

Molecular dynamics study of free energy of transfer of alcohol and amine from water phase to the micelle by thermodynamic integration method

K. Fujimoto, N. Yoshii, and S. Okazaki

Citation: *The Journal of Chemical Physics* **137**, 094902 (2012); doi: 10.1063/1.4747491

View online: <http://dx.doi.org/10.1063/1.4747491>

View Table of Contents: <http://scitation.aip.org/content/aip/journal/jcp/137/9?ver=pdfcov>

Published by the [AIP Publishing](#)

Articles you may be interested in

[Adapting SAFT- \$\gamma\$ perturbation theory to site-based molecular dynamics simulation. III. Molecules with partial charges at bulk phases, confined geometries and interfaces](#)

J. Chem. Phys. **141**, 094708 (2014); 10.1063/1.4893966

[Free energy profiles for penetration of methane and water molecules into spherical sodium dodecyl sulfate micelles obtained using the thermodynamic integration method combined with molecular dynamics calculations](#)

J. Chem. Phys. **136**, 014511 (2012); 10.1063/1.3671997

[Molecular dynamics study of solubilization of immiscible solutes by a micelle: Free energy of transfer of alkanes from water to the micelle core by thermodynamic integration method](#)

J. Chem. Phys. **133**, 074511 (2010); 10.1063/1.3469772

[Size-dependent hydrophobic to hydrophilic transition for nanoparticles: A molecular dynamics study](#)

J. Chem. Phys. **131**, 244706 (2009); 10.1063/1.3276915

[A molecular dynamics study of free energy of micelle formation for sodium dodecyl sulfate in water and its size distribution](#)

J. Chem. Phys. **124**, 184901 (2006); 10.1063/1.2179074



Molecular dynamics study of free energy of transfer of alcohol and amine from water phase to the micelle by thermodynamic integration method

K. Fujimoto,¹ N. Yoshii,^{1,2} and S. Okazaki^{1,a)}

¹Department of Applied Chemistry, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

²Center for Computational Science, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

(Received 27 June 2012; accepted 8 August 2012; published online 6 September 2012)

Free energy of transfer of methylamine, octylamine, methanol, and octanol from water phase to sodium dodecyl sulfate (SDS) micelle has been calculated using thermodynamic integration method combined with molecular dynamics calculations. Together with the results for alkanes obtained in our previous study [K. Fujimoto, N. Yoshii, and S. Okazaki, *J. Chem. Phys.* **133**, 074511 (2010)], the effect of polar group on the partition of hydrophilic solutes between water phase and the micelle has been investigated in detail at a molecular level. The calculations showed that the molecules with octyl group are more stable in the SDS micelle than in the water phase due to their hydrophobicity of long alkyl chain. In contrast, methanol and methylamine are stable in the water phase as well as in the micelle because of their high hydrophilicity. The spatial distribution of methylamine, octylamine, methanol, and octanol has also been evaluated as a function of the distance, R , from the center of mass of SDS micelle to the solutes. The distribution shows that the methylamine molecule is adsorbed on the SDS micelle surface, while the methanol molecule is delocalized among the whole system, i.e., in the water phase, on the surface of the micelle, and in the hydrophobic core of the micelle. The octylamine and octanol molecules are solubilized in the SDS micelle with palisade layer structure and are not found in the water phase. © 2012 American Institute of Physics. [<http://dx.doi.org/10.1063/1.4747491>]

I. INTRODUCTION

When spherical micelles consisting of surfactant molecules are dissolved in water, water-insoluble substances can be dispersed in the solution by binding to the micelle. This phenomenon is called “solubilization” and is applied to disperse perfumes, drugs, ink, and agrichemicals in water.^{1–6} Drug delivery systems by micelles have also been developed.^{7–9} For scientific research, water-insoluble membrane proteins were extracted from cell membranes using the protein solubilization to the micelle.^{10–12} Furthermore, highly selective and efficient syntheses are performed in the reactant-solubilizing micelles.^{13,14} Despite such utilities of solubilization in a wide range of fields, molecular picture of the solubilization, for example, to what extent, how, and where the substance is bound to the micelle is still unclear.

In our previous works,^{15–18} two extremes of solubilization of water and hydrocarbons were investigated. First, we performed molecular dynamics (MD) calculations and found that the free energy of transfer of a water molecule from bulk water to sodium dodecyl sulfate (SDS) micelle has a large positive value, $+28 \text{ kJ mol}^{-1}$, and that the water molecule is seldom contained in the SDS micelle.¹⁵ In contrast, for alkanes such as methane, ethane, butane, hexane, and octane molecules,¹⁶ the calculated free energy of transfer was $-5.4 - -28 \text{ kJ mol}^{-1}$, indicating that the alkanes are well solubilized by the micelle. The free energy decreases linearly as the number of carbon atoms in the alkane molecule increases. The

