(X\), which is 25.0 at \(X = 0\) and 12.3 at \(X = 0.3\) for \(\alpha_3 = 1.1\) (16.19 at...
$f_n$ tends to 1 for $n_p$ increasing $\alpha$ at and In (c), for the one-component solvent case, we can be obtained at higher pressures (up to $0.8$ at $23^\circ C$). In (a), for the one-component solvent case, we can be increased up to a liquid density. Thus, the second species plays a role of cosolvent improving the solute solubility.

In Fig. 6, we show that the pressure $p_{\text{ex}}$ increases with increasing $n_2^0$ in gas-liquid coexistence fixed $T$ and $X^\alpha$. In (a), for the one-component solvent case, we plot $p_{\text{ex}}$ vs $n_3$ for $\alpha_3 = 0.9$ and 1.1. Also for $X^\alpha = 0.2$, we plot $p_{\text{ex}}$ vs $n_3$ for three values of $\alpha_3$ at $\epsilon_{23}/k_B = 300$ K in (b) and for three values of $\epsilon_{23}$ at $\alpha_3 = 0.9$ in (c). For each $n_3^2$, $p_{\text{ex}}$ largely increases with increasing the solute hydrophobicity. In (d), the ratio $(p_{\text{ex}} - p_{\text{ex}}^0)/k_BTn_3^2$ tends to 1 for $n_3^2d_3^1 \ll 1$ (see Eq.(65)), while it is between $[1, 1.5]$ at $n_3^2d_3^1 \sim 0.1$ due to the solute-solute repulsion. Larger $n_3^2$ can be obtained at higher pressures (up to $0.337d_3^1$ in Fig.9(b)). Furthermore, we include the attractive interaction among the solute particles ($\epsilon_{33} > 0$), $n_3^2$ can be increased up to a liquid density.

In the dilute limit $n_3^2 \ll d_3^1$, $p_{\text{ex}}$ is simply given by $p_{\text{ex}} = p_{\text{ex}}^0 + k_BTn_3^2 = k_BTn_3^2 = f_3$ (GL),

$$n_3^2 = L_0(\bar{p} - p_{\text{ex}}^0)/k_BT \quad (\text{GL}), \quad (66)$$

Recall that instability occurs for $n_3 > n_3^0$, where $n_3^0$ is the spinodal solute density in Eq.(38). For very small $L_0$ and $\bar{p} - p_{\text{ex}}^0$, $n_3^0$ can be extremely small. We may also change $\bar{p}$ fixing $n_3$, where the liquid is metastable for $\bar{p} < p_n(n_3)$. This $p_n$ is the bubble-point pressure,

$$p_n = p_{\text{ex}}^0 + k_BTn_3^2 \quad (\text{GL}), \quad (67)$$

which is equivalent to Eq.(65). For example, $p_n \sim 10^3$ atm if the solute molar fraction is of order $L_0$. In pure water at $T \sim 300$ K, in contrast, bubble nucleation was observed for large negative pressures ($\sim -10^4$ atm).

**B. Phase transitions at fixed $V$-$N_i$-$T$**

We also examine phase separation at fixed particle numbers $N_i$ in a fixed volume $V$, where the initial one-phase state with densities $n_i = N_i/V$ is metastable or unstable. For $\alpha_3 = 0.9$ and $\epsilon_{23}/k_B = 300$ K, we then encounter both gas-liquid and liquid-liquid phase transitions. The latter was also found for $\alpha_3 = 1.1$ and not for $\alpha_3 = 1.3$ if the other parameters were unchanged. This liquid-liquid phase separation occurs in a wider parameter region for larger $\epsilon_{23}$, but disappears as $\epsilon_{23} \to 0$. 

FIG. 5: Results in one-component solvent ($X = 0$) slightly outside the coexistence curve at $T = 300$ K and $p = 1$ atm. As functions of diameter ratio $\alpha_3 = d_3/d_1(\leq 3)$, displayed are (a) spinodal solute density $n_{3\text{sp}}^0(= -1/2B_2)$ divided by $n_1$, (b) Kirkwood-Buff integral in the dilute limit $G_{33}^0(= -2B_2)$ multiplied by $n_1$, (c) $G_{33}^0/n_2$, and (d) $(\nu_3^0)^2/(\kappa_2U_{33})$ in $-U_{33}^0/U_{33}$ (see Eq.(36)). Here, $\epsilon_{13}/k_B$ takes three values (0, 250, and 400 K), which is 0 in the other figures in this paper. In (c), $G_{33}^0 \propto n_2$ for large $\alpha_3(\geq 2)$ and $G_{33}^0$ changes its sign at $\alpha_3 = 1.22$ for $\epsilon_{13} = 0.8$ at $23^\circ C$. In (d), the ratio tends to a constant larger than 1 with increasing $\alpha_3$, leading to $G_{33}^0 > 0$.

$X^\alpha = 0$ and 9.81 at $X^\alpha = 0.2$ for $\alpha_3 = 0.9$). The ratio $n_2^0/n_2^0$ stays close to its dilute limit ($n_2 \to 0$) given by $\exp(-\Delta G_{23}/k_BT) \sim e^\beta$. Thus, the second species plays the role of a cosolvent improving the solute solubility.

