

Spontaneous vesicle formation by mixed surfactants

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Abstract: Although single surfactants rarely form vesicles spontaneously, mixtures of two surfactants can lead to spontaneous vesicle formation. By considering the curvature elasticity of the surfactant bilayer, we show theoretically how the energetic stabilization of mixed vesicles can occur. Interactions between the two species (of the proper sign and magnitude) are crucial to stabilizing these vesicles. These interactions lead to composition asymmetries and effective spontaneous curvatures of the inner and outer layers that are of equal and opposite signs.

Key words: Vesicle; surfactant; selfassociation

I. Introduction

Since vesicles rarely form as the equilibrium structure of simple surfactant-water systems, non-equilibrium methods, such as sonication of lamellar liquid crystalline phases, are usually necessary to obtain a metastable phase of vesicles, which may reequilibrate back into the multilamellar, liquid crystalline structure. Recently, however, Kaler et al. [1] have reported a general method for producing equilibrium phases of vesicles of a controlled size. The vesicles form spontaneously upon mixing simple surfactants with oppositely charged head groups. Most previous reports of spontaneous vesicle formation have also involved surfactant mixtures [2–5]. Using the charge as a control parameter has both chemical and physical advantages since a wide variety of head group, counterion, and salt chemistries can be prepared and studied.

In this paper, we use the concepts of curvature elastic theory [6] to explain the stability of vesicles formed in mixed surfactant systems. In systems composed of a single surfactant, the curvature energy of a bilayer dictates that the energy of a phase of spherical vesicles is never lower than that of a multilamellar, liquid crystalline phase [7, 8]. This is because the bilayer is composed of two am-

phiphilic monolayers which, in the single surfactant case, have the same spontaneous curvature [6]. Since the two layers have curvature of opposite sign (e.g., the inner one being concave with respect to the water, and the outer one convex), the system is frustrated. Small vesicles, where the vesicle radius is of the order of the surfactant size, can be of lower energy than flat bilayer, as discussed in [9–12]. However, they may be of higher free energy than small micelles. In this work, we consider the case of large vesicles and discuss their stability with respect to lamellar phases; this feature can be compared with the experimental phase diagrams [13]. We find [7, 8] that the stabilization of the vesicles by surfactant mixtures only occurs when interactions of the surfactants is considered; ideal mixing of the two components does not yield vesicles as the ground state. These results can be used to see how the interactions can be exploited to control and stabilize the vesicle phase.

II. Mixed vesicles

In contrast to the situation for single amphiphiles, where large vesicles are usually not energetically stable in comparison with flat bilayers, vesicles

composed of two amphiphiles can have lower curvature energies than flat films. The curvature energy [6–8] per unit area of the vesicle is given by

$$f_c = 2K [(c + c_0)^2 + (c - c_i)^2], \quad (1)$$

where K is the bending elastic modulus [7, 8], c_i and c_0 are the spontaneous curvatures of the inner and outer monolayers, and c is the actual curvature of the inner layer. For the case of single surfactant systems, in the limit of small curvatures, $c_0 = c_i$. In this case, the minimum of f_c with respect to c implies that $c = 0$; flat bilayers are the lowest bending energy state. For mixed surfactants, constitutive relations for effective spontaneous curvatures of the inner and outer layers, c_i and c_0 are needed.

For simplicity, we consider a model where the spontaneous curvatures of films composed of each, single surfactant are equal, $c_1 = c_2$, and define ψ as the volume fraction of surfactant type "2" in the system. In addition, we define ψ_i and ψ_0 as the volume fraction of surfactant "2" in the inner and outer layers, respectively. The composition difference between these two layers is $\varphi = 1/2(\psi_0 - \psi_i)$, with the constraint of fixed $\psi = 1/2(\psi_0 + \psi_i)$.

We now describe a simple statistical model for the surfactant head-head interactions which allows for a unified treatment of the free energy of the system including both the elastic, entropic, and interaction contributions. Our basic assumption is that the interaction between head groups alone determines the spacing between surfactants at the interfaces, while the resulting compression of the surfactant tails determines the spontaneous curvature of each monolayer. (In [11], we shall relax this assumption.) In this case, the spontaneous curvature depends directly on the mean spacing between surfactant head groups as a function of composition, ψ .

We first consider a monolayer with a repulsive interaction $+J$ between like head groups, and an attractive interaction, $-J$ between opposite head groups. This suggests an Ising model description for the energy H of a two-component mixture:

$$H = \sum_{\langle ij \rangle} JS_i S_j, \quad (2)$$

where the sum over $\langle ij \rangle$ includes only nearest neighbor pairs. The constituents are labeled by i , and $S_i = +1$ (-1) denotes the presence of surfactant (2). Furthermore, the attractive or repulsive

interactions result in a local deformation of the bond distances compared to their values for the pure surfactants (which are assumed to have the same bond lengths). We describe this by a quantity Δ_{ij} , which is the *change* in the bond length between surfactants at nearest-neighbor sites i and j . Finally, there is an elastic-restoring force, with spring constant k :

$$H = \sum_{\langle ij \rangle} \left(JS_i S_j - B(1 - S_i S_j) \Delta_{ij} + \frac{k}{2} \Delta_{ij}^2 \right). \quad (3)$$

Here, B represents the strength of the coupling between the composition and elastic degrees of freedom. Equation (3) represents the compressible Ising model.

