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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

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Free energy of transfer, $\Delta G_{w \rightarrow m}$, from water phase to a sodium dodecyl sulfate (SDS) micelle core has been calculated for a series of hydrophobic solutes originally immiscible with water by thermodynamic integration method combined with molecular dynamics calculations. The calculated free energy of transfer is in good correspondence to the experiment as well as the theoretical free energy of transfer. The calculated $\Delta G_{w \rightarrow m}$'s are all negative, implying that the alkane molecules are more stable in the micelle than in the water phase. It decreases almost linearly as a function of the number of carbon atoms of the alkanes longer than methane with a decrement of 3.3 kJ mol⁻¹ per one methylene group. The calculated free energy of transfer indicates that, for example, at the micelle concentration of 50 CMC (critical micelle concentration), about only 1 of 6 micelles or 1 of 32 000 micelles does not contain a solute methane or n-octane molecule, respectively. © 2010 American Institute of Physics. [doi:10.1063/1.3469772]

I. INTRODUCTION

In a series of our molecular dynamics (MD) studies of a spherical sodium dodecyl sulfate (SDS) micelle, stability of the micelle in water has been investigated in detail including calculation of free energy of micelle formation.¹⁻³ Along with this, free energy of transfer of a water molecule from water phase to the micelle core has been calculated.³ The calculated value was +28 kJ mol⁻¹, which indicates that the water molecule seldom permeates into the core. The behavior clearly comes from the hydrophobic nature of the micelle core which is made of hydrocarbon chains.

On the contrary, hydrophobic solutes are expected to be more stable in the micelle core than in the water phase. In fact, the solutes immiscible with water may be solubilized by the micelle. The phenomenon is called solubilization. Application of this solubilization is wide in various industries. For example, coloring matters and perfumes in cosmetics are solubilized by the surfactants. Medicines in drug delivery systems,⁴ extracted cell membrane proteins,⁵⁻⁷ and reactant molecules of chemical reactions in the micelles^{8,9} are also the examples.

Scientifically, too, the solubilization has been attracting much interest of physical chemists for recent decades. A number of studies have been done to understand the phenomenon for simple solutes such as alkanes. For example, free energy of transfer of the alkanes from water to the micelle core has been obtained based on the solubility measurement of the solutes.¹⁰⁻¹² The measured value of the free energy of transfer of the alkanes from water to the micelles corresponded to the free energy of transfer from water to the

liquid alkanes at high pressures. This clearly shows enhancement of the solubility by the micelle. From a theoretical view point, however, only phenomenological methods such as the phase-separation model and the mass action model, which are popular in the field of colloid chemistry, have been applied to this solubilization, although little has been clarified at a molecular level.¹³

As stated above, in our previous work, free energy of transfer of a water molecule from water phase to the micelle core has been calculated by thermodynamic integration method combined with molecular dynamics calculations. In the present study, we extend this calculation to a series of hydrophobic solute molecules, i.e., methane, ethane, n-butane, n-hexane, and n-octane, in order to investigate the solubilization of immiscible solutes by the spherical SDS micelle. The calculated free energy is compared with the experimental one¹⁰⁻¹² as well as the theoretical one for methane by Matubayasi *et al.*¹⁴ based on their distribution function theory in the energy representation.

After computational details are described in Sec. II, thermodynamics of the solubilization and a molecular picture for it are discussed in Sec. III. We conclude in Sec. IV.

II. METHOD

In the present study, free energy of transfer of an alkane molecule from water phase in a micellar solution to the micelle core, $\Delta G_{w \rightarrow m}$, has been evaluated by

$$\Delta G_{w \rightarrow m} = \Delta G_{id \rightarrow m} - \Delta G_{id \rightarrow w}, \quad (1)$$

where $\Delta G_{id \rightarrow m}$ and $\Delta G_{id \rightarrow w}$ are free energy of transfer of the alkane molecule from an ideal gas state to the micelle core and the one from the ideal gas to the water phase, respectively. Figure 1 shows this thermodynamic cycle. The value

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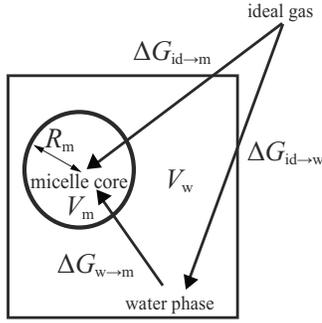