enthalpy, ΔH , and entropy, ΔS , of transfer also decrease linearly with increasing number of carbon atoms.¹⁷ Second, in order to clarify the penetrating process of molecules into the micelle, the free energy profile of hydrophobic methane and hydrophilic water was evaluated as a function of distance between the centers of mass of the SDS micelle and that of the solute by calculating mean force acting on them.¹⁸ No free energy barrier is observed for methane so that the methane molecule easily penetrates into the micelle in order to avoid the hydrophobic hydration. Then the solubilized methane may move about in the micelle core since free energy profile is almost constant in the micelle. By contrast, the free energy barrier of the penetrating water was evaluated to be $+24-35 \text{ kJ mol}^{-1}$ such that penetration of water into the micelle hardly occurs because of the disadvantage of breaking hydrogen-bonding with solvent water.

However, the solute molecules of practical use stated above are intermediates between the two extremes, i.e., they are, in most cases, organic compounds having hydrophobic alkyl groups and hydrophilic functional groups simultaneously. Thus, in the present study, in order to clarify the solubilization of solute molecules with alkyl chain and polar groups in the micellar solution, the free energy of transfer of methylamine, octylamine, methanol, and octanol from the water phase to the SDS micelle has been calculated using thermodynamic integration method combined with MD calculations. Effect of the polar groups and the length of the alkyl chain on the solubilization have been investigated. The binding sites of alkanes, amines, and alcohols in the SDS micelle have also been analyzed.

^{a)} Author to whom correspondence should be addressed. Electronic mail: okazaki@apchem.nagoya-u.ac.jp.

Computational details are given in Sec. II. The calculated free energy of transfer and radial distribution of the solutes are discussed in Sec. III. We conclude in Sec. IV.

II. METHOD

In the present study, free energy of transfer of methylamine, octylamine, methanol, and octanol molecules from water phase to SDS micelle has been calculated using thermodynamic integration method combined with molecular dynamics (MD) calculations.

A. Free energy of transfer

We consider the system composed of a SDS micelle in water and one solute molecule. Here, the solute is the methylamine, octylamine, methanol, and octanol molecule. A thermodynamic cycle shown in Fig. 1 of Ref. 16 in our previous study is considered in order to calculate free energy of transfer of the solute molecule from the water phase to the SDS micelle core and/or to the micelle surface, $\Delta G_{w \rightarrow m}$. $\Delta G_{id \rightarrow w}$ and $\Delta G_{id \rightarrow m}$ represent the free energy of transfer from the ideal gas state to the water phase and the one from the ideal gas state to the micelle. Then, $\Delta G_{w \rightarrow m}$ can be evaluated by

$$\Delta G_{w \rightarrow m} = \Delta G_{id \rightarrow m} - \Delta G_{id \rightarrow w}. \quad (2.1)$$

Here, the total free energy of transfer, $\Delta G_{w \rightarrow m}$, from the water phase to the SDS micelle core can also be evaluated by

$$\Delta G_{w \rightarrow m} = \Delta G_{w \rightarrow m}^{ex} - k_B T \ln \frac{V_m}{V_w}. \quad (2.2)$$

First and second terms of Eq. (2.2) are called the ‘‘excess term’’ and the ‘‘ideal term,’’ respectively. k_B and T are the Boltzmann constant and the absolute temperature, respectively. V_m is the volume of the SDS micelle calculated by $\frac{4}{3}\pi R_m^3$, where R_m is the radius of the SDS micelle. A fixed value of 2.8 nm was adopted for the present R_m , which corresponds to the distance from the center of mass of SDS micelle to the outer end of the distribution of hydrophilic group. It reflects roughness of the micelle surface as well as the breathing of the micelle itself. V_w is the volume of the water phase evaluated by $V - V_m$, where V is the volume of the total system, i.e., the simulation box. $\Delta G_{id \rightarrow w}^{ex}$ and $\Delta G_{id \rightarrow m}^{ex}$ may be calculated by thermodynamic integration method described in the previous study.¹⁶

The excess free energy difference, ΔG^{ex} , between the states at $\lambda_1 = \lambda_2 = 0$ and $\lambda_1 = \lambda_2 = 1$ can be calculated by

$$\begin{aligned} \Delta G^{ex} &= G^{ex}(\lambda_1 = \lambda_2 = 1) - G^{ex}(\lambda_1 = \lambda_2 = 0) \\ &= \int_C \left\{ \left\langle \frac{\partial V}{\partial \lambda_1} \right\rangle_{\lambda_1, \lambda_2} d\lambda_1 + \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} d\lambda_2 \right\}, \quad (2.3) \end{aligned}$$

where λ_1 and λ_2 are the coupling parameters for Coulomb interaction and Lennard-Jones interaction, respectively, as shown in Eq. (3) in Ref. 16. The solute molecule does not interact with the other molecules at $\lambda_1 = \lambda_2 = 0$, where the solute molecule is in the ideal gas state. On the other hand, the