FIG. 6: Results of solute-induced gas-liquid coexistence at $T = 300$ K and $p = 1$ atm, where $\alpha_3 = 1.1$, $\epsilon_{13} = \epsilon_{33} = 0$, and $\epsilon_{23}/k_B = 300$ K. (a) Densities in liquid $n_1^0$ (dotted lines) and those in gas $n_1^0$ (bold lines) in units of $d_3^1$ vs the cosolvent molar fraction in liquid $X^\alpha = n_2^0/(n_1^0 + n_2^0)(\leq 0.3)$, where the solute density in liquid $n_1^0$ is extremely small. (b) Density ratios $n_2^0/n_1^0$ vs $X^\alpha$, where those for the solvent ($i = 1, 2$) depend on $X^\alpha$ rather weakly but that for the solute ($=\text{the Ostwald coefficient } L$) depends on $X^\alpha$ very strongly.
FIG. 7: Gas-liquid coexistence pressure $p_{cx}$ in units of atm with addition of a hydrophobic solute with $\epsilon_{33} = \epsilon_{33} = 0$ at $T = 300$ K. As functions of $n_{i}^{3}d_{i}^{3}$ on logarithmic scales, $p_{cx}$ is plotted (a) for $X = 0$ with $\alpha_{3} = 0.9$ and 1.1, (b) for $X = 0.2$ with $\alpha_{3} = 0.9, 1.1$, and 1.3 at $\epsilon_{23}/k_{B} = 300$, and (c) for $X = 0.2$ with $\epsilon_{23}/k_{B} = 0, 300$, and 400 K at $\alpha_{3} = 0.9$. Here, $p_{cx} \to p_{cx}^{0} \ll 1$ atm as $n_{i}^{3}d_{i}^{3} \to 0$ (d) Ratio $\Delta p_{cx}/k_{B}Tn_{i}^{3}$ vs $n_{i}^{3}d_{i}^{3}$ for five cases in (a) and (b) on a semi-logarithmic scale, where $\Delta p_{cx} = p_{cx} - p_{cx}^{0}$ is the pressure increase due to solute.

At fixed $N_{i}$ and $V$, we consider the Helmholtz free energy. Its change after phase separation is written as

$$\mathcal{F} = V[\phi_{\gamma}f_{\gamma} + (1 - \phi_{\gamma})f_{\alpha} - f],$$

(68)

where $\phi_{\gamma}$ is the volume fraction of the $\gamma$ phase, $f_{\alpha}$ and $f_{\gamma}$ are the values of $f$ in Eq.(52) in the two phases, and $f$ is the initial value of $f$. We seek minima of $\mathcal{F}$ imposing the conditions $(1 - \phi_{\gamma})n_{i}^{{\alpha}} + \phi_{\gamma}n_{i}^{{\gamma}} = n_{i} (i = 1, 2, 3)$. To this end, we change $\phi_{\gamma} \to \phi_{\gamma} + \delta\phi_{\gamma}$ and $n_{i}^{{\gamma}} \to n_{i}^{{\gamma}} + \delta n_{i}^{{\gamma}}$ infinitesimally to obtain the incremental change in $\mathcal{F}$ as

$$\delta\mathcal{F} = \sum_{i}(\mu_{i}^{\alpha} - \mu_{i}^{\gamma})\delta n_{i}^{\gamma} + V(p_{\alpha} - p_{\gamma})\delta\phi_{\gamma},$$

(69)

where $(\mu_{i}^{\alpha}, \mu_{i}^{\gamma})$ and $(\phi_{\gamma})_{i}$ are the values of $(p, \mu_{i})$ in the two phases and $N_{i}^{{\gamma}} = V\phi_{\gamma}n_{i}^{\gamma}$ are the particle numbers in the $\gamma$ phase. Thus, from $\delta\mathcal{F}/\delta\phi_{\gamma} = \delta\mathcal{F}/\delta n_{i}^{\gamma} = 0$, we obtain common values of $p$ and $\mu_{i}$ in the two phases.

Figure 8 displays $p_{cx}$ vs $\bar{x}_{3} = N_{i}/(N_{i} + N_{j})$ at $X = N_{i}/(N_{i} + N_{j}) = 0.2$ in the two phase transitions. We set $\bar{n}_{i} = N_{i}/V$ equal to (a) 0.6416$d_{i}^{-3}$ and (b) 0.6327$d_{i}^{-3}$, for which the initial pressure $p_{0} = p(\bar{n}_{i}, \bar{n}_{j}, 0)$ (without solute) is (a) 1 and (b) $-613.5$ atm. In (a), at $\bar{x}_{3} = 10^{-4}$, $p_{cx}$ is still 90 atm due to the presence of a gas

fraction ($\sim 10^{-3}$ in Fig.9(c)) on the gas-liquid branch but is close to $p_{0} = 1$ atm on the liquid-liquid branch. In (b), as $\bar{x}_{3}$ is decreased, $p_{cx}$ tends to $p_{cx}^{0} = 0.075$ atm on the gas-liquid branch and to $p_{0} = -613.5$ atm on the liquid-liquid branch. Thus, in our model fluid, we can realize equilibrium liquid-liquid coexistence at negative pressures.

Here, $p_{cx}$ depends on $n_{i}^{3}$ sensitively because $\gamma_{3}$ in Eq.(6) is large ($\sim 40$) in liquid as in Fig.2(c).

In Fig.9, we further show (a) $n_{i}^{3}$, (b) $n_{i}^{3}$, (c) $\phi_{\gamma}$, and (d) $\mathcal{F}$ vs $\bar{x}_{3}$ for the case of Fig.8(a). The gas-liquid branch exists in the range $4 \times 10^{-8} < n_{i}^{3}d_{i}^{3} < 0.337$ here, on which the $\gamma$ phase consists mostly of the solute. On the liquid-liquid branch, $n_{i}^{3}d_{i}^{3}$ ($\sim 0.3$) and $n_{i}^{3}d_{i}^{3}$ ($\sim 0.2$) are nearly constant (both increasing by 3% at $\bar{x}_{3} = 10^{-2}$), while $n_{i}^{3}d_{i}^{3}$ ($\sim 0.005$) is small. In (c), $\phi_{\gamma}$ shrinks as $\bar{x}_{3}$ $\to$ 0. In (d), $\mathcal{F}$ is slightly lower (higher) on the gas-liquid branch than on the liquid-liquid branch in the left (right) of the vertical line at $\bar{x}_{3} ~ 2.5 \times 10^{-3}$. However, from $\mathcal{F}$, we cannot decide which transition occurs in real situations.