FIG. 1. Thermodynamic cycle for solubilization. Free energy of transfer of alkane from water phase to the micelle core, $\Delta G_{w \rightarrow m}$, may be calculated from the one from an ideal gas state to the water phase, $\Delta G_{id \rightarrow w}$, and the one from the ideal gas state to the micelle core, $\Delta G_{id \rightarrow m}$. R_m is the radius of the spherical micelle, and V_m and V_w are the volume of the micelle and the water phase, respectively.

of $\Delta G_{id \rightarrow m}$ and $\Delta G_{id \rightarrow w}$ may be calculated by the standard thermodynamic integration method combined with molecular dynamics calculations since $\lambda_1 = \lambda_2 = 0$ state, as stated below, is actually the ideal gas state with the volume allowed for the alkane.

A. Thermodynamic integration method for solubilization

Now, we consider a system composed of $N+1$ molecules. The first N molecules constitute one spherical micelle in solution and the $(N+1)$ -th molecule is an alkane molecule. Suppose that the alkane molecule interacts with the micelle molecules as well as the solvent water through a set of ordinary interaction functions with coupling parameters, λ , such that the potential energy of the whole system, $V(\mathbf{r}^{N+1}; \lambda)$, may be written as

$$V(\mathbf{r}^{N+1}; \lambda) = V_N(\mathbf{r}^N) + \Delta V(\mathbf{r}_{N+1}, \mathbf{r}^N; \lambda) + V_{N+1}^{\text{intra}} \quad (2)$$

where $V_N(\mathbf{r}^N)$, $\Delta V(\mathbf{r}_{N+1}, \mathbf{r}^N; \lambda)$, and V_{N+1}^{intra} represent the sum of intra- and intermolecular interactions over the first N molecules, the intermolecular interaction between the $(N+1)$ -th molecule and the rest of the N molecules, and the intramolecular interaction of the $(N+1)$ -th molecule, respectively. In the present study, a two-parameter formula by Zacharias *et al.*¹⁵ was adopted for the intermolecular potential function between the $(N+1)$ -th alkane molecule and the rest of N micelle and solvent molecules,

$$\begin{aligned} \Delta V(\mathbf{r}_{N+1}, \mathbf{r}^N; \lambda_1, \lambda_2) = & \lambda_1 \sum_{i \in M^N} \sum_{j \in M_{N+1}} \frac{1}{4\pi\epsilon_0} \frac{q_i q_j}{r_{ij}} \\ & + \lambda_2 \sum_{i \in M^N} \sum_{j \in M_{N+1}} \left\{ \frac{A_{ij}}{[r_{ij}^2 + \delta(1 - \lambda_2)]^6} \right. \\ & \left. - \frac{B_{ij}}{[r_{ij}^2 + \delta(1 - \lambda_2)]^3} \right\}, \quad (3) \end{aligned}$$

where $i \in M^N$ represents the i -th atom in one of the N molecules and $j \in M_{N+1}$ the j -th atom in the $(N+1)$ -th molecule. ϵ_0 is the dielectric constant of vacuum, q_i and q_j are the point charges of the i -th and j -th atoms, respectively, and A_{ij} and B_{ij} are the Lennard-Jones parameters between the i -th and

j -th atoms. δ is a parameter which prevents divergence of the Lennard-Jones potential caused by the overlap of the $(N+1)$ -th molecule with any of the other N molecules. Here, the value of δ was set to be 0.05 nm^2 .

At $\lambda_1 = \lambda_2 = 0$, the $(N+1)$ -th molecule does not interact with the other N molecules. Then, the $(N+1)$ -th molecule can be regarded to form an ideal gas. On the other hand, at $\lambda_1 = \lambda_2 = 1$, the $(N+1)$ -th molecule fully interacts with the rest of the whole system. Then, we can write the free energy difference ΔG between the states at $\lambda_1 = \lambda_2 = 1$ and 0 to be

$$\begin{aligned} \Delta G = & G(\lambda_1 = \lambda_2 = 1) - G(\lambda_1 = \lambda_2 = 0) \\ = & \int_C \left\{ \left\langle \frac{\partial V}{\partial \lambda_1} \right\rangle_{\lambda_1, \lambda_2} d\lambda_1 + \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} d\lambda_2 \right\}, \quad (4) \end{aligned}$$

where $\langle \dots \rangle_{\lambda_1, \lambda_2}$ denotes the isothermal-isobaric ensemble average at fixed λ_1 and λ_2 , and C is an integration path from $\lambda_1 = \lambda_2 = 0$ to $\lambda_1 = \lambda_2 = 1$. Integrands of Eq. (4) may easily be evaluated by ordinary molecular dynamics calculations.

