Temperature-Controlled Vesicle Aggregation in the Mixed System of Sodium n-Dodecyl Sulfate/ n-Dodecyltributylammonium Bromide

Haqing Yin,† Jianbin Huang,*,† Yuqian Gao,† and Honglan Fu†

State Key Laboratory for Structural Chemistry of Unstable and Stable Species, College of Chemistry and Molecular Engineering, and College of Life Science, Peking University, Beijing 100871, People’s Republic of China

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Temperature-controlled vesicle aggregation was investigated in a catanionic surfactant system of sodium n-dodecyl sulfate/n-dodecyltributylammonium bromide. Vesicle aggregation took place as the temperature reached the critical value ($T_c$). $T_c$ can be adjusted by the variations of the total surfactant concentration and the mixed molar ratio. It was also found that the temperature variation above $T_c$ can greatly influence the vesicle aggregation rate. The vesicle aggregation process was irreversible as long as $T \geq T_c$, whereas the vesicle disaggregation process occurred only below $T_c$.

Introduction

Vesicles are widely used as the models for cell membranes and drug delivery systems.1,2 Living cells in a multicellular organism preserve their individuality. However, in certain physiological conditions their aggregation or fusion occurs. In the past few decades, the aggregation of vesicles has attracted special attention not only for its close relations to these biological processes as the analogous model,3,4 but also for its practical importance in pharmacy and so on.5–7 Normally, vesicle aggregation is induced by external additives. Salt-induced and polymer-induced vesicle aggregations have been well-investigated in numerous papers.8–12 Recently, vesicle aggregation induced by the specific molecular recognition13 (or referred to as the “host–guest” complexation)14 also aroused much interest. However, no research on the temperature-induced vesicle aggregation has been reported so far, although temperature variation can provide quite a simple way to tailor assemblies.15,16 In fact, in most vesicular systems, phase transition or vesicle disruption will take place upon increasing the temperature.17,18

In this work, temperature-controlled vesicle aggregation is for the first time reported in a catanionic surfactant system of sodium n-dodecyl sulfate (SDS)/n-dodecyltributylammonium bromide (DTBAB). Vesicle aggregation occurred as the temperature reached the critical value. The critical temperature showed a strong dependence on the total surfactant concentration and the surfactant mixed molar ratio. The aggregation rate can also be greatly influenced by the temperature variation above the critical temperature.

Experimental Section

SDS was bought from ACROS ORGANICS Co., 99% purity. Quaternary ammonium bromide was prepared by reaction of 1-bromododecane and the corresponding trialkylamine. Turbidity was carried out with a Shimadzu UV-250 spectrophotometer at 514.5 nm. Dynamic light scattering (DLS) measurements were performed with a spectrometer (ALV-5000/E/WIN Multiple Tau Digital Correlator) and a Spectra-Physics 2017 Ar laser (514.5-nm wavelength). The intensity autocorrelation functions were analyzed using the Contin method, and the average hydrodynamic radius ($R_h$) was deduced from the diffusion coefficient ($D$) by the Stokes–Einstein formula

$$D = \frac{k_BT_c}{6\pi R_h n}$$

The temperature of turbidimetric and DLS measurements was controlled by an external thermostatic bath, and the time needed for the temperature changes was less than 2 min in the study. A negative-staining technique (with uranyl acetate water solution) was used, and a JEM-100CX electron microscope was employed in the microscopic observation. Differential scanning calorimetry (DSC) measurements were carried out (1 °C/min) using a Micro DSC III (Setaram-France) instrument. Zeta potentials were measured using a temperature-controlled ZetaPlus (Brook Heaton Co.) zeta potential analyzer.

Results and Discussion

At 30 °C, the formation of microstructures in the mixed system of SDS/DTBAB was investigated at the total surfactant concentration (C$_{total}$) of 10 mM and the mixed molar ratio of 2:1 (SDS/DTBAB). Separated spherical vesicles with the radius of 50–100 nm were observed by transmission electron microscopy (TEM) (Figure 1a), and

* Corresponding author. E-mail: jhhuang@pku.edu.cn. Fax: 86-10-62751708. Tel.: 86-10-62753557.

† College of Chemistry and Molecular Engineering, Peking University.

‡ College of Life Science, Peking University.

§ College of Life Science, Peking University.

1 College of Chemistry and Molecular Engineering, Peking University.


vesicle aggregation was very scarce, if at all. Combined with the result of DLS (see Figure 1 in the Supporting Information), it can be demonstrated that spherical vesicles with the average hydrodynamic radius (\(\langle R_h \rangle\)) of 60 nm were the dominating aggregates in the system. The zeta potential of the system was about \(-96\) mV at 30 °C, which indicates that the electrostatic repulsion between vesicles was relatively strong.19 This kind of repulsive force together with the repulsive hydration force between the hydration layers of vesicles20 may be responsible for the stability of the system.