To examine the metastability, we introduce the grand potential density $\omega(n_{i1}, n_{j2}, n_{j3})$ by

$$\omega = f - \sum_{i}\mu_{i}n_{i} + \bar{p} = \sum_{i}(\mu_{i} - \bar{\mu}_{i})n_{i} + \bar{p} - p,$$

(70)

where $\bar{\mu}_{i}$ and $\bar{p}$ are the values of $\mu_{i}$ and $p$ in the reference state with $n_{i} = \bar{n}_{i}$. Then, $\mathcal{F}$ is rewritten as

$$\mathcal{F} = V[\phi_{\gamma}\omega_{\gamma} + (1 - \phi_{\gamma})\omega_{\alpha}],$$

(71)

where $\omega_{\alpha}$ and $\omega_{\gamma}$ are the values of $\omega$ in the two phases. Here, $\omega_{\alpha}$ is of the second order in the deviations $n_{i}^{3} - \bar{n}_{i}(\times \phi_{\gamma})$ as $\delta f_{i}$ in Eq.(26), so $\omega_{\alpha} \propto \phi_{\gamma}^{2}$ as $\phi_{\gamma} \to 0$. On the other hand, we have $\omega_{\gamma} < 0$ when the initial state with $n_{i} = \bar{n}_{i}$ is metastable or unstable.
FIG. 9: Gas-liquid and liquid-liquid coexistence with varying \( \tilde{x}_3 = N_3 / (N_1 + N_2) \) at \( T = 300 \text{ K} \), where particle numbers \( N_1 = \tilde{n}_1 V \) and volume \( V \) are fixed with \( X = N_2 / (N_1 + N_2) = 0.2 \) and \( \tilde{n}_1 d_i^3 = 0.6416 \) as in Fig.8(a). Here, \( \alpha_3 = 0.9, \varepsilon_{13} = \varepsilon_{33} = 0, \) and \( \varepsilon_{23} / k_B T = 300 \text{ K} \). Plotted are (a) \( N_2^2 / N_3 \) (\( i = 1, 2, 3 \)) in the \( \alpha \) phase on the gas-liquid branch (dotted lines) and on the liquid-liquid branch (bold lines), (b) \( n_i^2 / d_i^3 \) in the \( \gamma \) phase, (c) volume fraction \( \phi_\gamma \) of the \( \gamma \) phase, and (d) free energy change \( F \) in Eq.(68) multiplied by \( d_i^3 / k_B T \). In (c), solute number \( N_2^2 / V \phi_\gamma n_3^2 \) in the \( \gamma \) phase divided by \( N_3 \) is also plotted (inset), which tends to 1 with increasing \( \tilde{x}_3 \). In (d), difference of \( F \) between the two phases is very small.

In Fig.10, we plot \( \omega_\gamma \) vs \( \tilde{x}_3 \) at \( X^\alpha = 0.2 \) and 0.4. For curves at fixed \( V \) we used the data in Figs.8(a) and 9, on which \( \omega_\gamma < 0 \). On the gas-liquid branch, \( \omega_\gamma \to 0 \) as \( \phi_\gamma \to 0 \), since \( \rho_0 = p(\tilde{n}_1, \tilde{n}_2, 0) = 1 \) atm is close to \( p_c^0 \). The liquid-liquid branch exists only for \( \tilde{x}_3 > x_3^\text{min} \), where \( \phi_\gamma \to 0 \) and \( \tilde{n}_3 \to n_3^\alpha \) as \( \tilde{x}_3 \to x_3^\text{min} \). In Fig.10, \( x_3^\text{min} \) is \( 1.41 \times 10^{-5} \) at \( X = 0.2 \) and \( 7.20 \times 10^{-4} \) at \( X = 0.4 \).

C. Phase transitions at fixed \( p-N_i-T \)

We next seek two-phase coexistence in the isobaric condition requiring \( \mu_i^\alpha = \mu_i^\gamma \) and \( \rho_0 = \rho_\gamma = 1 \) atm. The average densities \( \tilde{n}_i \) are chosen to satisfy \( \tilde{\rho} = p(\tilde{n}_1, \tilde{n}_2, \tilde{n}_3) = 1 \) atm. This is needed since \( \rho_0 \to \tilde{\rho} \) as \( \phi_\gamma \to 0 \). If we increase \( \tilde{n}_3 \) gradually, \( \tilde{n}_1 \) and \( \tilde{n}_2 \) decrease according to Eq.(12) for each fixed \( X = \tilde{n}_2 / (\tilde{n}_1 + \tilde{n}_2) \). In this method, we vary the volumes of the two phases, \( V_\alpha \) and \( V_\gamma \), at fixed total particle numbers \( N_i = \tilde{n}_i V \), where \( V \) is the initial volume. Using \( \omega \) in Eq.(70), we write the change in the Gibbs free energy after phase separation as

\[
\mathcal{G} = V_\alpha \omega_\alpha + V_\gamma \omega_\gamma. \tag{72}
\]

The particle numbers \( N_i^\alpha = V_\alpha n_i^\alpha \) and \( N_i^\gamma = V_\gamma n_i^\gamma \) in the two phases satisfy \( N_i^\alpha + N_i^\gamma = N_i \). For infinitesimal changes in these quantities, \( \mathcal{G} \) changes by

\[
\delta \mathcal{G} = \sum_i (\mu_i^\alpha - \mu_i^\gamma) \delta N_i^\gamma + (\bar{\rho} - \rho_\alpha) \delta V_\alpha + (\bar{\rho} - \rho_\gamma) \delta V_\gamma. \tag{73}
\]

Thus, from \( \partial \mathcal{G} / \partial n_i^\alpha = \partial \mathcal{G} / \partial V_\gamma = \partial \mathcal{G} / \partial V_\alpha = 0 \), we obtain \( \mu_i^\alpha = \mu_i^\gamma \) and \( \rho_0 = \rho_\gamma = \bar{\rho} \). On the gas-liquid branch, we have \( V_\alpha \approx V_\gamma \approx V \). On the liquid-liquid branch, \( n_i^\gamma \) are nearly constant satisfying the space-filling relation in Eq.(12), which are slightly smaller than those at fixed \( V \).