solute molecule fully interacts with the other molecules at $\lambda_1 = \lambda_2 = 1$, that is, the solute molecule is in the micelle or in the water phase. $\langle \cdots \rangle_{\lambda_1, \lambda_2}$ represents isothermal-isobaric ensemble average at fixed λ_1 and λ_2 , and C is an arbitrary integral path from $(\lambda_1, \lambda_2) = (0, 0)$ to $(1, 1)$. Here, a two-steps integral path $(0, 0) \rightarrow (0, 0.5) \rightarrow (1, 1)$ was adopted. At the second step, λ_2 was set to be $\lambda_2 = 0.5\lambda_1 + 0.5$. Then, the integral may be described by

$$\begin{aligned} \Delta G^{ex} &= \int_0^{0.5} \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} d\lambda_2 \\ &+ \int_0^1 \left[\left\langle \frac{\partial V}{\partial \lambda_1} \right\rangle_{\lambda_1, \lambda_2} + 0.5 \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} \right] d\lambda_1. \quad (2.4) \end{aligned}$$

The excess free energy of transfer of the solute molecule from the ideal gas state to the water phase, $\Delta G_{id \rightarrow w}^{ex}$, and the one from the ideal gas state to the SDS micelle core, $\Delta G_{id \rightarrow m}^{ex}$, were evaluated using Eq. (2.4). The parameter, δ , was introduced to $\partial V / \partial \lambda_2$, and set to be 0.05 nm² in order to avoid the divergence of the Lennard-Jones potential due to the overlap of the solute molecule with the other molecules at small λ_2 value.¹⁹ Now, the excess free energy of transfer from the water phase to the SDS micelle core, $\Delta G_{w \rightarrow m}^{ex}$, is obtained by

$$\Delta G_{w \rightarrow m}^{ex} = \Delta G_{id \rightarrow m}^{ex} - \Delta G_{id \rightarrow w}^{ex}. \quad (2.5)$$

B. Restriction on the space for the solute

In order to evaluate $\Delta G_{id \rightarrow w}^{ex}$ and $\Delta G_{id \rightarrow m}^{ex}$, accessible configurational space for the solute must be restricted in the water phase or in the micelle, respectively, during the MD calculation. We introduced a soft-core wall potential for the solute,

$$\phi_{\text{wall}}(R, R_m) = \frac{A}{(R - R_m)^{12}}, \quad (2.6)$$

where R is the distance between the center of mass of the micelle and that of the solute. A is the interaction parameter, which was adopted to be the same as the repulsion between the oxygen atoms of SDS.

C. Molecular dynamics calculation

The aggregation number of SDS micelle was set to be 60 in the present study since our previous work²⁰ as well as the light scattering experiments^{21,22} and time-resolved fluorescence spectroscopy²³ indicated that the micelle composed of 60 SDS molecules is thermodynamically most stable in water. The 60 SDS molecules, 8360 water molecules, and a solute are contained in a cubic simulation box with periodic boundary condition. Since the critical micellar concentration (CMC) of SDS is 8.1 mM, the concentration of our system corresponds to 50 CMC. TIP4P²⁴ and CHARMM potential^{25,26} were used for water and other molecules, respectively. The pressure and temperature were controlled at $P = 0.1$ MPa and $T = 300$ K, respectively, using algorithms proposed by Martyna *et al.*^{27,28} Inertial constant of the barostat was set to be 6.7×10^{-17} J s² such that the

relevant time constant is 2.0 ps. Nosé-Hoover chain thermostat of five chains was connected to the particle degrees of freedom and barostat, separately. The inertial constant of the thermostat for the former was set to be $3.6 \times 10^{-21} \text{ J s}^2$ for the first chain and $1.2 \times 10^{-21} \text{ J s}^2$ for the remaining higher order chains and that for the latter to be $4.2 \times 10^{-18} \text{ J s}^2$ for the first chain and $7.5 \times 10^{-23} \text{ J s}^2$ for the remaining chains. The time constants are all 0.5 ps.^{27,29} The time step, Δt , was set to be 2 fs. The particle mesh ewald (PME) method was used in order to calculate the coulomb interaction. The cutoff distance of the Lennard-Jones interaction and that of the real space of PME method were both 1 nm. The parameter α and the grid points of PME method were $0.4 \times 10^{10} \text{ m}^{-1}$ and $64 \times 64 \times 64$, respectively.³⁰ SHAKE/ROLL and RATTLE/ROLL methods were used to constrain the bond length between heavy atoms (carbon, oxygen, and nitrogen) and hydrogen (H) atoms in dodecyl sulfate (DS) ions, solute, and water. Hydrogen-hydrogen distance constraints were also used in order to constrain the bending angles H–C–H of methylene groups, H–O–H of water, and H–N–H of amine.