The integration path C in Eq. (4) may be chosen arbitrarily under the condition that the starting and ending terminal points are fixed at $\lambda_1 = \lambda_2 = 0$ and 1, respectively. Here, we adopted a numerical integration path made of two straight lines. First, λ_2 changes its value from 0 to 0.1 at an interval of 0.025, and from 0.1 to 0.3 at an interval of 0.1 with λ_1 fixed at 0. Then, both λ_1 and λ_2 are changed simultaneously from 0 to 1 and from 0.3 to 1 at intervals of 0.1 and 0.07, respectively, following the equation $\lambda_2 = 0.7\lambda_1 + 0.3$. Thus, Eq. (4) can be expressed as

$$\begin{aligned} \Delta G = & \int_0^{0.3} \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} d\lambda_2 \\ & + \int_0^1 \left[\left\langle \frac{\partial V}{\partial \lambda_1} \right\rangle_{\lambda_1, \lambda_2} + 0.7 \left\langle \frac{\partial V}{\partial \lambda_2} \right\rangle_{\lambda_1, \lambda_2} \right] d\lambda_1. \quad (5) \end{aligned}$$

This is the formula we adopted for the present numerical line integration. In order to evaluate $\Delta G_{id \rightarrow w}$ and $\Delta G_{id \rightarrow m}$ separately by the thermodynamic integration method, integration space for the alkane molecule of interest must be divided into the water phase and the micelle core. We defined that the alkane is in the micelle core where the distance from the center of mass of the micelle to that of the alkane is shorter than the radius of the micelle $R_m = 2.8 \text{ nm}$, i.e., the average distance from the center of mass of the micelle to the interface between the micelle and water,² see Fig. 1. When the distance is longer than R_m , the alkane is considered to be located in the water phase.

Suppose that the spaces of the micelle core and the water phase are represented by the volume $V_m (= \frac{4}{3}\pi R_m^3)$ and $V_w (= V - V_m)$, respectively, where V is the volume of the MD box. Then, excess free energy of transfer of the alkane from an ideal gas to the water phase $\Delta G_{id \rightarrow w}^{\text{ex}}$ and to the micelle core $\Delta G_{id \rightarrow m}^{\text{ex}}$ may be calculated by

$$\Delta G_{id \rightarrow w}^{ex} = \Delta G(\mathbf{r}_{N+1} \in V_w), \quad (6)$$

$$\Delta G_{id \rightarrow m}^{ex} = \Delta G(\mathbf{r}_{N+1} \in V_m), \quad (7)$$

where $\Delta G(\mathbf{r}_{N+1} \in V_w)$ and $\Delta G(\mathbf{r}_{N+1} \in V_m)$ represent the free energy difference ΔG in Eq. (5) for which the sampling of the integrands is made for the location of the alkane $\mathbf{r}_{N+1} \in V_w$ and $\mathbf{r}_{N+1} \in V_m$, respectively.

Then, the total free energy of transfer $\Delta G_{id \rightarrow w} (= \Delta G_{id \rightarrow w}^{id} + \Delta G_{id \rightarrow w}^{ex})$ and $\Delta G_{id \rightarrow m} (= \Delta G_{id \rightarrow m}^{id} + \Delta G_{id \rightarrow m}^{ex})$ may be written as

$$\Delta G_{id \rightarrow w} = \Delta G_{id \rightarrow w}^{ex} - k_B T \ln \frac{V_w}{V}, \quad (8)$$

$$\Delta G_{id \rightarrow m} = \Delta G_{id \rightarrow m}^{ex} - k_B T \ln \frac{V_m}{V}. \quad (9)$$

Now, the total free energy of transfer $\Delta G_{w \rightarrow m}$ of the alkane from the water phase to the micelle core is of the form

$$\Delta G_{w \rightarrow m} = \Delta G_{w \rightarrow m}^{ex} - k_B T \ln \frac{V_m}{V_w}, \quad (10)$$

where

$$\Delta G_{w \rightarrow m}^{ex} = \Delta G_{id \rightarrow m}^{ex} - \Delta G_{id \rightarrow w}^{ex}. \quad (11)$$