In Fig.10, we additionally plot curves of \( \omega_\gamma \) vs \( \tilde{x}_3 \) for \( \bar{x}_3 = 0.2 \) and 0.4 at fixed \( p \) as well as those at fixed \( V \). On the gas-liquid branch at fixed \( p \), \( \omega_\gamma \) nearly vanishes at any \( \bar{x}_3 \), because \( n_i^\gamma \) remains small (\( \sim 6 \times 10^{-4} d_i^{-3} \)). On the liquid-liquid branch, the two curves of \( \omega_\gamma \) at fixed \( V \) and \( p \) almost coincide and depend on \( \tilde{x}_3 \) logarithmically. These are because \( n_i^\gamma \) is changed only by a small amount (\( \lesssim 3\% \) in the figure) and the term \( -\mu_i n_i^\gamma \) in \( \omega_\gamma \) gives rise to the contribution \(-k_B T n_i^\gamma \ln \bar{x}_3 \) (see Eq.(80)).

D. Phase diagrams at fixed \( p-T \)

In Fig.11, the phase behaviors are illustrated for \( \alpha_3 = 0.9 \) at \( T = 300 \text{ K} \) and \( p = 1 \) atm. In (a), stable and metastable regions of the liquid-liquid phase transition are separated by the binodal line \( n_3^m = n_3^\text{min} \) in the \( X-n_3 \) plane. Here, \( n_3^\text{min} \) is the minimum of \( n_3 = \bar{x}_3 (n_1 + n_2) \) on the isobaric liquid-liquid branch with \( \bar{\rho} = p(\tilde{n}_1, \tilde{n}_2, \tilde{n}_3) = \rho_0 \), and \( \bar{x}_3 \) in the **** phase density. On the gas-liquid branch, \( \omega_\gamma \) is nearly zero at fixed \( p \) (purple filled circle). On the liquid-liquid branch, \( \omega_\gamma \) is nearly the same for fixed \( V \) (red +) and \( p \) (blue ×). At fixed \( V \) in (a), the data are common to those in Fig.9. Here, \( \alpha_3 = 0.9, \varepsilon_{13} = \varepsilon_{33} = 0, \) and \( \varepsilon_{23} / k_B T = 300 \text{ K} \).
FIG. 11: Phase behaviors at $T = 300$ K and $p = 1$ atm for $\alpha_3 = 0.9$, $\epsilon_{13} - \epsilon_{33} = 0$, and $\epsilon_{23}/k_B = 300$ K. (a) Phase diagram in the $X$-$n_3d_1^3$ plane on a semi-logarithmic scale. Line $n_3^{\alpha}$ vs $X$ separates stable and metastable (blue) regions of liquid-liquid transition, on which $X = X^\alpha$. Unstable region is above line $n_3^{\text{sp}}$ (yellow). Liquid-liquid critical point is marked by *. Binodal line is in red (blue) in the left (right) of the critical point. Liquid-liquid phase separation occurs above its binodal line $n_3^{\min}$ (in blue and yellow). Line $n_3^{\min}$ represents bubble line at $p = 1$ atm for gas-liquid transition in Eq.(66). (b) Coexisting densities $n_i^{\alpha}$ and $n_i^{\text{sp}}$ vs $X^\alpha = n_2^{\alpha}/(n_1^{\alpha} + n_2^{\alpha})$ in units of $d_i^{\alpha/3}$, which coincide at the critical point. (c) Triangular phase diagram, where tie-lines (in green) connect coexisting two states. In (d), it is expanded near the critical point, where the metastable region (in green) is between the binodal and spinodal lines. In (a), (c), and (d), dotted lines represent spinodal.

In liquid-liquid coexistence, the differential relation $\sum_i(n_i^{\alpha} - n_i^{\text{sp}})d\mu_i^{\alpha} = 0$ holds, where $\mu_i^{\alpha}$ are the phase chemical potentials with $\mu_i^{\alpha} \equiv k_BT[\ln(n_i^{\alpha}X_i^{\alpha}) + \nu_i(n_i^{\alpha}, n_2^{\alpha})]$ from Eq.(5). We treat the binodal density $n_3^{\min} = n_3^{\alpha}$ as a function of $X^\alpha$ at fixed $T$ and $p$ to find

$$\left(\frac{\partial \ln n_3^{\min}}{\partial X^\alpha}\right)_{T,p} = -g_3 + \frac{n_3^{\alpha}n_2^{\alpha} - n_1^{\alpha}n_2^{\alpha}}{(n_3^{\alpha} - n_3^{\text{sp}})^2} \chi_{\text{LL}},$$

using Eqs.(30) and (A13). Here, $g_3$ and $\chi$ are the $\alpha$-phase values and $n_3 = n_1^{\alpha} + n_2^{\alpha}$. In Fig.11(a), the above derivative is close to $-g_3$, where the second term in Eq.(74) is about $0.1g_3$ and the critical value of $g_3$ is $-10.4$.

In Fig.12, we plot the mean-field concentration variance $\chi_R$ in Eq.(41) in one-phase states in the stable and metastable regions, where $\alpha_3 = 0.9$, $T = 300$ K, and $p = 1$ atm. This $\chi_R$ does not include the contribution from phase-separated domains, but increases above $\chi$ due to the solute-concentration coupling in Eq.(29). We can approach the critical point in Fig.11 passing through the stable region with respect to the liquid-liquid transition to encounter the critical scattering.

Previously, Moriyoshi et al. found a solute-induced critical point in a mixture of water, ethanol, and C8-alcanol. Recently, Anisimov’s group measured the surface tension near a critical point in a mixture of water, TBA, and cyclohexane, where the correlation length increased up to 9.5 nm. Singular behaviors around such a unique critical point are of great interest.

