PHYSICAL REVIEW E VOLUME 49, NUMBER 5 MAY 1994

Interactions between monolayers and the stability of mixed surfactant vesicles

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(Received 17 March 1993; revised manuscript received 23 November 1993)

Safran *et al.* pointed out that the contribution of interaction between two species within a monolayer can be described by the spontaneous curvature of the monolayer which plays a crucial role for the stability of the mixed surfactant vesicles [S. Safran *et al.*, Phys. Rev. A **43**, 1071 (1991)]. In this paper, reconsidering the relation between the spontaneous curvature and mismatching interactions between two species, we find a case in which this interaction cannot be represented completely by spontaneous curvature, even though the spontaneous curvature accounts for part of its contributions. We analyze the effects of intermonolayer interaction as well as that of intramonolayer interaction on the stability of bilayer vesicles. Our results on the ranges of parameters for stable vesicles give a clue to estimate the interaction strength from the compositional distribution analysis of stable mixed surfactant vesicles.

PACS number(s): 87.10.+e, 83.70.Hq, 68.10.Et, 81.30.Dz

I. INTRODUCTION

Several years ago, using single-tailed cationic and anionic surfactants, Kaler *et al.* [1] found a way to produce spontaneous stable vesicles whose size distributions can be well controlled. They concluded that the vesicle formation comes from the production of loose anion-cation surfactant pairs that acted as pseudo double-tailed zwitterionic surfactants.

Lately, Safran *et al.* [2] proposed a phenomenological theory for spontaneous vesicles formation in surfactant mixtures. In their theory, the total free energy of the mixed vesicles consists of three parts: the curvature energy f_c, the entropy part of mixing f_m, and f_i—the direct interactions between the two species of surfactants within the same monolayer with the contribution to spontaneous curvature excluded. In the large rigidity and low temperature limit, they neglected the last two parts f_m and f_i, and analyzed the phase behavior of the spherical vesicles by assuming that the properties of bilayer are given by adding that of two monolayers together.

In this paper, we discuss the condition for the validity of the approximation made in Ref. [2] in which f_i is neglected. We find that, when f_i is retained, the spontaneous curvatures of two monolayers are no longer equal. As there are strong interactions (which are important in the combination of bilayer) between two monolayers, we study their effects on the spontaneous curvatures and stability of bilayer vesicles. Our results for the phase diagram imply a possible method of estimating the interaction strength from the compositional distribution analysis of stable vesicles.

This manuscript is organized as follows. In Sec. II, we review briefly the theory of Safran *et al.* [2] and discuss the relation between spontaneous curvature and the mismatching interaction within monolayer. In Sec. III, we introduce interactions between two monolayers into the total free energy of mixed surfactant vesicles. Their effects on the spontaneous curvature and stability of mixed surfactant vesicles are studied. We find that, for certain range of parameters, our phase diagrams are different from that in Ref. [2]. We conclude our paper in Sec. IV with a summary of our results.

II. PHENOMENOLOGICAL THEORY FOR MIXED SURFACTANT VESICLES

We denote two kinds of surfactants as "1" and "2", and define the volume fraction of surfactant "2" in inner and outer layers as ψ_i and ψ_o, respectively. The compositional difference between these two layers is $\phi = (\psi_o - \psi_i)/2$, and the average ratio of composition $\psi = (\psi_o + \psi_i)/2$ is set *fixed*. The spontaneous curvatures of the inner and the outer layers are denoted by c_i and c_o. The total curvature energy per unit area of the midplane for the spherical vesicles is [2]

$$f_c = 2K[(c + c_o)^2 + (c - c_i)^2] \ , \tag{1}$$

where c is the actual curvature of the inner layer and K is the rigid modulus of the monolayers. Expanding c_o and c_i in terms of ϕ up to the second order, we have

$$\begin{aligned} c_o &= \bar{c}(\psi) - \alpha(\psi)\phi - \beta(\psi)\phi^2 \ , \\ c_i &= \bar{c}(\psi) + \alpha(\psi)\phi - \beta(\psi)\phi^2 \ . \end{aligned} \tag{2}$$

Since our discussions are in low temperature limit, the entropy part of free energy f_m from mixing is neglected hereafter.