The mean-field value of $\langle \Delta_{ij} \rangle$ is found by minimizing Eq. (3) with respect to $\langle \Delta_{ij} \rangle$:

$$\langle \Delta_{ij} \rangle = B(1 - \langle S_i S_j \rangle)/k; \quad (4)$$

the resulting expression for the free energy per surfactant h is

$$h = J \langle S_i S_j \rangle - \frac{B^2}{2k} (1 - \langle S_i S_j \rangle)^2. \quad (5)$$

In random mixing, the nearest-neighbor correlation function $\langle S_i S_j \rangle$ can be found by weighting the two possible values by the appropriate product of independent probabilities for finding surfactants 1 and 2 at each site:

$$\begin{aligned} \langle S_i S_j \rangle &= (1 - \psi)^2 + \psi^2 - 2\psi(1 - \psi) \\ &= (1 - 2\psi)^2. \end{aligned} \quad (6)$$

Simple models for the packing of surfactant molecules at a surface yield a spontaneous curvature which depends linearly on the mean spacing between polar head groups. Within the model of the previous section, the change in the spontaneous curvature depends on $\langle \Delta_{ij} \rangle$, and hence on $\langle S_i S_j \rangle$:

$$c(\psi) - c(0) = \frac{\beta}{4} (1 - \langle S_i S_j \rangle) = \beta\psi(1 - \psi). \quad (7)$$

The parameter β is of order a^{-1} , where a is a microscopic length. The precise value of β can be obtained, although it is somewhat model specific [11].

Considering now the properties of a bilayer, and using the definitions of the composition asymmetries discussed above, we arrive at the following expressions for the effective spontaneous curvatures:

$$c_i = \bar{c}(\psi) + a(\psi)\varphi - \beta(\psi)\varphi^2 \quad (8)$$

$$c_0 = \bar{c}(\psi) - a(\psi)\varphi - \beta(\psi)\varphi^2 \quad (9)$$

where

$$\bar{c} = c_1(1 - \psi) + c_2\psi + \beta\psi(1 - \psi), \quad (10a)$$

$$a = (c_1 - c_2) - \beta(1 - 2\psi), \quad (10b)$$

These formulae are written for the general case where the individual spontaneous curvatures are unequal. For the case where $c_1 = c_2$, the effective spontaneous curvature of the interacting system is reduced (for $\beta > 0$) compared with c_1 . This reduction is just what is necessary to stabilize the vesicle so that the effective spontaneous curvatures of the inner and outer layers are equal and opposite, thus relieving the frustration present in the single surfactant case. For ideally mixed, or non-interacting surfactants ($\beta = 0$), a vesicle composed of a single surfactant has an outer layer which satisfies the spontaneous curvature, but a frustrated inner layer. Interactions between the two surfactants, however, can result in a contribution to the spontaneous curvature which is opposite in sign to both c_1 and c_2 . If more of these pairs are placed on the inner layer, one can stabilize the vesicle so that when $c = c_i = -c_0$, the system is at its lowest curvature energy state and the frustration is relieved. This is seen quantitatively from Eqs. (8) and (9) where the choice

$$\varphi = \pm (\bar{c}/\beta)^{1/2} \quad (11)$$

results in $c_i = -c_0$. Note that this stabilization is only possible if the interaction terms are considered.

With this model, the curvature free energy of Eq. (1) then becomes

$$f_c = 4K[(c - a\varphi)^2 + (\bar{c}(\psi) - \beta\varphi^2)^2]. \quad (12)$$

Thus, the spontaneous curvature of the bilayer is $c = a\varphi$. This describes a flat bilayer, unless $\varphi \neq 0$. We must now determine the value φ^* , which minimizes

the free energy as a function of φ . When $c = a\varphi$, the free energy per surfactant F_c is

$$\begin{aligned} F_c &= 2K\sigma(c(\psi) - \beta\varphi^2)^2 \\ &= 2K\sigma[c(\psi)^2 - 2\beta c(\psi)\varphi^2 + \beta^2\varphi^4], \end{aligned} \quad (13)$$

where σ is the area per polar head group. The contribution of the interaction terms of Eq. (5) to the free energy per surfactant is

$$\begin{aligned} F_i &= J(1 - 2\psi)^2 - \frac{8B^2}{k} \psi^2(1 - \psi)^2 \\ &+ \left[4J - 8 \frac{B^2}{k} (1 - 6\psi(1 - \psi)) \right] \varphi^2 \\ &- 8 \frac{B^2}{k} \varphi^4. \end{aligned} \quad (14)$$