B. Restriction on the space for alkane molecule

In order to sample the integrands in Eq. (5) efficiently, space for the alkane molecule of interest must be restricted in the water phase or in the micelle core during the MD calculations. In order to do so, we introduced soft core wall potential for the alkane,

$$\phi_{\text{wall}}(R, R_m; \lambda) = \lambda \frac{A}{[(R - R_m)^2 + \delta(1 - \lambda)]^6}, \quad (12)$$

where R is the distance between the center of mass of the micelle and that of the alkane. R_m is the distance from the center of mass of the micelle to the wall, for which the radius of the micelle is adopted. A is the interaction parameter between the alkane molecule and the wall, which was adopted to be the same as that for the oxygen atom of SDS. Here, λ was set to be the same as λ_2 . Then, at $\lambda_1 = \lambda_2 = 0$, the alkane can go through the wall freely to be anywhere in the simulation box, whereas at $\lambda_1 = \lambda_2 = 1$, the position of the alkane is restricted in the micelle or in the water phase, being separated by the wall. This wall potential causes an extra free energy to the system. However, this is very small such that it may be neglected in the present study.

C. Molecular dynamics calculation

Free energy of transfer from water phase to the SDS micelle core has been calculated by thermodynamic integration method combined with molecular dynamics calculations for methane, ethane, n-butane, n-pentane, and n-octane. In these calculations, the aggregation number of the SDS micelle was adopted to be 60 since our previous work¹ as well as the experiments^{16,17} showed that the aggregation number

around 60 is thermodynamically most stable in the micellar solution. One alkane molecule, one spherical micelle, and 8360 water molecules were contained in a cubic simulation box with the periodic boundary condition. The micelle concentration of the present SDS corresponds to about 50 CMC, i.e., about 10 wt %, where the SDS is found in the stable spherical micelle phase. CHARMM force field^{18,19} was used for the SDS and alkane molecules and TIP4P model²⁰ for water. The temperature and pressure were controlled at $T = 300$ K and $P = 0.1$ MPa, respectively, using the algorithm proposed by Martyna *et al.*^{21,22} Inertia of thermostat and barostat was set to be 3.0×10^{-12} and 0.5×10^{-12} s, respectively. The SHAKE/ROLL and RATTLE/ROLL algorithms were used to impose the constraints on the bond lengths relevant to the hydrogen atoms.²² Particle mesh Ewald (PME) method was adopted for the calculation of the long range interaction.²³ The Ewald dispersion parameter, α , was $0.375 \times 10^{10} \text{ m}^{-1}$ with the cutoff distance of 1 nm and the $128 \times 128 \times 128$ grids for PME. The time step Δt was 1 fs. First, the molecular dynamics calculation was performed for 2 ns for equilibration of the micelle structure and spatial distribution of Na^+ ion. Then, in order to obtain sufficient statistics for the thermodynamic integration, molecular dynamics calculation was performed for 250–350 ps for each set of λ , for which the first 50 ps trajectory was excluded from the average.

During the MD calculations, location of the alkane molecule was monitored to decide at every step time whether it is in the water phase or in the micelle core according to the criterion described in the previous subsection. Following the decision, the integrand either for the alkane in the water phase or in the micelle core was summed up, respectively, see Eqs. (6) and (7). Here, we sampled the MD trajectories starting from two initial configurations. In one case, the alkane was located at $t=0$ inside the wall, i.e., in the micelle, and, in the other case, it was set outside it, i.e., in the water phase. The former is to sample the configurations important for $\Delta G_{id \rightarrow m}^{ex}$ efficiently and the latter is for $\Delta G_{id \rightarrow w}^{ex}$.

Free energy of transfer $\Delta G_{id \rightarrow pw}$ of the alkanes from their ideal gas state to pure water has also been calculated in the same way as the case of the micelle solutions, where one alkane molecule was dissolved in 1300 water molecules in the periodic boundary condition. In this case, the system is homogeneous such that no wall potential is needed.