Though constructing a theory of surfactant-free microemulsions is a future project, we make some comments. If the second species is amphiphilic, emulsification can occur in the metastable region $n_3^{\min} < n_3 < n_3^{\text{sp}}$, while long-wavelength fluctuations grow up to macroscopic sizes in the unstable region $n_3 > n_3^{\text{sp}}$. (i) To support this simple scenario, Vitale and Katz observed micrometer-sized Ouzo droplets in a narrow metastable region and macroscopic phase sep-
aration in an unstable region in the phase diagram for strongly hydrophobic solutes in water-ethanol solvents. This was displayed in a plane of the ethanol fraction and the logarithm of the solute fraction as in Fig.11(a). (ii) Anisimov’s group\textsuperscript{13,14} observed droplets with sizes of order 100 nm in a narrow region in the triangular phase diagram at small cyclohexane fractions outside the binodal in a water-TBA solvent. They also observed mesoscopic droplets in wider regions outside the binodal for less hydrophobic solutes in the same solvent.\textsuperscript{14} (iii) Through the Ouzo process, mesoscopic articles with sizes of order 100 nm can be produced for various hydrophobic solutes including polymers\textsuperscript{31,32} in water-hydrotrope mixtures.

E. Solute-induced nucleation

We now discuss homogeneous nucleation\textsuperscript{45,83,84,93,94} in a reference metastable state with densities \( \bar{n}_i \) and pressure \( \bar{p} \). We suppose a spherical domain with radius \( R \) in the limit \( \phi_n \rightarrow 0 \). The droplet free energy is given by

\[
F(R) = (4 \pi / 3) R^3 \omega_n + 4 \pi R^2 \sigma,
\]

where \( \omega_n \) is defined in Eq.(70) and the second term is the surface free energy. The surface tension \( \sigma \) is assumed to be a constant. This \( F(R) \) depends on \( R, n_i^7, \) and \( \bar{n}_i \). For small changes in \( R \) and \( n_i^7 \) at fixed \( \bar{n}_i \), \( F(R) \) changes as

\[
\frac{\delta F(R)}{4 \pi R} = (R \omega_n + 2 \pi R^2 \sigma - 3 \sum_i (\mu_i^7 - \mu_\bar{i}) \delta n_i^7.
\]

(76)

We determine \( n_i^7 \) setting \( \mu_i^7 = \mu_\bar{i} \) to seek a critical droplet. Then, Eq.(70) gives a simple relation,

\[
\omega_n = \bar{p} - p_\gamma < 0.
\]

(77)

Since the second term in Eq.(76) vanishes, \( F(R) \) has a maximum \( F_c = F(R_c) \) at a critical radius \( R_c \), where

\[
R_c = 2 \pi / (p_\gamma - \bar{p}), \quad F_c = (4 \pi / 3) \sigma R_c^2.
\]

(78)

These relations are general. In particular, we find \( \omega_n \equiv (1 - n_i^7 / n_0^7)(\bar{p} - p_\gamma) \) for weak metastability in one-component fluid\textsuperscript{45,94}, where the condition \( \mu_i^7 = \mu_\bar{i} \) becomes \( (p_\gamma - p_\gamma^0)/(n_i^7) \equiv (\bar{p} - p_\gamma^0)/n_0^7 \).

At the gas-liquid transition with \( n_i^3 \ll d_i^{-3} \), we find \( n_i^3 \approx L_0^{-1} n_3 \) from \( \mu_\bar{i} = \bar{p} \) in Eq.(67) yields

\[
\omega_n \approx \bar{p} - p_n \quad \text{(GL)}.
\]

(79)

At the liquid-liquid transition, we use the relation \( \omega_n \equiv \sum_i (n_i^0 - n_i^3)(\bar{p} - p_\gamma) \delta n_i^3 \delta (\bar{p} - p_\gamma) \delta n_i^3 \) with \( \mu_3^0 \approx \mu_3(\bar{n}_3, \bar{n}_2, n_3^\text{min}) \). Here, \( n_3^\text{min}(\bar{n}_3, \bar{n}_2) \) is the binodal solute density for densities \( \bar{n}_1 \) and \( \bar{n}_2 \).

\[
\omega_n \equiv -k_B T (n_i^3 - n_i^0) \ln(\bar{n}_3/n_3^\text{min}) \quad \text{(LL)}.
\]

(80)

which is negative for \( \bar{n}_3 > n_3^\text{min} \). The curves of \( \omega_n \) at fixed \( p \) in Fig.10 can well be fitted to Eq.(80).

In our problem, we should note that \( \sigma \) depends on the composition \( x^\alpha \) and take different values in gas-liquid and liquid-liquid phase transitions. Hence, we write \( \sigma = \sigma_{gL} \) for the gas-liquid case and \( \sigma = \sigma_{ll} \) for the liquid-liquid case. (i) For binary water-alcohol mixtures, \( \sigma_{gL} \) is decreased by interfacial adsorption of alcohol\textsuperscript{95-98}. For example, at \( X = 0.05 \), it is 32 mN/m for ethanol and 25 mN/m for TBA, which are considerably below the pure-water value \( \sigma_{w} = 72 \) mN/m. (ii) For ternary mixtures of water, alcohol, and a hydrophobic solute, \( \sigma_{ll} \) should be decreased more strongly since the oil side contains hydrophobic molecules\textsuperscript{99}. It was well below 1 mN/m as the critical pint was approached\textsuperscript{2,10,15}.

In Fig.13, we plot \( R_c \) in Eq.(77) vs \( \bar{x}_3 = \bar{n}_3/(\bar{n}_1 + \bar{n}_2) \) in metastable states with densities \( \bar{n}_i \) at \( T = 300 \) K and \( p = 1 \) atm. Here, \( \bar{x} = \bar{n}_2/(\bar{n}_1 + \bar{n}_2) \) is (a) 0.2 and (b) 0.8 with \( \alpha_3 = 0.9, \epsilon_1 = \epsilon_3 = 0 \), and \( \epsilon_{23} / k_B = 300 \) K. In units of mN/m, the gas-liquid surface tension \( \sigma_{gL} \) is (a) 72 and 50 and (b) 72 and 25, while the liquid-liquid surface tension \( \sigma_{ll} \) is 72, 30, and 5 in (a).