Suitable sets of the coupling parameters (λ_1, λ_2) were selected in order to execute the numerical integration of Eq. (2.4) with high accuracy. For two small solutes (methylamine and methanol molecules), 1ns-long molecular dynamics calculations have been performed for 12 sets of λ : (λ_1, λ_2) = (0, 0), (0, 0.05), (0, 0.1), (0, 0.2), (0, 0.3), (0, 0.4), (0, 0.5), (0.2, 0.6), (0.4, 0.7), (0.6, 0.8), (0.8, 0.9), and (1, 1). For long solutes (octanol and octylamine molecules), additional 1ns-long MD calculations have been performed for two sets of the parameters, (λ_1, λ_2) = (0, 0.01) and (0.025), in addition to the previous 12 (λ_1, λ_2) sets. The first 0.5-ns trajectory was excluded from the analysis.

In order to calculate the radial distribution of the solute in the micelle solution (see in subsection III C), another 15 ns-long normal MD calculations ($\lambda_1 = \lambda_2 = 1$) have been performed, too, without wall potential $\varphi_{\text{wall}}(R, R_m)$. The simulation box contains again 60 SDS molecules, 8360 water molecules, and one solute (methylamine, octylamine, methanol, or octanol) molecule. Other calculation conditions were the same as the above free energy calculations. The last 10-ns trajectory was used for the analysis.

III. RESULTS AND DISCUSSION

Figure 1 shows the instantaneous value of $\partial V/\partial \lambda_2$, the integrand of the first term of Eq. (2.4), and its cumulative average

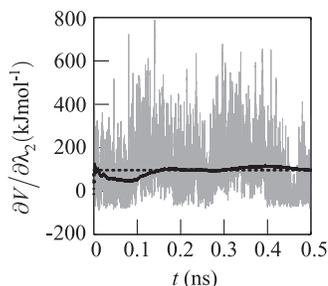


FIG. 1. The calculated $\partial V/\partial \lambda_2$ in Eq. (2.4) for the octylamine at $\lambda_1 = 0$ and $\lambda_2 = 0.05$ as a function of time (gray line) as well as its cumulative average (black line). Dashed line is the average.

erage for octylamine as a function of time at $\lambda_1 = 0$ and $\lambda_2 = 0.05$, where convergence of the cumulative average is the slowest and the error in $\langle \partial V/\partial \lambda_2 \rangle_{\lambda_1, \lambda_2}$ is the largest among the λ 's. A dashed line in Fig. 1 represents the average value obtained from 0.5-ns MD calculation. As shown in the figure, the cumulative average converged well, implying that the 0.5-ns MD calculation is sufficiently long to obtain satisfactory statistics for the integrand.

A. Excess free energy of transfer from the ideal gas state to the water phase and to the SDS micelle

Excess free energy of transfer of methylamine, octylamine, methanol, and octanol from the ideal gas state to the water phase, $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$, and to the SDS micelle, $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$, has been calculated by numerical integration according to Eq. (2.4). The calculated $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ and $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ are shown in Fig. 2 as an energy level diagram. In Fig. 2, blue and red lines represent $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ and $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$, respectively. Solid circles are experimental hydration free energy obtained by solubility measurement for these molecules in pure water.³¹ It is interesting to find that $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ is in good agreement with the experimental hydration free energy despite difference between the water phase in the micellar solution and pure water. For instance, the calculated $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ of octanol is $-14 \pm 3 \text{ kJ mol}^{-1}$, and the corresponding experimental value is -17 kJ mol^{-1} . Within the error, these values agree well with each other. The other solutes also show a similar level agreement. The solutes may be considered to interact weakly with the present sodium ions in the water phase.

$\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ of hydrophobic methane and octane molecules are 9.8 ± 0.6 and $15 \pm 1 \text{ kJ mol}^{-1}$, respectively. These molecules are less stable in the water phase than in the ideal gas state due to the hydrophobic hydration. In contrast, $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ of methylamine, octylamine, methanol, and octanol molecules which also have hydrophilicity are -15 ± 2 , -21 ± 1 , -12 ± 4 , and $-14 \pm 3 \text{ kJ mol}^{-1}$, respectively, i.e.,

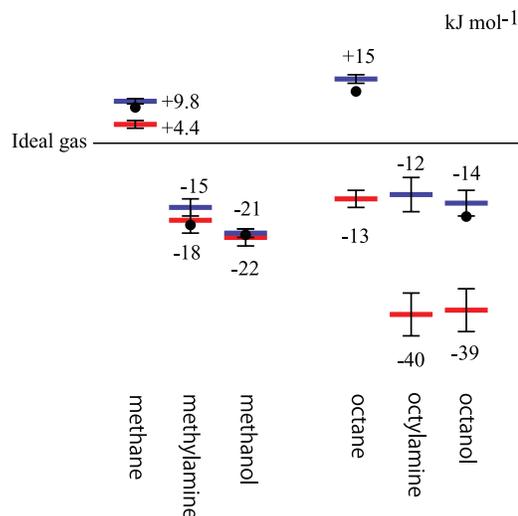


FIG. 2. The calculated free energy of transfer from the ideal gas state to the water phase $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ (blue) and to the SDS micelle $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ (red) for methane, octane, methylamine, octylamine, methanol, and octanol molecules. Solid circle is the experimental hydration free energy.

negative values. This is because hydrogen bond is formed between amino or hydroxyl group and the solvent water. These solutes are more stable in the water phase than in the ideal gas state.

