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Molecular dynamics simulation of micelle formation in amphiphilic solution

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The micelle formation in amphiphilic solution is investigated by molecular dynamics (MD) simulation of coarse-grained rigid amphiphiles with explicit solvent molecules. In our simulation model, the intensity of the hydrophilic interaction and the hydrophobic interaction can be varied independently. Our simulations show that various kinds of micellar structures are formed at a lower temperature by quenching from a random configuration of amphiphilic molecules in solution at a higher temperature. The micellar shape changes from a disc (bilayer) into a cylinder and then into a sphere as the intensity of the hydrophilic interaction increases. It is also found that the micelle formation proceeds in a stepwise fashion through the coalescence of smaller micelles. From the analysis of the orientational order for the amphiphilic molecules, it is concluded that the orientational order parameters can be used to distinguish the micellar shapes clearly.

Keywords: Molecular dynamics simulation; Micelle formation; Amphiphilic solution; Asphericity; Orientational order

1. Introduction

Amphiphilic molecules such as surfactants and lipids consist of both a hydrophilic part and a hydrophobic part. In aqueous solutions, these molecules can form various structures such as micelles, bilayer membranes and bicontinuous cubic structures and can transform from one to another when the solution conditions are changed [1–3]. Self-assembly of amphiphilic molecules plays important roles in many biological and industrial processes. For example, phospholipids are one of the major components in the cell membrane and surfactants are indispensable in the textile and the metal industry.

Over the last decade, numerous computer simulations have been carried out in relation to self-assembly of amphiphilic solutions. The equilibrium size and shape distributions of self-assembled micelles were studied using Monte Carlo simulation by Nelson *et al.* [4] and Kenward *et al.* [5]. Molecular dynamics (MD) simulations of coarse-grained amphiphilic molecules in solution were performed by Goetz *et al.* [6] in order to investigate the

spontaneous self-assembly of amphiphilic molecules into bilayer membranes. Several computer simulations were carried out to clarify the molecular mechanism of membrane fusion. Noguchi *et al.* [7] studied the fusion dynamics of vesicles using a Brownian dynamics simulation of trimer amphiphiles without solvent. Stevens *et al.* [8] carried out coarse-grained MD simulations to get direct insight into the dynamics of individual lipids during membrane fusion. Dissipative particle dynamics simulations were also performed to investigate the phase behaviour of amphiphilic solution [9,10] and budding and fission dynamics of two-component vesicles [11]. Although simulation studies on the dynamics of amphiphilic molecules in solution have thus been done intensively, little is known about the detailed mechanism of micelle formation in amphiphilic solution at the molecular level.

The purpose of this paper is to clarify the molecular mechanism of micelle formation in amphiphilic solution. With a view to investigating the micelle formation process in amphiphilic solution *at the molecular level*, we carry

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out the MD simulations of coarse-grained amphiphilic molecules with explicit solvent molecules and analyse the micelle formation process systematically.

2. Simulation model and method

The present computational model is the same as that used in the previous work [12]. An amphiphile is modeled as a rigid linear molecule, which consists of one hydrophilic head particle and two hydrophobic tail particles. A solvent molecule is considered to be a hydrophilic particle. The interaction between a hydrophilic particle and a hydrophobic particle is modeled by a repulsive soft core potential:

$$U_{\text{SC}}(r) = 4\epsilon_{\text{SC}} \left(\frac{\sigma_{\text{SC}}}{r} \right)^9, \quad (1)$$

the interaction between a hydrophilic head particle and a solvent particle is modeled by a Lennard–Jones potential:

$$U_{\text{LJ}}^{\text{hs}}(r) = 4\epsilon_{\text{hs}} \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right], \quad (2)$$

and all other interactions are modeled by a Lennard–Jones potential:

$$U_{\text{LJ}}(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right], \quad (3)$$

where r is the interparticle distance, ϵ_{SC} is an interaction parameter for the intensity of the hydrophobic interaction and ϵ_{hs} is that for the intensity of the hydrophilic interaction. The parameter σ_{SC} is set to be $\sigma_{\text{SC}} = 1.05\sigma$ as in Ref. [6]. The cutoff distance for these potentials is $r_c = 3.0\sigma$ and we use the shifted force variant of these potentials: $V(r) = U(r) - U(r_c) - (\partial U / \partial r)|_{r=r_c}(r - r_c)$, in order to avoid discontinuities both in the potential energy and in the force. In what follows, we represent dimensionless quantities by an asterisk, e.g. number density $\rho^* = \rho\sigma^3$, time $t^* = t\sqrt{\epsilon/m\sigma^2}$ and temperature $T^* = k_B T / \epsilon$, where k_B is the Boltzmann constant. The equations of motion for all particles are solved numerically using the leap-frog algorithm at constant