In water-alcohol solvents, nanometer-sized solute-rich aggregates preexist with alcohol molecules covering them in one-phase states\textsuperscript{8,11,13}. Then, they should play the role of embryos of critical liquid droplets consisting of solute and alcohol molecules. This much amplifies the prefactor \( J_0 \) of the nucleation rate \( I = J_0 \exp(-F_c/k_B T) \) of the liquid-liquid transition\textsuperscript{45,94}. However, we can well expect occurrence of the gas-liquid transition for weak solute-cosolvent attraction (for smaller \( \epsilon_{23} \) in our scheme) (see the first paragraph in Sec.IV.B).
Jin et al. reported observations of air nanobubbles in mixtures of water and a neutral organic water-soluble species such as tetrahydrofuran, where the latter has an amphiphilic nature and accumulates at gas-liquid interfaces. These bubbles were removed by repeated filtration and regenerated by air injection. Note that the method of gas injection is widely used to produce nanobubbles, where large bubbles are fragmented into small ones.

V. SUMMARY AND REMARKS

We have studied a continuum theory of solvation and phase transitions in nonionic ternary mixtures varying the solvent composition $X$ and the solute density $n_3$. Main results are summarized as follows.

1. In Sec.II, we have presented a theory of ternary mixtures using the second virial expansion of the free energy density $f$ with respect to $n_3$. We have clarified relationship among the solvation chemical potential $k_B T \nu_3$, the partial volumes $v_i$, the Kirkwood-Buff integrals $G_{ij}$ (and the dilute limits $G_{ij}^0$), the solute spinodal density $n_3^{sp}$, the second virial osmotic coefficient $B_2$, and the Gibbs transfer free energy $\Delta G$. We have confirmed the space-filling relation $\sum_j v_j n_i = 1$ for slowly varying densities $n_i$ in the limit of small compressibility. In nearly incompressible mixtures, the solute-concentration coupling grows as in Fig.4 when the solute interacts with the two solvent species differently. It is much amplified in water–alcohol mixtures in the presence of micelle-like aggregates.

2. In Sec.III, we have investigated the solvation properties using the MCSL model. The parameters of our model have been chosen to realize the following at $T = 300$ K. (i) The saturated vapor pressure $p_0^s$ is very small ($\ll 1$ atm), (ii) the two solvent species are miscible in any proportion at $p = 1$ atm, and (iii) the solute interacts repulsively with the first species but attractively with the second. In this situation, the solvent-mediated solute-solute interaction mainly arises from the solute-concentration coupling for not small $X$. In the case of one-component solvents ($X = 0$), we have examined the effective solute interaction vs the diameter ratio $d_3 / d_1$ in Fig.5.

3. In Sec.IV, we have examined solute-induced gas-liquid and liquid-liquid phase transitions. We have determined the solute spinodal density, the metastability conditions, and the binodal conditions. We have presented phase diagrams in Fig.11 and discussed homogeneous nucleation.

Finally, we give some remarks. (1) We need to calculate the surface tension for amphiphilic cosolvents. There should be significant differences between methanol, ethanol, and TBA in the formation of Ouzo domains. In the pre-Ouzo regime, the hydrotrpoe molecules consist of those forming micells and those in monomeric states. (2) Kinetics of solute-induced phase transitions should be investigated, where slow solute diffusion is crucial. (3) We can add a salt to water-hydrotrope mixtures. It is of interest how an antagonistic salt (composed of hydrophilic and hydrophobic ions) can induce aggregates in such mixture solvents, where an electric field can be applied. (4) Microscopically, the hydrogen-bonding structures in aqueous mixtures are strongly deformed around amphiphilic and hydrophobic molecules. Thus, inputs from molecular dynamics simulations are highly informative.

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Appendix A: General relations of partial volumes and Kirkwood-Buff integrals

Let a nonionic fluid mixture be in a macroscopic volume $V$ with particle numbers $N_i = n_i V$. The partial volumes, written as $\bar{v}_i$ here, are defined by

$$\bar{v}_i = (\partial V / \partial N_i)_{T, p, \{N_j \neq i\}}.$$  \hspace{1cm} (A1)

where $N_j$ with $j \neq i$ are fixed in the derivative with respect to $N_i$. We obtain $\bar{v}_i = (\partial \mu_i / \partial \mu_j)_{T, \{N_j \neq i\}}$ from $dG = -V dp + \sum_i \mu_i dN_i$ at fixed $T$ for the Gibbs free energy $G$. Since $V$ is an extensive quantity, we find the sum rule,

$$\sum_j \bar{v}_j n_j = 1.$$  \hspace{1cm} (A2)

The differential form of $V$ is then given by

$$dV = \sum_j \bar{v}_j dN_j - \kappa V dp + \alpha_p V dT.$$  \hspace{1cm} (A3)

Here, $\kappa = -\left( \partial V / \partial p \right)_{T, \{N_j \}} / V$ is the isothermal compressibility and $\alpha_p$ is the isobaric thermal expansion coefficient. In Eq.(A3) we set $N_j = V n_j$ to obtain

$$\sum_j \bar{v}_j dN_j - \kappa dp + \alpha_p dT = 0,$$  \hspace{1cm} (A4)

with the aid of Eq.(A2). Thus, we can express $\bar{v}_i$ as

$$\bar{v}_i = \kappa (\partial \mu_i / \partial \mu_j)_{T, \{N_j \neq i\}}.$$  \hspace{1cm} (A5)

$$k_B T \kappa \sum_j \bar{v}_j I^{ij}.$$  \hspace{1cm} (A6)

In deriving Eq.(A6) we use the Gibbs-Duhem relation $(dp = \sum_j n_j d\mu_j$ at fixed $T$) and define

$$I^{ij} = (k_B T)^{-1} (\partial \mu_j / \partial n_i)_{T, \{N_k \neq j\}}.$$  \hspace{1cm} (A7)

We obtain Eqs.(10) and (11) from Eq.(A5).
In the grand canonical ensemble, we may consider the fluctuations of the particle numbers, written as $δN_i$, in a region with volume $V$. The $I_{ij}$ in Eq.(15) can be related to the variances of $δN_i$ as

$$I_{ij} = V^{-1}(δN_i δN_j) = k_B T (∂n_i/∂μ_j)_{T, (μ_k, z_k)}.$$  \hspace{1cm} (A8)