III. RESULTS AND DISCUSSION

Figure 2 shows the time evolution of the first term of Eq. (5) for n-octane at $\lambda_1 = 0$ and $\lambda_2 = 0.05$. Since this alkane is the longest among the solute molecules studied in the present study and, further, the values of λ_1 and λ_2 are small, convergence of the cumulative average shown in the figure is expected to be slow compared with the other systems. As an example, ensemble averages of $\langle \partial V / \partial \lambda_2 \rangle_{\lambda_1, \lambda_2}$ and $\langle \partial V / \partial \lambda_1 \rangle_{\lambda_1, \lambda_2} + 0.7 \langle \partial V / \partial \lambda_2 \rangle_{\lambda_1, \lambda_2}$ for n-octane transferring from the ideal gas state to the micelle core are presented for a series of (λ_1, λ_2) values in Fig. 3. The resultant $\Delta G_{id \rightarrow m}^{ex}$ was -13 kJ mol^{-1} .

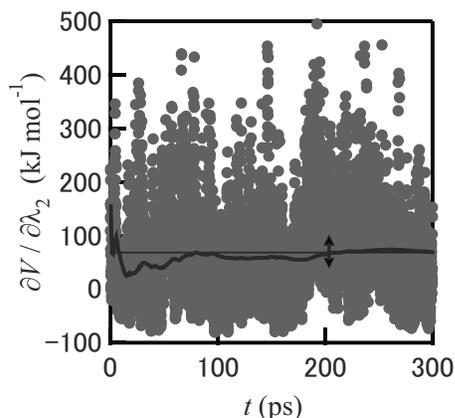


FIG. 2. An example of the calculated first term of Eq. (5) as a function of time (gray dots) for n-octane at $\lambda_1=0$, $\lambda_2=0.05$ as well as its cumulative average (black line). The arrow represents the tolerance of the error, 10 kJ mol^{-1} , which results in the error of 2 kJ mol^{-1} in the calculated free energy difference (see the text).

The error in $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ and $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ should be smaller than 3 kJ mol^{-1} in order to discuss, at least, the carbon number dependence of the free energy of transfer $\Delta G_{\text{w} \rightarrow \text{m}}$ of the alkanes from the water phase to the micelle core. However, average of the integrands over 200–300 ps in the present study might be too short to attain satisfactory statistics for the resultant $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ and $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$. In order to test this, additional long-time MD calculations for 3.5 ns have been done for two conditions in Fig. 3, $\lambda_1=0$, $\lambda_2=0.025$ and $\lambda_1=0$, $\lambda_2=0.05$, for n-octane. The error of the integrand may be considered to be great for these two systems compared with the other conditions in the present study, i.e., the longest alkane and the smallest two λ_1 and λ_2 's.

The average $\langle \partial V / \partial \lambda_2 \rangle$ from the 3.5 ns MD trajectory for $\lambda_1=0$ and $\lambda_2=0.025$ were 165 and 166 kJ mol^{-1} for n-octane molecule in the micelle core and in the water phase, respectively, the residence time being 0.75 and 2.75 ns, respectively. On the other hand, from the 300 ps trajectories, these were 154 and 167 kJ mol^{-1} for the former and for the latter, respectively. Thus, the differences were 11 and 1 kJ mol^{-1} , respectively. For $\lambda_1=0$, $\lambda_2=0.05$, the differences were calculated to be 8 and 5 kJ mol^{-1} for the alkane in the micelle core and in the water phase, respectively. Thus, we

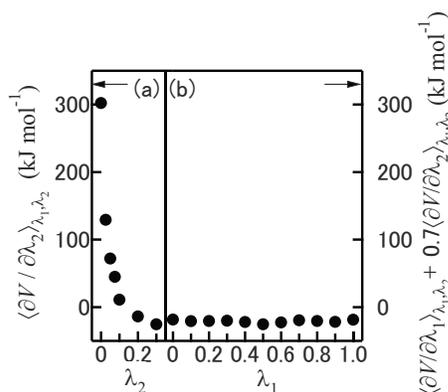


FIG. 3. The averaged $\langle \partial V / \partial \lambda_2 \rangle_{\lambda_1, \lambda_2}$ and $\langle \partial V / \partial \lambda_1 \rangle_{\lambda_1, \lambda_2} + 0.7 \langle \partial V / \partial \lambda_2 \rangle_{\lambda_1, \lambda_2}$, the integrands of the thermodynamic integration method in Eq. (5), for n-octane transferred from the ideal gas state to the micelle core.