temperature with a time step of $\Delta t^* = 0.0025$ and the temperature is controlled at every 10 time steps by *ad hoc* velocity scaling [13]. We apply the periodic boundary conditions and the number density is set to $\rho^* = 0.75$. Initially, we provide a randomly distributed configuration of 97 amphiphilic molecules in solution at high temperature ($T^* = 10$) for various values of the interaction parameters ϵ_{SC}^* and ϵ_{hs}^* ($1.0 \leq \epsilon_{\text{SC}}^*, \epsilon_{\text{hs}}^* \leq 3.0$). The number of solvent molecules is 5541, which leads to the amphiphilic concentration of 0.05. The system is then quenched to $T^* = 1.3$ and MD simulations of $t^* = 2.0 \times 10^4$ (8.0×10^6 time steps) are carried out for each simulation run. In this paper, we focus our attention on the results of $\epsilon_{\text{SC}}^* = 1.0$.

3. Simulation results

3.1 Micellar shape

We show, in figure 1, the snapshots of micelles formed by amphiphilic molecules in solution in the cases of $(\epsilon_{\text{SC}}^*, \epsilon_{\text{hs}}^*) = (1.0, 1.0)$, $(1.0, 1.5)$ and $(1.0, 2.0)$. In the figure, grey shadows of the largest micelle projected on three planes are also depicted to clarify the micellar shape. Note that solvent molecules are not displayed. This figure indicates that the micellar shape changes from a disc (bilayer) into a cylinder and then into a sphere as the intensity of the hydrophilic interaction (ϵ_{hs}^*) increases.

3.2 Micelle formation

We first examine the energy relaxation during the micelle formation process. The time evolution of the potential energy in the case of $(\epsilon_{\text{SC}}^*, \epsilon_{\text{hs}}^*) = (1.0, 1.0)$ is plotted in figure 2. We find, from figure 2, that the potential energy relaxes in a stepwise manner. This kind of stepwise behaviour is also found in the cases of $(\epsilon_{\text{SC}}^*, \epsilon_{\text{hs}}^*) = (1.0, 1.5)$ and $(1.0, 2.0)$.

In order to investigate the micelle formation process more clearly, we then define a *micelle* as a collection of amphiphilic molecules whose tail particles are located close to each other [14]. Our precise definition of a micelle

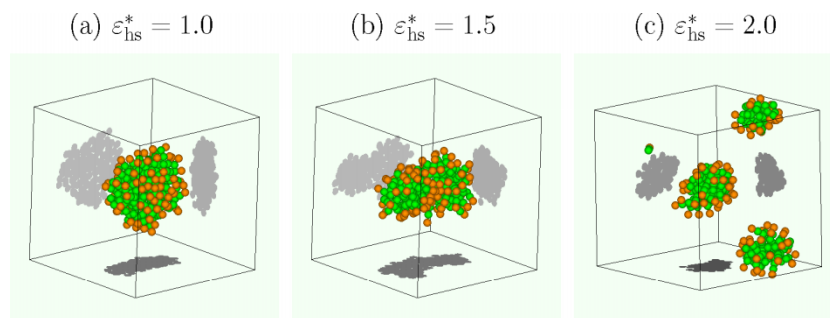


Figure 1. Snapshots of micelles formed by amphiphilic molecules in solution in the case of $\epsilon_{\text{SC}}^* = 1.0$: (a) a disc micelle (bilayer) for $\epsilon_{\text{hs}}^* = 1.0$; (b) a cylindrical micelle for $\epsilon_{\text{hs}}^* = 1.5$; and (c) spherical micelles for $\epsilon_{\text{hs}}^* = 2.0$. Orange and green particles denote hydrophilic head groups and hydrophobic tail groups, respectively. Grey shadows of the largest micelle projected on three planes are also shown to clarify the micellar shape. Note that solvent molecules are not displayed for clarity (colour in online version).