We notice that the matrix $I^{ij}$ in Eq.(A7) is equal to the inverse of the variance matrix $I_{ij}$ in Eq.(A8). Then,

$$k_B T n_i = \sum_j I_{ij} \bar{v}_j,$$ \hspace{1cm} (A9)

and

$$k_B T K = \sum_{jk} I^{jk} n_j = \sum_{jk} I_{jk} \bar{v}_j \bar{v}_k.$$ \hspace{1cm} (A10)

It is easy to express $I^{ij}$ in terms of $I_{ij}$ for three component systems. Furthermore, for small $n_3$, $I_{ij}$ and $I^{ij}$ for the solvent components $(i,j = 1,2)$ smoothly tend to those of $n_3 = 0$, while $I^{13}$ grows as $n_3^{-1}$ and

$$I^{13} = -I^{13} n_1 G_{13} - I^{12} n_2 G_{23} + \cdots \hspace{1cm} (i = 1,2).$$ \hspace{1cm} (A11)

From Eqs.(4), (7), (A7), and (A11) we find

$$\nu_{31} = (k_B T)^{-1} \lim_{n_3 \to 0} (\partial μ_i/\partial n_3)_{T, n_1, n_2} = -\lim_{n_3 \to 0} [I^{11} n_1 G_{13} + I^{12} n_2 G_{23}].$$ \hspace{1cm} (A12)

We then obtain Eqs.(17) and (31).

We finally consider the composition $X$ for binary mixtures. Using Eqs.(A6) and (24), we rewrite its differential relation $dX = (n_1 dn_2 - n_2 dn_1)/n^2$ at fixed $T$ as

$$dX = (n^2 \gamma/k_B T)(\bar{v}_1 d\mu_2 - \bar{v}_2 d\mu_1) = (n^2 \gamma/k_B T)[(\bar{v}_1 - \bar{v}_2) dp + d\Delta].$$ \hspace{1cm} (A13)

with $\Delta = μ_2 - μ_1$. For $dp = 0$ we find Eqs.(23) and (74).

Appendix B: Gas-liquid coexistence in one-component solvent: Corrections to $L$ and $k_B$

In a one-component solvent, we examine gas-liquid coexistence with a solute to linear order in its density. The solvent and solute densities are $n_i^0$ and $n_3^0$ in liquid and $n_i^g$ and $n_3^g$ in gas. Without solute, the solvent density is $n_i$ in liquid and $n_g$ in gas. After the doping, it is changed by $δn_i^0 = n_i^0 - n_i$ in liquid and $δn_i^g = n_i^g - n_g$ in gas.

The deviations $δμ_1$, $δμ_3$, and $δp_{cx}$ assume constant values in the two phases. The Gibbs-Duhem relation gives

$$δp_{cx} = n_i δμ_1 + k_B T n_3^0 = n_g δμ_1 + k_B T n_3^0,$$ \hspace{1cm} (B1)

Here, for any physical quantity $\mathcal{A}$, we use the symbol $[\mathcal{A}] = \mathcal{A}_α - \mathcal{A}_γ$, where the values of $\mathcal{A}$ in the two phases are written with $α$ and $γ$. We then solve Eq.(B1) as

$$δμ_1/k_B T = -[n_3]/[n_1],$$ \hspace{1cm} (B2)

$$δp_{cx}/k_B T = (n_i^0 n_3^0 - n_g^0 n_3^0)/[n_1] = (n_γ/L_o - n_α) n_3^0/(n_γ - n_α).$$ \hspace{1cm} (B3)

Thus, $δp_{cx}$ is positive (negative) for $L_o n_α/n_γ < 1 (> 1)$. This occurs for $(ΔG)/k_B T > -10.6 (< -10.6)$ for ambient water. Far from the criticality, we have $δp_{cx} \equiv k_B T n_3^0$ for hydrophobic solutes as in Eq.(66), but the shift is small for hydrophilic solutes with $L_o \gg 1$.

From Eq.(4) $δμ_1$ is written as

$$δμ_1/k_B T = δn_i^0/K_\ell + ν_3 n_3^0 = δn_i^0/K_γ + ν_g n_3^0,$$ \hspace{1cm} (B4)

where $(K_\ell, ν_3)$ and $(K_γ, ν_g)$ are the values of $K = n_2^0 k_B T K$ and $ν_{31} = (\partial ν_3/\partial n_1)$ in liquid and gas, respectively, with $κ$ being the compressibility. Here, Eq.(34) gives $Kν_{31} = n_1 v_3^α$. From Eqs.(B2) and (B4) we find

$$δn_i^0 = -K_\ell [n_3]/[n_1] + ν_3 n_3^0,$$ \hspace{1cm} (B5)

$$δn_i^g = -K_γ [n_3]/[n_1] + ν_g n_3^0.$$ \hspace{1cm} (B6)

In gas, $K_γ ≡ n_γ$ and $ν_g = lim_{n_3 \to 0} (\partial^2 p/\partial n_3 d n_3)$. Far from the criticality, $δn_i^γ$ is very small ($\sim (n_γ/n_ε)n_3^0$). For the solute we use Eqs.(5) and (48) to obtain

$$ln n_3) + ΔG/k_B T = -[n_3 δn_1] - [U_{313} n_3]/k_B T,$$ \hspace{1cm} (B7)

where the left hand side is $ln(L/L_0)$. With the aid of Eqs.(34) and (36), substitution of Eqs.(B5) and (B6) into the right hand side yields

$$L/L_0 - 1 = [n_1 v_3^α]/[n_1] - 2[B_2 n_3],$$ \hspace{1cm} (B8)

The correction to $k_B$ can be calculated from

$$ln(k_B/k_B^0) = (δn_i^α + δn_i^γ)/[n_γ] + ν_3 δn_i^0 + U_{313} n_3/k_B T,$$ \hspace{1cm} (B9)

where the quantities in liquid appear and the first term arises from $ln(n_i^α + n_i^γ)/[n_γ]$. We thus find Eq.(51).