Comparing octyl group with methyl one, $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ of the solute with octyl group is 3–7 kJ mol⁻¹ larger than that with methyl one. Increase of the alkyl chain length causes the stronger hydrophobic hydration in the water phase, and has an influence on the stability of the solutes. However, for the case of $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$, the instability is less than this as stated below.

Concerning $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$, methane has a positive value (4.4 ± 0.9 kJ mol⁻¹), and is unstable in the SDS micelle. In contrast, $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ of the other solutes has negative values. These molecules are 17–22 kJ mol⁻¹ more stable in the SDS micelle than in the ideal gas state. The trend is the opposite to the case of $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$. The longer the alkyl chain of the solute is, the stronger the interaction between the alkyl chain and the hydrophobic core of the SDS micelle becomes.

B. Stability of the solutes in the SDS micelle

In this subsection, we discuss the stability of the solutes by comparing it between in the SDS micelle and in the water phase. Table I lists the free energy of transfer, $\Delta G_{\text{w} \rightarrow \text{m}}$, from the water phase to the SDS micelle. Here, it is noted that $\Delta G_{\text{w} \rightarrow \text{m}}$ obtained by Eq. (2.2) includes the ideal term of the free energy calculated as a function of the ratio of volume of the SDS micelle (V_{m}) to that of the water phase (V_{w}). In this paper, the concentration of SDS in the simulation box corresponds to 50 CMC. Then, the value of $k_{\text{B}}T \ln \frac{V_{\text{m}}}{V_{\text{w}}}$ is 1.8 kJ mol⁻¹.

We can see from $\Delta G_{\text{w} \rightarrow \text{m}}$ in Table I that the solutes except for methanol are more stable in the SDS micelle than in the water phase. The stability may come from the alkyl chain of the solutes interacting with the micelle core by hydrophobic interaction. It is remarkable for the solute molecules with long alkyl chain. The difference of the $\Delta G_{\text{w} \rightarrow \text{m}}$ becomes as great as 23–26 kJ mol⁻¹ for octyl group. On the other hand, in the case of the short alkyl chain, i.e., methyl group, the stability of the solutes in the SDS micelle is relatively small. For example, $\Delta G_{\text{w} \rightarrow \text{m}}$ of methylamine and methanol are -1 ± 4 and $+1 \pm 3$ kJ mol⁻¹, respectively.

When one methylene group is added to the chain, the increment of $\Delta G_{\text{w} \rightarrow \text{m}}$ of amine and alcohol may be roughly

estimated to be 3 kJ mol⁻¹. This is in good agreement with the case of alkane (3.3 kJ mol⁻¹).¹⁶ The result indicates that alkyl chain length of the solute plays a very important role in the stabilization of the solute in the micelle.

The difference, $\Delta G_{\text{w} \rightarrow \text{m}}$, of the $\Delta G_{\text{w} \rightarrow \text{m}}$ between alkane and amine or alcohol having the same carbon chain length as alkane is listed in Table I. $\Delta G_{\text{w} \rightarrow \text{m}}$ of methanol is almost equal to that of the methylamine. Similarly, $\Delta G_{\text{w} \rightarrow \text{m}}$ of octanol is similar to that of octylamine. This implies that hydrophilicity of the hydroxyl group is similar to that of the amino group. This is due to the strong hydrogen bonding ability of alcohol and amine, which affects the binding ratio of the solute to the micelle.

The binding ratio of the solutes in the SDS micelle to that in the water phase is also listed in Table I. Here, the binding ratio was evaluated from $\exp(-\Delta G_{\text{w} \rightarrow \text{m}}/RT)$, where R and T are the gas constant and the temperature, respectively. The binding ratio of small solutes (methane, methyl amine, and methanol) is small ranging between 0.7 and 5. The molecules must be widely distributed in the whole region of the micellar solution, i.e., both in the micelle core and in the water phase. In contrast, the binding ratio of the solutes having a long alkyl chain such as octane, octylamine, and octanol is several ten thousands, such that the solute molecules may penetrate into the SDS micelle and are localized there because of the hydrophobic nature of the long alkyl chain.