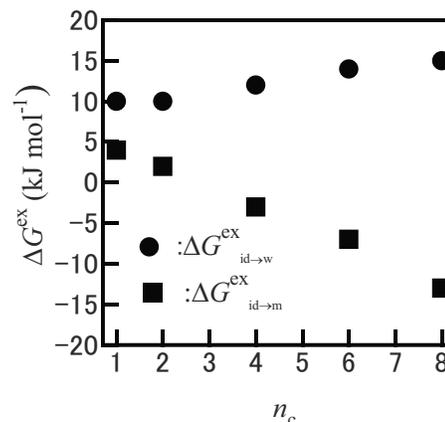


FIG. 4. The calculated excess free energy of transfer from an ideal gas state with the volume V to the water phase of the micellar solution (\bullet) at 50 CMC and from the ideal gas to the micelle core (\blacksquare) as a function of number of carbon atoms, n_c .

can assume that the measure of the error in the calculated integrands in Fig. 3, for example, is, at most, 10 kJ mol^{-1} on average for $\lambda_2 \leq 0.1$. For $\lambda_2 > 0.1$, it can be assumed, at most, to be 5 kJ mol^{-1} since the value of the integrand itself is much smaller than that found for $\lambda_2 \leq 0.1$.

In the present case, the free energy difference we calculate is a summation of the integrands in Eq. (5) of the form $\Delta G = \sum_i \Delta \lambda_i \langle \partial V / \partial \lambda_i \rangle_{\lambda_i}$, the numerical integration, where, for simplicity, only one term is written. However, since the trajectories of the MD calculations with different λ_i are independent of each other, the calculated integrands may be considered to be independent of each other too. Then the error $\sigma_{\Delta G}$ included in ΔG must be $\sigma_{\Delta G}^2 = \sum_i \Delta \lambda_i^2 \sigma_{\lambda_i}^2$, where σ_{λ_i} is the error in the i -th integrand since the covariances are all zero. The estimated value of $\sigma_{\Delta G}$ following the above equation was as small as 2 kJ mol^{-1} even for the present very largely assumed values of σ_{λ_i} . The measure of σ_{λ_i} assumed in the present analysis, 10 kJ mol^{-1} , is presented by an arrow in Fig. 2. The figure clearly shows that the convergence of the cumulative average of the integrand is satisfactory based on the present 200–300 ps long MD calculation.

Figure 4 shows the excess free energy of transfer from an ideal gas state to the water phase in the micellar solution, $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$, and the one from the ideal gas state to the micelle core, $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$, for a series of alkanes. It is found from the figure that $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ is smaller than $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ for all the alkanes from methane to n-octane. The alkanes are, thus, configurationally more stable in the micelle core than in the water phase. Further, the value of $\Delta G_{\text{id} \rightarrow \text{m}}^{\text{ex}}$ decreases monotonically as a function of number of carbon atoms, n_c , and becomes negative for $n_c \geq 4$, at this micelle concentration, ~ 50 CMC, indicating that except for methane and ethane, the alkanes are thermodynamically more stable in the micelle than in the ideal gas state with the volume V . On the other hand, $\Delta G_{\text{id} \rightarrow \text{w}}^{\text{ex}}$ is positive for all the alkanes.

In Fig. 5, the calculated total free energy of transfer of the guest solute from water phase in the present micellar solution at 50 CMC to the micelle core, $\Delta G_{\text{w} \rightarrow \text{m}}$, calculated by Eq. (1) is plotted for each alkane together with the experimental value at 8 CMC (Refs. 10 and 11) and that at 5 CMC

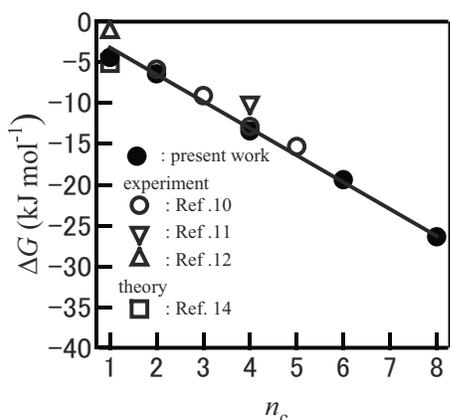


FIG. 5. The calculated total free energy of transfer from the water phase of the micellar solution to the micelle core. (●) Present study, (□) theory by Matubayasi *et al.* (Ref. 14), and [(○), (▽), and (△)] experiments by Wishniya (Ref. 10), Han *et al.* (Ref. 11), and Hai *et al.* (Ref. 12), respectively.