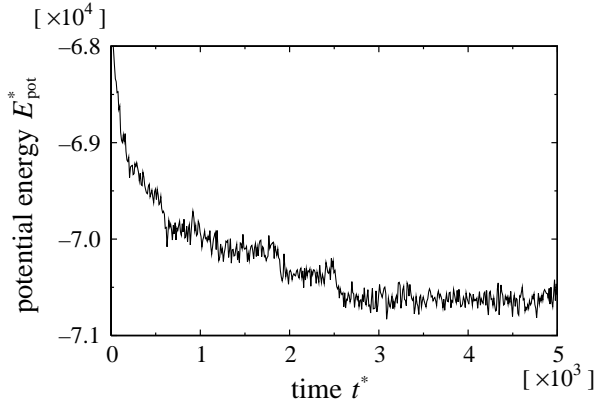


Figure 2. Potential energy E_{pot}^* vs. time t^* in the case of $\varepsilon_{\text{SC}}^* = 1.0$ and $\varepsilon_{\text{hs}}^* = 1.0$.

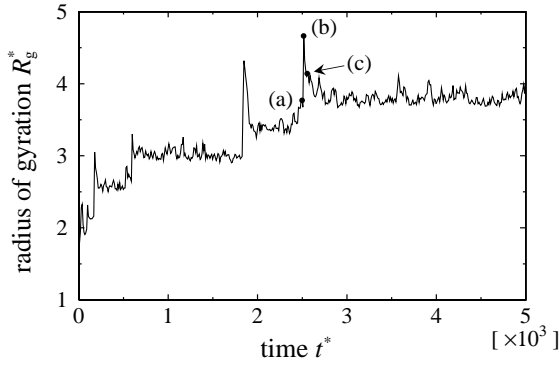


Figure 3. Radius of gyration R_g^* vs. time t^* in the case of $\varepsilon_{\text{SC}}^* = 1.0$ and $\varepsilon_{\text{hs}}^* = 1.0$. Filled circles (a), (b) and (c) correspond to $t^* = 2500$, 2515 and 2560, respectively (figure 4).

is as follows. Two amphiphilic molecules, i and j , belong to the same micelle if the following condition is satisfied: $\min_{k,l} |\mathbf{r}_k^i - \mathbf{r}_l^j| < r_0$, where \mathbf{r}_k^i is the position vector of the k -th tail particle in the i -th amphiphilic molecule. In our calculations, we set $r_0 = 1.4\sigma$. In figure 3, we show the radius of gyration R_g^* of the largest micelle as a function of time in the case of $(\varepsilon_{\text{SC}}^*, \varepsilon_{\text{hs}}^*) = (1.0, 1.0)$. R_g^* is found to increase in a stepwise fashion in connection with the energy relaxation (figure 2). We also find several sharp bumps in the time evolution of R_g^* , which implies that the

micelle formation proceeds through the coalescence of smaller micelles.

Here, we study the coalescence of micelles. We show micelles at $t^* = 2500$, 2515 and 2560 in the case of $(\varepsilon_{\text{SC}}^*, \varepsilon_{\text{hs}}^*) = (1.0, 1.0)$ in figure 4. It is found from this figure that two micelles at $t^* = 2500$ contact at $t^* = 2515$, which corresponds to the time for the peak of R_g^* in figure 3 and coalesce into a large micelle at $t^* = 2560$. The time for coalescence is so short that the micelle formation proceeds in a stepwise fashion.

3.3 Asphericity

We calculate the distribution of asphericity to characterize the micellar shape. Here, we introduce the coordinate system with three principal axes of inertia of the largest micelle. In this coordinate system, the origin is located at the centre-of-mass position of the micelle, the x -axis is the principal axis with the largest moment of inertia and the z -axis is that with the smallest moment of inertia. The asphericity A is defined by

$$A = \frac{(R_{\text{gx}}^2 - R_{\text{gy}}^2)^2 + (R_{\text{gy}}^2 - R_{\text{gz}}^2)^2 + (R_{\text{gz}}^2 - R_{\text{gx}}^2)^2}{2R_{\text{g}}^4}, \quad (4)$$

where R_{gx} , R_{gy} and R_{gz} are, respectively the radii of gyration parallel to individual principal axes and the relation $R_{\text{g}}^2 = R_{\text{gx}}^2 + R_{\text{gy}}^2 + R_{\text{gz}}^2$ holds. It should be noted that we take only the tail particles into account in the calculation of the principal axes of inertia and asphericity. The asphericity A is a measure of deformation from spherical symmetry: $A = 0.25$ for an infinitely thin disc, $A = 1.0$ for an infinitely thin rod and $A = 0.0$ for a perfect sphere. The distribution function of asphericity $P(A)$ is shown in figure 5 in the cases of $(\varepsilon_{\text{SC}}^*, \varepsilon_{\text{hs}}^*) = (1.0, 1.0)$, $(1.0, 1.5)$ and $(1.0, 2.0)$. This figure tells us that A is between 0.1 and 0.2 for a disc micelle, A is larger than 0.2 for a cylindrical micelle and A is less than 0.2 for a spherical micelle. This result indicates that disc micelles are not clearly distinguishable from spherical micelles by the asphericity A because the distribution functions $P(A)$ for disc micelles and spherical micelles overlap significantly each other (figure 5(a) and (c)). We, therefore, need