Similarly, for small values of φ , the contribution due to the entropy of mixing is

$$\begin{aligned} F_m &= kT \left[\psi \log \psi + (1 - \psi) \log(1 - \psi) \right. \\ &+ \frac{1}{2} \left(\frac{1}{\psi(1 - \psi)} \right) \varphi^2 \\ &\left. + \frac{1}{12} \left(\frac{1}{\psi^3} + \frac{1}{(1 - \psi)^3} \right) \varphi^4 \right]. \end{aligned} \quad (15)$$

The total free energy per surfactant can be written as

$$F = F_0 - \varepsilon\varphi^2 + A\varphi^4, \quad (16a)$$

where

$$\begin{aligned} \varepsilon &= 4K\sigma\beta c(\psi) - 4J + \frac{8}{k} B^2(1 - 6\psi(1 - \psi)) \\ &- \frac{kT}{2} \left(\frac{1}{\psi(1 - \psi)} \right), \end{aligned} \quad (16b)$$

$$A = \frac{kT}{12} \left(\frac{1}{\psi^3} + \frac{1}{(1 - \psi)^3} \right) - 8 \frac{B^2}{k}, \quad (16c)$$

and F_0 is independent of φ . Equations (15) and (16) are valid in the high "temperature" limit. This corresponds to interaction terms J and B/k , which are small compared with kT . In this limit, $\varepsilon \sim (T_c - T)$ and $B \sim T$, where $T_c \approx K\sigma\beta c(\psi)$. Then, a spontaneous vesicle phase characterized by $\varphi \neq 0$ will occur below a second order phase transition at $T = T_c$. This suggests that it will be fruitful to more fully examine the case of low temperatures, or the case of strong interactions between the constituents [11].

III. Discussion

For $\varepsilon < 0$, the minimum free energy state is composed of flat bilayers where the two monolayers have identical compositions ($\varphi = c = 0$). When $\varepsilon > 0$, the free energy is minimized by a non zero value of φ and hence a non-zero curvature. However, the vesicle phase is limited to a finite region of the phase diagram as a function of the relative composition ψ , as well as the absolute concentration of amphiphile φ_s . This limitation arises from the imposition of packing constraints on the vesicles. This enables an estimate of the phase diagram at fixed values of temperature, β , c_1 , and c_2 as a function of concentration. Neglecting polydispersity, the volume fraction of the system occupied by vesicles is

$$\Phi = \frac{4\pi}{3} nR^3, \quad (17)$$

where $R = 1/c^*$ is the vesicle radius and n is the number density of vesicles. For large vesicles, the volume fraction of surfactant is

$$\varphi_s = 8\pi n\delta R^2. \quad (18)$$

Eliminating n , we find that $6\delta/R = \varphi_s/\Phi$. The vesicles cannot be overpacked (Φ must be less than one); we take the value of $\Phi = 1$ as the bound of stability of the vesicles with respect to the lamellar phase where steric constraints are much weaker. An approximation to the phase boundary as a function of φ_s (the total volume fraction of surfactant) and ψ (the fraction of surfactant that is type "2") is then given by the locus of points which satisfy

$$\varphi_s = 6\delta c^*(\psi), \quad (19)$$

where

$$c^* = a(\psi)\varphi^*, \quad (20)$$

where $\varphi^*(\psi)$ is the value of φ that minimize Eq. (16). A more detailed discussion of the phase diagram can be found in [8, 11].

In summary, we have shown how interactions between surfactants can stabilize a phase of spherical vesicles with respect to a flat lamellar phase. These interactions require that the effective spontaneous curvature of the film have a term quadratic in the composition. The physical origin of this stabilization is the tendency of "1-2" surfactant pairs to have a different bond distance from the average of "1-1" and "2-2" pairs. It is then possible for the effective spontaneous curvature of a film composed mostly of "1-2" pairs to be quite different (even in sign) from the spontaneous curvature of the pure films. In the case where the curvature energy dominates, the vesicle is then stable; the outer layer, for example, may consist mostly of "1-1" pairs and the inner layer of the vesicle may be mostly "1-2". The concentration asymmetry of the two layers is such that the effective spontaneous curvatures of the inner and outer layer are equal and opposite; the frustration of one of the layers that destabilizes vesicles composed of a single surfactant is thus prevented.

Even within the context of this model, several outstanding issues remain. The first is to explore the interactions and mixing effects more generally for both the strong and weak interaction case [11]. In addition, the case of mixed amphiphiles of long and short chains should be studied. Finally, the microscopic interactions which determine the different head spacings in ionic systems should be explored so that the interaction parameters β can be related to charge and salinity.

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