C. Distribution of the solutes

In order to clarify what part of the SDS micelle the solute is bound to, the radial distribution of the solute in the SDS micellar solution has been calculated using the trajectory of MD run for 15 ns without wall potential (see Sec. II). The radial distribution $f(R)$ of the hydrophobic part and sulfate ion of the SDS micelle, sodium ion, and water molecule are shown as a function of the distance, R , from the center of mass of the SDS micelle in Fig. 3(a). The calculated radial distribution functions, $f(R)$, of alkane, amine, and alcohol are presented in Figs. 3(b)–3(d), respectively. Each $f(R)$ was obtained from the number density profile $\rho(R)$ of the solute divided by Jacobian $4\pi R^2$: $f(R) = \rho(R)/4\pi R^2$. Then, $f(R)$ should be in proportion to $\exp(-\Delta G_{\text{w} \rightarrow \text{m}}^{\text{ex}}/RT)$. It is noted that $\rho(R)$ is proportional to $\exp(-\Delta G_{\text{w} \rightarrow \text{m}}/RT)$. The red and black lines in Figs. 3(b)–3(d) represent methyl and octyl groups in the solutes, respectively. The solid and dotted lines are the $f(R)$ of hydrophobic

TABLE I. The total free energy of transfer, $\Delta G_{\text{w} \rightarrow \text{m}}$, from the water phase to the SDS micelle calculated by Eq. (2.2) and the difference $\Delta G_{\text{w} \rightarrow \text{m}}$ between $\Delta G_{\text{w} \rightarrow \text{m}}$ of the alkanes and that of the amines and alcohols with the same carbon chain length. The binding ratio of the solute in the SDS micelle to that in the water phase was calculated by $\exp(-\Delta G_{\text{w} \rightarrow \text{m}}/RT)$. H, NH₂, and OH represent alkane, amine, and alcohol, respectively. The errors of methane and octane are re-evaluated using our previous data.¹⁶ The error in the present work represents 80% confidence interval.

| | Methyl groups | | | Octyl groups | | |
|----------------------------------------------------------------------|---------------|-----------------|------------|--------------|-----------------|-------------|
| | H | NH ₂ | OH | H | NH ₂ | OH |
| $\Delta G_{\text{w} \rightarrow \text{m}}/\text{kJ mol}^{-1}$ | -4 ± 1 | -1 ± 4 | $+1 \pm 3$ | -26 ± 2 | -26 ± 8 | -23 ± 6 |
| $\Delta \Delta G_{\text{w} \rightarrow \text{m}}/\text{kJ mol}^{-1}$ | ... | $+3 \pm 4$ | $+5 \pm 3$ | ... | 0 ± 8 | $+3 \pm 6$ |
| Binding ratio | 5 | 1 | 0.7 | 30 000 | 30 000 | 10 000 |

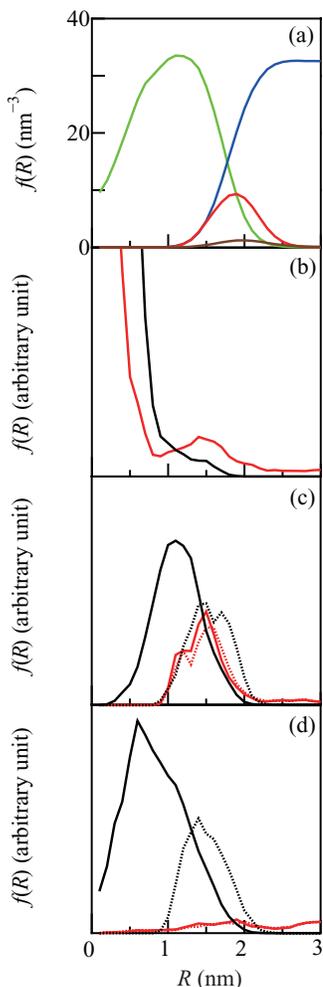


FIG. 3. (a) Radial distribution $f(R)$ of SDS micelles as a function of radial distance R from the center of mass of the SDS micelle (green: hydrophobic carbon atom, red: sulfur and oxygen atom of the sulfate ion, blue: water molecule, and brown: sodium ion). Radial distribution $f(R)$ of alkane (b), amine (c), and alcohol (d) as a function of radial distance R . The red and black lines represent $f(R)$ of methyl and octyl groups of the solutes, respectively. The solid and dashed lines are $f(R)$ of hydrophobic carbon chain and hydrophilic group of the solutes, respectively.

carbon chain and hydrophilic group, respectively. Here, the above two distributions are compared directly with each other, though, in a similar way, a comparison of the free energy can also be made.

As shown in Fig. 3(b), methane and octane molecules are distributed more in the SDS micelle than in the water phase. In particular, binding probability increases in the vicinity of the center of mass of the SDS micelle where the density of the hydrophobic alkyl chain is low. In the water phase, $f(R)$ for methane is small, and that for the octane is almost 0. $\Delta G_{w \rightarrow m}^{\text{ex}}$ of methane is $-5 \pm 1 \text{ kJ mol}^{-1}$, only twice as large as thermal fluctuation energy (2.5 kJ mol^{-1}) at $T = 300 \text{ K}$ such that methane can be distributed in the water phase, too. In contrast, octane has a large value, $-28 \pm 6 \text{ kJ mol}^{-1}$, and is localized and stabilized in the SDS micelle core avoiding the contact with the solvent water molecules.