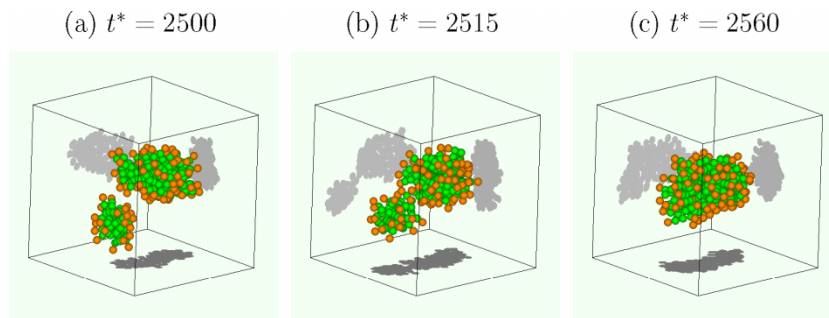


Figure 4. Coalescence of micelles: (a) $t^* = 2500$; (b) $t^* = 2515$; and (c) $t^* = 2560$, which are indicated by filled circles in figure 3.

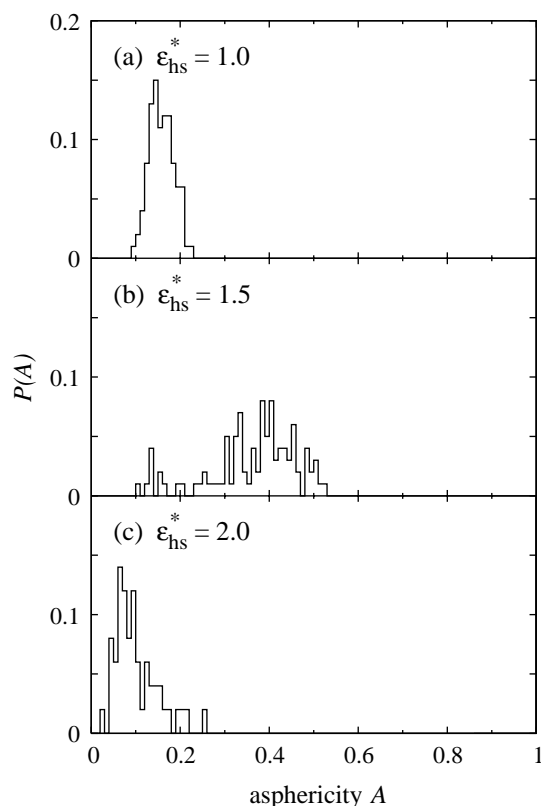


Figure 5. Distribution function of asphericity $P(A)$ in the case of $\epsilon_{SC}^* = 1.0$: (a) $\epsilon_{hs}^* = 1.0$; (b) $\epsilon_{hs}^* = 1.5$; and (c) $\epsilon_{hs}^* = 2.0$. Time average is taken during $t^* = 9500 - 10,000$ in (a) and (c) and during $t^* = 19,500 - 20,000$ in (b).

another parameter to clearly distinguish three types of micellar shapes.

3.4 Orientational order

We focus on the orientational order of amphiphilic molecules in order to characterize the three types of micelles: disc (bilayer), cylindrical and spherical micelles. The orientational order parameters p_x , p_y and p_z are defined by

$$p_i = \left\langle \frac{3 \cos^2 \theta_i - 1}{2} \right\rangle \quad (i = x, y, z), \quad (5)$$