Appendix C: Phase diagram from CS model
For one-component fluids with density $n_1$, Fig. 14(a) displays a phase diagram, where the steric part is given by the Carnahan-Starling (CS) model and the attractive part by the van der Waals model\textsuperscript{102-104} with $d_1$ and $w_{11}$ being independent of $T$ and $p$. The pressure is given by

$$p = k_B T n_1 \left[ 1 + \frac{4\eta_1 - 2\eta_1^2}{(1 - \eta_1)^2} \right] - \frac{1}{2} w_{11} n_1^2, \quad (C1)$$

where $\eta_1 = \pi d_1^3 n_1 / 6$. The critical temperature $T_c$, density $n_c$, and pressure $p_c$ are calculated as\textsuperscript{103,104}

$$k_B T_c = 9.01 \times 10^{-2} w_{11} d_1^{-3}, \quad n_c = 0.249 d_1^{-3}, \quad p_c / n_c k_B T_c = 0.359. \quad (C2)$$

In this paper, $d_1$ and $w_{11}$ are given by Eq. (62), which yield the coexistence pressure $p^c_{ex} = 0.031$ atm of water at $T = 300$ K (CS1 fitting). This gives $T_c = 838$ K and $n_c = 0.247 d_1^{-3} = 9.1$ nm$^{-3}$, which are not far from the water values ($T_c = 647.1$ K and $n_c = 10.8$ nm$^{-3}$). We can also determine $d_1$ and $w_{11}$ to obtain $T_c$ and $n_c$ of water (CS2 fitting), for which $p^c_{ex} = 0.72$ atm at $T = 300$ K. In Fig. 14(b), curves CS1 and CS2 give the coexisting densities $n_i$ and $n_g$ vs $T$ from these fittings, which are compared with curve vdW from the critical-point fitting of the van der Waals model. In the CS model, the gas density $n_g / (p^c_{ex} / k_B T)$ can be very small far below $T_c$.

**Appendix D: Summary of MCSL model**

We summarize the multi-component MCSL model\textsuperscript{15}. Using $d_i$, we write the hard-sphere volume fractions as $\eta_i = \pi n_i d_i^3 / 6$ and the total one as $\eta = \sum_j n_j$. The hard-sphere free energy density $f_h$ in Eq. (52) can be simply expressed in terms of $u = \eta / (1 - \eta)$ as

$$f_h / k_B T n = 4u + u^2 - 3g_1 u - 3(y_1 + y_2) u^2 / 2 + (y_3 - 1)(u - u^2 / 2 - \ln(1 + u)), \quad (D1)$$

where $n = \sum_j n_j$. We define $y_1$, $y_2$, and $y_3$ as

$$y_1 = \sum_{i > j} (d_i + d_j) \Delta_{ij} / (d_i d_j)^{1/2}, \quad y_2 = \frac{\xi_2}{\eta} \sum_{i > j} \Delta_{ij} (d_i d_j)^{1/2}, \quad y_3 = \frac{6 \xi_2^2}{\pi \eta^2} n, \quad (D2)$$

with $\Delta_{ij} = (\pi / 6)(d_i - d_j)(d_i d_j)^{1/2} n_i n_j / n_\eta$, and $\xi_\ell = (\pi / 6) \sum_j n_j d_j^{\ell} (\ell = 1, 2, 3)$.

We then calculate the hard-sphere part of the chemical potential $\mu_{hi} = \partial f_h / \partial n_i$ in Eq. (56) as

$$\frac{\mu_{hi}}{k_B T} = \frac{3 \xi_2 d_i}{1 - \eta_1} \left[ x_1 d_1 + \frac{\xi_2 d_2}{3 \xi_2} + \frac{\gamma_i d_i^3}{1 - \eta} \right], \quad (D3)$$

where $\gamma_i = \xi_2 d_i / \eta$. In ternary mixtures, $\mu_{hi}$ yields $\nu_3$ and $U_{33}$ as $n_3 \to 0$ from Eqs. (57) and (58). They have third-order and sixth-order polynomial forms as\textsuperscript{85}

$$\nu_3 = -\ln(1 - \eta) + D_1 \alpha_3 + D_2 \alpha_3^2 + D_3 \alpha_3^3, \quad (D4)$$

$$n U_{33} = k_B T \sum_{0 \leq k \leq 6} W_k \alpha_3^k, \quad (D5)$$

where the coefficients $D_k$ and $W_k$ depend on $n_1$ and $n_2$. Note that $n_3$ appears in the form of $d_3^2 n_3$ in $f_h$ in Eq. (D1), yielding the $\alpha_3^3$ term in $\nu_3$ and the $\alpha_6^3$ term in $U_{33}$ (see Figs. 2 and 5). In particular, we express $D_3$ and $W_6$ as

$$D_3 = B^3 [2u^3 + u^2 - 2u - 2 \ln(1 - \eta)] + 3A_1 BU^2 / A_3 + u / A_3 - (8\sqrt{2} / 3) (c_{13} \eta + c_{23} \alpha_3^6 \eta_2) / k_B T, \quad (D6)$$

$$W_6 = (B^3 / A_3) [5u^3 + 6u^2 - 6 \ln(1 - \eta)] + (1 + 6A_1 BU) u^2 / A_3, \quad (D7)$$

where $A_k = 2 + X (A_k - 1), B = A_2 / A_3, \eta = \eta_1 + \eta_2$, and $u = \eta / (1 - \eta)$. The $D_3$ and $W_6$ are large for $\eta \gtrsim 0.5$. For example, we have $D_3 = 8.05 - 1.98 \varepsilon_{13} / k_B T$ for $X = 0$ and $\eta = 0.526$ and $D_3 = 6.00 - (1.27 \varepsilon_{13} + 0.317 \varepsilon_{23}) / k_B T$ for $X = 0.2, \eta = 0.520$, and $\alpha_3 = 0.9$. Thus, the coupling coefficients $C_3$ in Eq. (8) and $g_3$ in Eq. (30) increase as $\alpha_3^3$ for $\alpha_3 \gtrsim 1$, leading to Eqs. (63) and (64).

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