Figure 3(c) shows the radial distribution $f(R)$ of methyl- and octylamine. Methylamine is distributed in the vicinity of the surface of the SDS micelle ($1 \leq R \leq 2 \text{ nm}$). This may

be considered as a result of the competition between the hydrophilicity of the polar amino group and the hydrophobicity of the non-polar methyl group. Furthermore, methylamine easily moves to the water phase, since $\Delta G_{w \rightarrow m}^{\text{ex}}$ of methylamine, $-3 \pm 4 \text{ kJ mol}^{-1}$, is as small as the thermal energy. In contrast, for the octylamine, its alkyl chain is buried in the hydrophobic part of the SDS micelle to avoid hydrophobic hydration, whereas the amino group keeps the hydrogen bond with the solvent water molecules. Thus, the octylamine is solubilized in the SDS micelle with the palisade layer structure.

Figure 3(d) shows the radial distribution $f(R)$ of methanol and octanol as a function of R . Methanol is distributed in the whole region of the micellar solution from the hydrophobic core of the micelle to the water phase. Although methanol molecule is found in the micelle, $\Delta G_{w \rightarrow m}^{\text{ex}}$ of the methanol molecule is $-1 \pm 3 \text{ kJ mol}^{-1}$, which is half of the thermal fluctuation energy (2.5 kJ mol^{-1}) at $T = 300 \text{ K}$. Then, the methanol can dissolve into the water phase and move about in the whole region of the micellar solution. On the other hand, the alkyl chain of octanol is buried in the hydrophobic SDS micelle core in the same way as the case of octylamine in order to avoid the hydrophobic hydration. Octanol is, then, solubilized in the SDS micelle with the palisade layer structure.

IV. CONCLUSION

The free energy of transfer of methylamine, octylamine, methanol, and octanol from the water phase to the SDS micelle has been calculated by MD calculation. The calculated free energy was compared with that of alkanes obtained in our previous work.

The calculated free energy of transfer, $\Delta G_{w \rightarrow m}$, showed that all the solute molecules are stable in the SDS micelle. With increasing alkyl chain length, the solute is more stable in the SDS micelle. Stability of the solutes is in the order, alkane $>$ amine \approx alcohol. Methanol and methylamine are stable in the water phase, too, at 50 CMC because of their high hydrophilicity. The binding ratio for the small solutes such as methane, methylamine, and methanol in the SDS micelle is small ranging from 0.7 to 5. In contrast, the ratio for the large solutes such as octane, octylamine, and octanol is as large as several tens of thousands.

The radial distribution of methane, octane, methylamine, octylamine, methanol, and octanol has been evaluated as a function of the radial distance, R , from the center of mass of SDS micelle to the solutes. The octane molecule is found only in the SDS micelle core. However, $\Delta G_{w \rightarrow m}^{\text{ex}}$ of methane is small enough for it to move about the whole solution, going in and out the SDS micelle. Methylamine was adsorbed on the SDS micelle surface. Methanol moves about from the surface of the SDS micelle to the water phase since $\Delta G_{w \rightarrow m}^{\text{ex}}$ of the methanol molecule is as small as $-1 \pm 3 \text{ kJ mol}^{-1}$, which corresponds to the half of the thermal fluctuation energy, 2.5 kJ mol^{-1} , at $T = 300 \text{ K}$. Octylamine and octanol are solubilized in the SDS micelle with the palisade layer structure.

ACKNOWLEDGMENTS

This work was supported by the Next Generation Super Computing Project, Nanoscience Program, and by

TCCI/CMSI in the Strategic Programs for Innovative Research, MEXT, Japan. The authors thank the Okazaki Research Center for Computational Science, the National Institute of Natural Science, the Center for Computational Science, University of Tsukuba, and the Information Technology Center of Nagoya University for the use of supercomputers.