Excluding the phenomenological spontaneous curvature energy, the remainder of the direct interactions between two species within each monolayer is of the form

$$f_i = -2J\psi(1 - \psi) + 2J\phi^2 \ , \tag{3}$$

where J represent the strength of interaction. We have used the assumption that the properties of the bilayer are given by summation of two monolayers, as in Ref. [2].

Safran *et al.* [2] minimized the total free energy $f = f_c + f_m + f_i$ with respect to the curvature c and got the curvature $c^* = \alpha\phi$ which minimizes the free energy for given ϕ. In the limit of large rigidity, they neglected the contributions from f_m and f_i, and obtained $\phi^* = \pm(\bar{c}/\beta)^{1/2}$ (so $c^* = \alpha\phi^*$). In this approximation, the spontaneous curvatures for two monolayers have the same magnitude, but opposite signs.

Generally speaking, in the low temperature limit, the free energy of any one of the monolayers (e.g., inner layer) is a function of ψ, the compositional difference ϕ and the curvature c, i.e., $f^{\text{in}}(\phi,\psi,c)$. For small c, we may expand $f^{\text{in}}(\phi,\psi,c)$ around $c = 0$ (to the second order of c):

$$f^{\text{in}}(\phi,\psi,c) = f^{\text{in}}(\phi,\psi,c=0) + \left.\frac{\partial f^{\text{in}}}{\partial c}\right|_{c=0} c + \frac{1}{2}\left.\frac{\partial^2 f^{\text{in}}}{\partial c^2}\right|_{c=0} c^2 . \tag{4}$$

Denoting

$$\frac{1}{2}\left.\frac{\partial^2 f^{\text{in}}}{\partial c^2}\right|_{c=0} = 2K , \quad \frac{1}{4K}\left.\frac{\partial f^{\text{in}}}{\partial c}\right|_{c=0} = -c_i , \tag{5}$$

we have

$$f^{\text{in}}(\phi,\psi,c) = 2K(c-c_i)^2 + f^{\text{in}}(\phi,\psi,c=0) - 2Kc_i^2 . \tag{6}$$

Comparing the free energy of this form with that Safran *et al.* used for monolayer, we find that the first term in Eq. (6) gives the curvature energy, and by definition, the last two terms, contribute to the remain part of direct interactions between two species excluding the spontaneous curvature energy. This part equals f_i of Eq. (3).

Now, we discuss the relation between spontaneous curvature of monolayer and mismatching interactions between two species within the monolayer. In our logic, the spontaneous curvature results from the mismatching of two species. But whether the total mismatching interaction energy between the two species can be represented by the phenomenological spontaneous curvature energy is worth studying.

It is clear that, in case the mismatching interaction energy can almost be included in the spontaneous curvature energy, the last two terms in Eq. (6) will cancel each other to give a very small residue. So the energy f_i of Eq. (3) will be very small and can be neglected compared with the bending energy. This corresponds to the case Safran *et al.* discussed [2].

However, there is another case in which the total interaction energy between two species cannot be described totally by the spontaneous curvature energy, even though the spontaneous curvature results from this mismatching interaction. In this case, the contribution of the last two terms in Eq. (6) is not very small, and f_i in Eq. (3) should not be neglected for its effect on the stability of vesicles. In general, we should retain f_i in the discussion on vesicle stability.

As it is well-known, a phenomenological formula for the free energy of monolayer usually consists of two parts: bending energy and tensile energy. The last two terms in Eq. (6) may be identified as the tensile energy. It is natural that the surface tension λ is a function of ψ and ϕ for mixed surfactant system. When the contribution of tensile energy can be neglected compared to bending energy, total free energy of vesicles is dominated by bending energy. This is the case discussed by Safran *et al.* For the second case the tensile energy is comparable with the bending energy.