(Ref. 12) from the solubility measurement as well as the theoretical one¹⁴ at 40 CMC based on the distribution function theory.

Comparison of the free energy of transfer at different micelle concentrations has been made by reducing the experimental and theoretical values to those at 50 CMC, i.e., by adding the correction term $-k_B T \ln(V_w^{50 \text{ CMC}}/V_w^c)$ to the experimental and theoretical free energies, where V_w^c represents the volume of the water phase at the concentrations adopted in the experiments and theory, respectively. Here, only the translational free energy of the alkane in the volume is taken into account assuming that the micelle concentration dependence of the configurational free energy of the dissolved alkane in the water phase may be neglected.

As clearly shown in the figure, the present study is in good agreement with both of the experiments and theory at the common micelle concentration, 50 CMC. Further, the figure clearly shows that $\Delta G_{w \rightarrow m}$ decreases almost linearly as a function of n_c except for methane. The decrement of $\Delta G_{w \rightarrow m}$ per methylene group ($-\text{CH}_2-$) of the alkanes, $\partial \Delta G_{w \rightarrow m} / \partial n_c$, was evaluated to be -3.3 kJ mol^{-1} by the linear fitting of $\Delta G_{w \rightarrow m}$ for $2 \leq n_c \leq 8$. The value is also in very good agreement with the experiment, -3.2 kJ mol^{-1} .¹⁰ The above agreement of the total free energy of transfer corrected for the different concentrations as the volume effect implies that the excess free energy of transfer without correction agrees well, too, among the present calculation, the experiments, and the theory.

The calculated free energy of transfer, $\Delta G_{id \rightarrow w}$ and $\Delta G_{id \rightarrow pw}$, from the ideal gas state with the volume V was corrected by adding $-k_B T \ln(V_0/V)$, where V_0 is the volume of the ideal gas at 0.1 MPa and 300 K, in order to obtain the free energy of transfer, $\Delta G_{id \rightarrow w}$ and $\Delta G_{id \rightarrow pw}$, from the ideal gas state at 0.1 MPa. In Fig. 6, the calculated total free energy of transfer from the ideal gas state at 0.1 MPa to the water phase in solution, $\Delta G_{id \rightarrow w}$, and to the pure water, $\Delta G_{id \rightarrow pw}$, calculated in this study is plotted for the alkanes together with the experimental free energy of transfer from the gas state at 0.1 MPa to pure water, $\Delta G_{g \rightarrow pw}$. First, the calculated $\Delta G_{id \rightarrow w}$ is in good agreement with the calculated

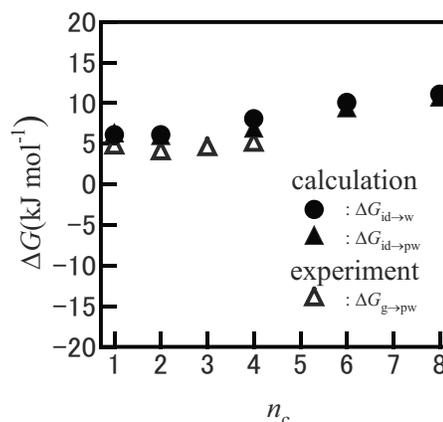


FIG. 6. The calculated total free energy of transfer from the ideal gas state at 0.1 MPa to the water phase of the micellar solution at 50 CMC (●) and from the ideal gas state to pure water (▲) compared with the experimental one (△) from the gas state to pure water (Ref. 25).

$\Delta G_{id \rightarrow pw}$, and second, the calculated $\Delta G_{id \rightarrow w}$ as well as the $\Delta G_{id \rightarrow pw}$ is in good correspondence to the experimental $\Delta G_{g \rightarrow pw}$. The former means that the presence of Na^+ ion in the micellar solution has little influence on $\Delta G_{id \rightarrow w}$. This may be caused by the rather weak interaction between Na^+ and alkane.