- ¹H. Nakajima, *Industrial Applications of Microemulsions*, Surfactant Science Series Vol. 66, edited by C. Solans and H. Kunieda (Marcel Dekker, New York, 1997), p. 175.
- ²Md. H. Uddin, N. Kanei, and H. Kunieda, *Langmuir* **16**, 6891 (2000).
- ³Y. Tokuoka, H. Uchiyama, M. Abe, and K. Ogino, *J. Colloid Interface Sci.* **152**, 402 (1992).
- ⁴Y. Tokuoka, H. Uchiyama, and M. Abe, *J. Phys. Chem.* **98**, 6167 (1992).
- ⁵Y. Tokuoka, H. Uchiyama, M. Abe, and S. D. Christian, *Langmuir* **11**, 725 (1995).
- ⁶M. J. Carcia-Celma, *Industrial Applications of Microemulsions*, Surfactant Science Series Vol. 66, edited by C. Solans and H. Kunieda (Marcel Dekker, New York, 1997), p. 123.
- ⁷M. Yokoyama, M. Miyauchi, N. Yamada, T. Okano, Y. Sakurai, K. Kataoka, and S. Inoue, *Cancer Res.* **50**, 1693 (1990).
- ⁸K. Kataoka, A. Harada, and Y. Nagasaki, *Adv. Drug Delivery Rev.* **47**, 113 (2001).
- ⁹H. Kuramochi, Y. Andoh, N. Yoshii, and S. Okazaki, *J. Phys. Chem.* **113**, 15181 (2009).
- ¹⁰D. L. Foster and R. H. Fillingame, *J. Biol. Chem.* **254**, 8230 (1979).
- ¹¹M. J. Newman, D. L. Foster, T. H. Wilson, and H. R. Kaback, *J. Biol. Chem.* **256**, 11804 (1981).
- ¹²H. Itami, Y. Sakaki, T. Shimamoto, M. T. H. Hama, and T. Tsuchiya, *J. Biochem. (Tokyo)* **105**, 785 (1989).
- ¹³V. Pillai and D. O. Shah, *Industrial Applications of Microemulsions*, Surfactant Science Series Vol. 66, edited by C. Solans and H. Kunieda (Marcel Dekker, New York, 1997), p. 227.
- ¹⁴M. A. López-Quintela, J. Quibén-Solla, and J. Rivas, *Industrial Applications of Microemulsions*, Surfactant Science Series Vol. 66, edited by C. Solans and H. Kunieda (Marcel Dekker, New York, 1997), p. 247.
- ¹⁵N. Yoshii and S. Okazaki, *J. Chem. Phys.* **126**, 096101 (2007).
- ¹⁶K. Fujimoto, N. Yoshii, and S. Okazaki, *J. Chem. Phys.* **133**, 074511 (2010).
- ¹⁷K. Fujimoto, N. Yoshii, and S. Okazaki, *Mol. Simul.* **38**, 342 (2012).
- ¹⁸K. Fujimoto, N. Yoshii, and S. Okazaki, *J. Chem. Phys.* **136**, 014511 (2012).
- ¹⁹M. Zacharias, T. P. Straatsma, and J. A. McCammon, *J. Chem. Phys.* **100**, 9025 (1994).
- ²⁰N. Yoshii, K. Iwahashi, and S. Okazaki, *J. Chem. Phys.* **124**, 184901 (2006).
- ²¹H. F. Huisman, *Proc. K. Ned. Akad. Wet., Ser. B: Phys. Sci.* **67**, 388 (1964).
- ²²S. Hayashi and S. Ikeda, *J. Phys. Chem.* **84**, 744 (1980).
- ²³P. Lianos and R. Zana, *J. Colloid Interface Sci.* **84**, 100 (1981).
- ²⁴W. L. Jorgensen, J. Chandrasekhar, J. D. Madura, R. W. Impey, and M. L. Klein, *J. Chem. Phys.* **79**, 926 (1983).
- ²⁵A. D. MacKerell, Jr., D. Bashford, M. Bellott, R. L. Dunbrack, Jr., J. D. Evanseck, M. J. Field, S. Fischer, J. Gao, H. Guo, S. Ha, D. Joseph-McCarthy, L. Kuchnir, K. Kuczera, F. T. K. Lau, C. Mattos, S. Michnick, T. Ngo, D. T. Nguyen, B. Prodhom, W. E. Reiher III, B. Roux, M. Schlenkrich, J. C. Smith, R. Stote, J. Straub, M. Watanabe, J. Wiórkiewicz-Kuczera, D. Yin, and M. Karplus, *J. Phys. Chem. B* **102**, 3586 (1998).
- ²⁶A. D. MacKerell, Jr., M. Feig, and C. L. Brooks III, *J. Comput. Chem.* **25**, 1400 (2004).
- ²⁷G. J. Martyna, D. J. Tobias, and M. L. Klein, *J. Chem. Phys.* **101**, 4177 (1994).
- ²⁸G. J. Martyna, M. E. Tuckerman, D. J. Tobias, and M. L. Klein, *Mol. Phys.* **87**, 1117 (1996).
- ²⁹G. J. Martyna, M. L. Klein, and M. E. Tuckerman, *J. Chem. Phys.* **97**, 2635 (1992).
- ³⁰U. Essmann, L. Perera, M. L. Berkowitz, T. A. Darden, H. Lee, and L. Pedersen, *J. Chem. Phys.* **103**, 8577 (1995).
- ³¹S. Cabani, P. Gianni, V. Mollica, and L. Lepori, *J. Solution Chem.* **10**, 563 (1981).