III. INTERACTIONS BETWEEN TWO MONOLAYERS AND PHASE DIAGRAMS

Until now, we have used the assumption that the properties of bilayer is merely the summation of two monolayers. However, a more complete theory should include the interaction between two monolayers which also depends on ϕ and ψ, and plays important role in the formation of bilayer structure of vesicles. In addition, if the chain lengths of two species are unequal, there will be interpenetrations of surfactant chains between two monolayers. These interpenetrations affect the distribution and packing of surfactants, and even the stability of vesicles.

Actually, it is not difficult to write out the phenomenological terms describing the intermonolayer interactions for mixed surfactant vesicles:

$$\begin{aligned} f_{\text{bi}} = {} & (2J_3 - J_1 - J_2)\phi^2 - (2J_3 - J_1 - J_2)\psi^2 \\ & -2(J_3 - J_2)\psi + J_2 , \end{aligned} \tag{7}$$

where, J_1, J_2, and J_3 are respectively proportional to the strength of interactions between surfactants "2-2", "1-1", "1-2" of the inner and outer layers. We have assumed that the strengths of interactions between "1"of inner and "2" of outer layers are the same as that between "2" of inner and "1" of outer layers.

The total free energy now becomes $f = f_c + f_i + f_{\text{bi}}$. Minimizing it with respect to the curvature c first, we find $c^* = \alpha\phi$. Inserting this expression back to f and omitting terms not involving ϕ, we get

$$f = 2K(-\tfrac{1}{2}\bar{\epsilon}\phi^2 + 2\beta^2\phi^4) , \tag{8}$$

where,

$$\bar{\epsilon} = 8\beta\bar{c} - \frac{J + 2J_3 - J_1 - J_2}{K} . \tag{9}$$

Hereafter we define

$$U \equiv \frac{J + 2J_3 - J_1 - J_2}{K}$$

to simplify our expressions.

From Eq. (8), we obtain the range of β in which the mixed vesicles are stable with respect to plain lamellar in the limit of low temperature. When $U \geq -2$ (in the same unit of Ref. [2]), the range of β for stable vesicles has similar features to that of Ref. [2]. But when $U < -2$, the phase diagrams are different. In Fig. 1, we give our results for $U = -4$. We find that, for negative U and large $|U|$, the stable vesicles will have small ψ or $(1-\psi)$. Accordingly, the ratios of two compositions within stable mixed vesicles have a large difference.

The range of U for stable vesicles is also constrained (Fig. 2). For positive and large U, ψ will be about 0.5 for stable spherical vesicles, and the ratios of two com-

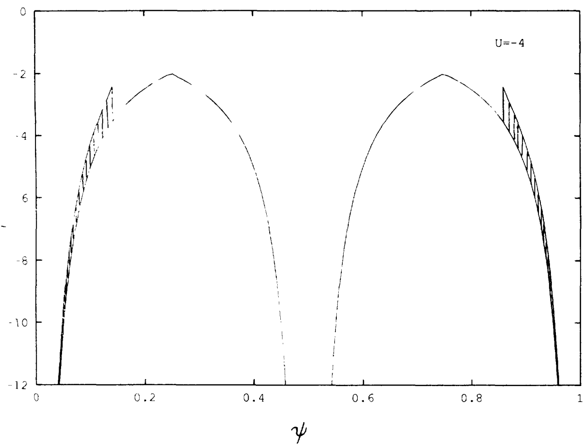

FIG. 1. β (see text) versus relative composition ψ. The shaded area represents range of β and ψ where vesicles are stable. The ψ is close to 0 or 1 for stable vesicles.