All the values plotted in Fig. 6 are positive due to the instability of hydrophobic hydration of the alkanes. Furthermore, the hydration free energy has a minimum value for ethane both in the calculation and experiment. Stability of the alkane in water may be related to the hydration or the cage formation by the solvent water molecules around it²⁴ since the cage structure itself clearly depends on the size of the alkane molecule. Thus, the present result indicates that the hydration structure of ethane is most stable among the alkanes studied here. Further, the carbon number dependence of $\Delta G_{id \rightarrow w}$ found in Fig. 6 is small compared with that of $\Delta G_{id \rightarrow m}$, see also Fig. 4. This implies that the free energy of transfer $\Delta G_{w \rightarrow m}$ in Fig. 5 is dominated by the dissolving process of the alkanes to the hydrophobic micelle core.

Free energy of transfer of methane and n-octane from the ideal gas state at 0.1 MPa to the micelle core and to the water phase in the micellar solution at the concentration of 50 CMC in the present calculation is illustrated in Fig. 7 as an energy level diagram. The result for the guest water molecule obtained in our previous study³ is also presented in the figure.

For methane, $\Delta G_{id \rightarrow m}$ and $\Delta G_{id \rightarrow w}$ are 2 and 6 kJ mol^{-1} ,

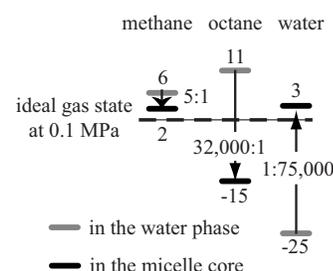


FIG. 7. The calculated free energy level for methane, n-octane, and water molecules in the ideal gas at 0.1 MPa, in the water phase of the micellar solution at 50 CMC, and in the micelle core.

respectively, showing that both processes are thermodynamically unfavorable. The instability is greater in water than in the micelle core. As a result, $\Delta G_{w \rightarrow m}$ has a negative value of -4 kJ mol^{-1} . That is, the methane prefers moving from the water phase into the micelle core to staying in the water phase under the condition that the methane is in the micellar solution. Calculating the $\exp(-\Delta G_{w \rightarrow m}/RT)$, we can estimate the probability that the guest solute is found in the micelle core assuming that the only one solute is accommodated in the micelle core. The value of $\Delta G_{w \rightarrow m}$ indicates that five of six methane molecules are found in the micelle at $T=300 \text{ K}$. On the other hand, for n-octane, $\Delta G_{id \rightarrow m}$ and $\Delta G_{id \rightarrow w}$ were evaluated to be -15 and 11 kJ mol^{-1} , respectively. Here, it must be pointed out that the n-octane molecule is more stable in the micelle core than in the ideal gas state at 0.1 MPa although it is unstable in water. The combined effect gives the considerably negative $\Delta G_{w \rightarrow m} = -26 \text{ kJ mol}^{-1}$, implying that almost all of the n-octane molecules are found in the micelle, only 1 of the 32 000 molecules being dissolved in the water phase. This may be understood by the concept of hydrophobicity too. Almost all the alkane molecules move from the water phase to the hydrophobic micelle core in order to avoid the contact with water molecules and reduce the hydrophobic hydration.

Here, it is interesting to compare the above findings with the case of the water molecule. In our previous work, the calculated $\Delta G_{w \rightarrow m}$ for water was $+28 \text{ kJ mol}^{-1}$. From this, we could evaluate that only 1 of the 75 000 water molecules is found inside the micelle core while the rest of the water molecules are free in the water phase. From the energetical point of view, water molecules do not like to cut their hydrogen bonds with other water molecules to move into the micelle core.

IV. CONCLUSION

In order to evaluate the solubilization free energy of alkanes, i.e., methane, ethane, n-butane, n-hexane, and n-octane by the spherical SDS micelle, thermodynamic integration has been done executing the isobaric and isothermal molecular dynamics calculations for the micellar solution which contains a single alkane molecule. Negative free energy of transfer $\Delta G_{w \rightarrow m}$ from water phase to the micelle core was obtained for all the alkane molecules in the present study, which indicates that alkanes are more stable in the micelle core than in the water phase. Reflecting this negative free energy, the alkane molecules resided in the micelle core all the time during the calculation for a few nanoseconds without wall potential.

The calculated free energy of transfer $\Delta G_{w \rightarrow m}$ decreases almost linearly as a function of number of carbon atoms of the alkanes. It decreases by 3.3 kJ mol^{-1} per methylene group for the alkanes longer than methane. The factor

$\exp(-\Delta G_{w \rightarrow m}/k_B T)$ at 300 K indicates that only 1 of the 32 000 n-octane molecules is dissolved in the water phase.

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