where θ_i is the angle between the vector along the molecular axis of an amphiphile and the i -axis ($i = x, y, z$) and $\langle \dots \rangle$ denotes the average over all amphiphilic molecules. Note that the average is taken for the amphiphilic molecules in the proximity of the centre-of-mass position of the largest micelle, that is, those in the region of $-\Delta r < x, y, z < \Delta r$. We set $\Delta r = 2.5\sigma$ in the calculation of p_i . Ideally, the orientational order parameters take the following values: $(p_x, p_y, p_z) = (0, 0, -0.5)$ for a disc (bilayer), $(p_x, p_y, p_z) = (1, -0.5, -0.5)$ for a cylinder and $(p_x, p_y, p_z) = (0, 0, 0)$ for a sphere. We show, in figure 6, the distribution functions $P(p_x)$, $P(p_y)$ and $P(p_z)$ in the cases of $(\epsilon_{SC}^*, \epsilon_{hs}^*) = (1.0, 1.0)$, $(1.0, 1.5)$ and $(1.0, 2.0)$. We find

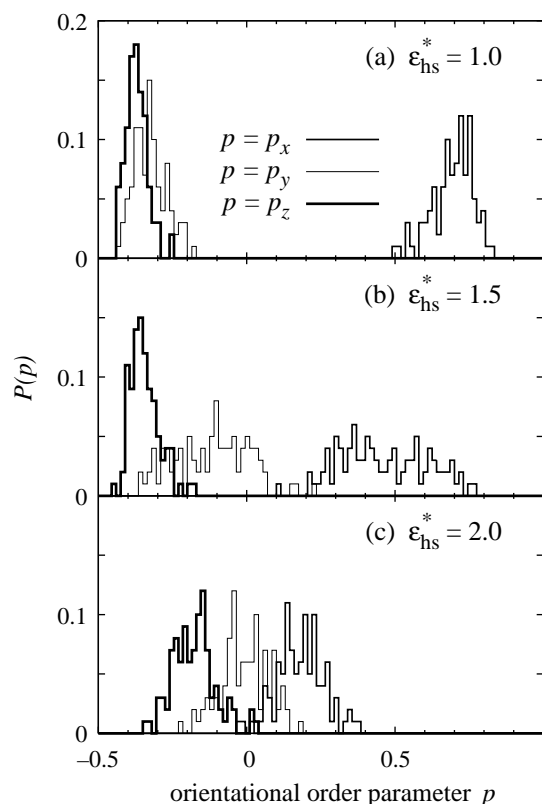


Figure 6. Distribution functions of orientational order parameter $P(p_x)$, $P(p_y)$ and $P(p_z)$ in the vicinity of the centre-of-mass of the largest micelle in the case of $\epsilon_{SC}^* = 1.0$: (a) $\epsilon_{hs}^* = 1.0$; (b) $\epsilon_{hs}^* = 1.5$; and (c) $\epsilon_{hs}^* = 2.0$. Time average is taken during the same time interval as in figure 5.

from this figure that three types of micellar shapes are clearly distinguishable by the orientational order parameters: $0.5 < p_x < 1.0$ and $-0.5 < p_y, p_z < -0.25$ for a disc micelle, $-0.25 < p_x, p_y < 0.5$ and $-0.5 < p_z < -0.25$ for a cylindrical micelle and $-0.25 < p_x, p_y, p_z < 0.5$ for a spherical micelle.

4. Summary and discussion

By performing MD simulations of coarse-grained amphiphilic molecules with explicit solvent molecules, we have obtained the following new results: (1) as the intensity of the hydrophilic interaction increases, the micellar shape changes from a disc (bilayer) into a cylinder and then into a sphere; (2) both the energy relaxation and the increase of the radius of gyration proceed in a stepwise manner; (3) the micelle formation proceeds through the coalescence of smaller micelles; and (4) three types of micellar shapes (disc, cylinder and sphere) are clearly distinguishable by the orientational order parameters p_x , p_y and p_z .

The first result can be interpreted in the following way. The hydrophilic interaction tends to increase the interfacial area per amphiphilic molecule (the effective headgroup area), which leads to the large interfacial curvature [2,3]. Therefore, the micelle with larger

interfacial curvature emerges as the intensity of the hydrophilic interaction increases.

Our simulation results lead to the conclusion that the orientational order parameters, concerning the principal axes of inertia of the micelle rather than the asphericity, are useful enough to distinguish the micellar shapes. The reason for this is that the asphericity fluctuates considerably with time, in the case of a thick disc or a thick cylinder, whereas the internal orientational structure of a micelle is not so sensitive to the shape fluctuation.

For the future work, we will carry out MD simulation of amphiphilic molecules with various chain rigidity in solution in order to investigate the effect of chain rigidity on the formation processes of micelles and mesophases systematically.

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