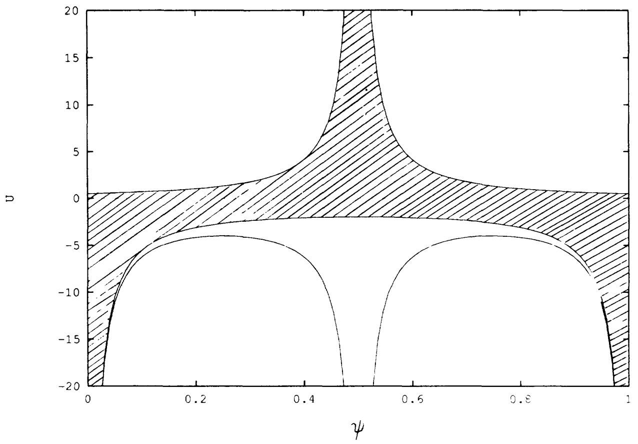

FIG. 2. U (see text) versus relative composition ψ. The shaded area represents range of U and ψ where vesicles are stable.

positions within stable mixed vesicles are almost equal. Again, we find that for negative U with large absolute value, the vesicles with small ψ or small $(1-\psi)$ are stable. This is a very interesting result. It implies that one may estimate U from the compositional distribution analysis of stable spherical vesicles.

Now let us have a discussion about the meaning of J's in U. For neutral surfactants, interactions within monolayer consist of steric interaction between headgroups, steric interaction between chains, and hydrophobic attractions along interface of monolayer [3]. For anionic-cationic surfactant mixtures, there is additional electric interaction between headgroups. All of these interactions contribute to J.

Hydrophobic attractive forces between monolayers along the normal directions of monolayers balanced by the steric interactions join two monolayers together into a bilayer. There is also electric interaction between headgroups of two monolayers for the ionic surfactants. These interactions are the origin of J_1, J_2, and J_3 in U.

It is pointed out that there is evidence of dynamic ion pairing of ionic single-tailed surfactants forming pseudo-double-tailed zwitterionic surfactant. However, this biding of pairing is not very tight, otherwise, they will behave as single-composition double-tailed surfactants and will not form unilamellar vesicles *spontaneously* [4].

The asymmetry of compositions and their packing are necessary for the interpretation of the spontaneous formation of mixed surfactant vesicles (which are only observed in surfactant mixtures [4]). Any compositional asymmetry of aforementioned interactions will contribute to the spontaneous curvature as well as to the stability of mixed surfactant vesicles.

IV. SUMMARY

We have discussed for two cases the relation between the spontaneous curvature of monolayer and mismatching interactions of two species. In one case, which corresponds to that discussed by Safran *et al.*, the total mismatching energy can be represented by the phenomenological spontaneous curvature energy, so f_i in Eq. (3) can be neglected. In the other case, the spontaneous curvature still results from the mismatching interaction, but the spontaneous curvature energy is no longer the main part of the total mismatching energy, so f_i should not be neglected in this situation.

Furthermore, we considered the interaction between monolayers, which is also crucial for the stability of bilayer vesicles. In the low temperature limit, we discuss the constraints on β, ψ, and U from the conditions that vesicles are stable. The range of β is different from that in Ref. [2] for $U < -2$. In addition, we find that U may be estimated by the compositional distribution analysis of stable spherical vesicles.

Even in the model used here, we have only discussed the stability of vesicles in comparison with the plain lamellar structures. There are still some issues unsettled, such as the surprising stability of anionic-cationic mixed vesicles against aggregation [4] and the stability of vesicles compared with multilamellar liposomes in the mixtures of anionic and cationic surfactants. Settlement of these issues relies on more general theory including interactions between vesicles and interactions between bilayers of multilamellar liposomes.

ACKNOWLEDGMENTS

This work is partially supported by the Grant No. LWTZ-1298 of Chinese Academy of Science and the National Natural Science Foundation of China. The author would like to thank Professor H. W. Peng, Professor Z. C. Ou-Yang, and Professor J. X. Liu for encouragement and Dr. T. Z. Qian for critical reading of this manuscript.

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