As the temperature changed from 30 to 33 °C, the turbidity dropped a little and there was no obvious change in the system. However, when the temperature increased to 34 °C, the turbidity began to increase with time (Figure 2a). By TEM, gradual aggregation of vesicles was observed (Figure 1b–d), which reveals that the increase of the turbidity was attributed to the vesicle aggregation at the critical temperature, 34 °C (named as \(T_c\) hereafter). In addition, the formation of larger vesicles by vesicle fusion can also be noticed during the process of vesicle aggregation.

It is interesting to find that temperature variation above \(T_c\) had great influences on the vesicle aggregation rate. In fact, the turbidity still increased slowly after 12 h at 34 °C, indicating that the vesicle aggregation rate was relatively slow at this temperature. However, the increase of turbidity became much faster when further heating to 35 or 36 °C (Figure 2). It just took \(~75\) min for the turbidity to reach the maximal value when the system was heated directly from 33 to 36 °C (Figure 2b), which suggests that the vesicle aggregation rate was remarkably accelerated by the increase of temperature. Further evidence was provided by the results of the light scattering intensity of the system measured at 90° \((I_{90};\) Figure 3). The temperature effect on the kinetics of vesicle aggregation above \(T_c\) is clearly shown in Figure 3, which is coincident with the turbidimetrical results. From Figure 2c, it is also noteworthy that, even as the temperature decreased but still remained above 34 °C, the turbidity still went on increasing but with a slower rate. Only as the temperature


aggregation was accompanied by an increase of entropy. Of this transition, it can also be deduced that the vesicle transition was positive. Considering the spontaneity (Figure 4), suggesting that the transfer of enthalpy during temperature of 34 °C is shown in the DSC heating curve this system. An obvious endothermic peak with the outset effect of the temperature-induced vesicle aggregation in

Disaggregation took place only below \( T_c \) while the vesicle aggregation occurred in the mixed systems of SDS/\( n \)-dodecyltrimethylammonium bromide (DTMAB), SDS/\( n \)-dodecyltrimethyl ammonium bromide (DTEAB), or SDS/\( n \)-dodecyltripropylammonium bromide (DTPAB) (see Figure 2 in the Supporting Information), indicating that the relatively large and hydrophilic headgroup (tributylammonium) of DTBAB may play an important role in this transition. In fact, owing to the steric restriction, it is not feasible for all three of the butyl groups to bend toward the inner hydrophobic region of the vesicle bilayer, and some butyl chains will stretch out to contact with water. Previous studies revealed that the cross-link of the exposed butyl groups due to the hydrophobic interaction among them was considered to account for the heating-induced micelle aggregation in some ionic surfactant systems using tetrabutylammonium as the counterion. Therefore, it is reasonable to think that the hydrophobic interaction among the exposed butyl groups also make a significant contribution to the vesicle aggregation in our case. When the temperature reaches \( T_c \), the exposed butyl groups of adjacent vesicles may link together to induce the aggregation of vesicles. As a result, the hydrated water molecules previously surrounding these hydrophobic groups will be released, which may be responsible for the increase of entropy during the transition. Further study is still going on in our lab.

It is for the first time reported that a temperature-controlled vesicle aggregation occurred in a surfactant system. The critical temperature can be adjusted by the variations of the total surfactant concentration and the surfactant mixed molar ratio. Moreover, the temperature variation above \( T_c \) can remarkably alter the kinetics of vesicle aggregation. This work provided a simple and effective way for the controlling of vesicle aggregation by temperature variation. We hope it may also advance the understanding on the inter-aggregate interactions and promote corresponding applications in other fields.

![Figure 3](image3.png)

Figure 3. Variations of the light scattering intensity at 90° (\( I_{90} \)) as a function of time when the system SDS/DTBAB = 2:1, \( C_{\text{total}} = 10 \text{ mM} \), was heated from 33 °C to 34 and 36 °C.

![Figure 4](image4.png)

Figure 4. DSC heating curve of the system SDS/DTBAB = 2:1, \( C_{\text{total}} = 10 \text{ mM} \).

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<th>Table 1. ( T_c ) of Several SDS/DTBAB = 2:1 Mixed Systems with Different Total Surfactant Concentrations</th>
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<th>Table 2. ( T_c ) of Several ( C_{\text{total}} = 10 \text{ mM} ) SDS/DTBAB Mixed Systems with Different Molar Ratios (SDS/DTBAB)</th>
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Supporting Information Available: $R_g$ distribution of the mixed system (SDS/DTRAB = 2:1, $C_{total} = 10$ mM) at 30 °C measured by DLS and turbidity heating curves of the vesicular systems of SDS/DTEAB and SDS/DTPAB. This material is available free of charge via the Internet at http://pubs.acs.org.