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Stability and phase behavior of mixed surfactant vesicles

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Although large, spherical surfactant vesicles are generally unstable to either lamellar or micellar phases, mixtures of two surfactants can lead to spontaneous vesicle formation. We show theoretically how the energetic stabilization of mixed vesicles can occur by considering the curvature elasticity of the surfactant bilayer. 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. The vesicles have a Gaussian distribution about an average size determined by the effective spontaneous curvature; the width of the distribution is calculated as a function of concentration. The stability of these vesicles with respect to a flat lamellar phase is estimated. The predictions of the ranges of stability of the various phases as a function of the three concentrations (solvent, e.g., water—and the two amphiphiles) are in qualitative agreement with recent experiments.

I. INTRODUCTION

Unilamellar vesicles consist of a surfactant bilayer that separates an inner region of a fluid (usually water) from a continuous phase of the same fluid. Industrial and biological applications such as cleaning, catalysis, and microencapsulation for drug delivery depend on a simple and controlled method for the generation of vesicles with a well-defined average size. In addition, vesicles are often studied as models for biological membranes. Although vesicles often form spontaneously in vivo, they rarely form as the equilibrium structure of simple surfactant-water systems. Nonequilibrium methods, such as sonication of lamellar, liquid-crystalline phases, are usually necessary to obtain a metastable phase of vesicles,[1] which may reequilibrate back into the multilamellar, liquid-crystalline structure. Recently, however, Kaler *et al.*[2] 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.[3-6] 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.

This experimental development motivated a new look[7] at the theory of vesicle formation using the concepts of curvature elastic theory.[8] 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. This is because the bilayer is composed of two amphiphilic monolayers which, in the single surfactant case, have the same spontaneous curvature.[8] Since the two layers have curvatures of opposite sign (e.g., the inner one being concave with respect to the water and the outer one convex), the system is frustrated. If, for example, the vesicle radius is chosen so that the outer layer has matched its curvature to the monolayer spontaneous curvature, the curvature energy cost of the inner layer with the curvature of the opposite sign is higher than the corresponding energy cost of a lamellar phase composed of flat bilayers. The only way that the lowering of the curvature energy by the outer layer can exceed the gain in energy of the inner layer is if the outer layer has *significantly* more molecules than the inner layer. However, this is not the case for large vesicles, whose radii are much greater than the surfactant size. Small vesicles, where the vesicle radius is of the order of the surfactant size, can be of lower energy than flat bilayers, as discussed in Refs. 9–11. 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 diagram.

While large vesicles composed of a single surfactant have higher free energy cost than flat bilayers, they can still be stabilized by their larger entropy of mixing. However, in the limit of large (with respect to the temperature k_BT) bending moduli,[8] these entropically stabilized vesicles[9] are extremely polydisperse and are only stable at exponentially small volume fractions. We have recently suggested[7] that mixtures of two surfactants can behave qualitatively differently. The additional degree of freedom of the composition of each monolayer of the bilayer allows the formation of an equilibrium phase of vesicles with an effective *negative* bending energy so the vesicles have lower curvature energy than the lamellar phase. Because the vesicles are *energetically* stabilized, a well-defined size is selected and the distribution is fairly monodisperse. In addition, we find that the stabilization of vesicles by surfactant mixtures only occurs when interactions of the surfactants are 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.

In Sec. II we discuss the free energy and distribution of large vesicles in systems consisting of a single amphiphile. We then consider mixed systems in Sec. III where we present our model and explore its implications. We predict the sign and magnitude of the interactions which will stabilize spontaneous vesicles in mixed surfactant systems[12] and estimate the stability of these mixed vesicles with respect to the lamellar phase, taking into account the excluded volume interactions of the vesicles. The resulting phase diagram (discussed in Sec. IV) as a function of the concentrations of the solvent (e.g., water) and the two amphiphilic species is qualitatively similar to that observed experimentally.[13] In Sec. V a Gaussian approximation is used to predict the distribution of vesicle sizes which is peaked at the effective spontaneous curvature of the mixed layer c^*, a quantity which depends on the concentrations of the two species as well as the interaction strength. The width of this distribution also depends on c^*, and we discuss the conditions under which the distribution is broad or narrow.

II. SINGLE SURFACTANT VESICLES

A. Curvature elasticity

We begin with a review of the curvature elasticity of surfactant films and consider a single monolayer[14] at a water/oil interface.[15] In the limit of large vesicles, with radii much larger than the surfactant size δ, the energy to deform the monolayer by shape or size changes can be written phenomenologically as an expansion in the two local curvatures $c_\parallel$ and $c_\perp$; the small parameter in this expansion is $c\delta$, where c is of the order of either $c_\parallel$ or $c_\perp$. Keeping terms up to quadratic order and noting that the curvature energy per unit area f_c must be symmetric in $c_\parallel$ and $c_\perp$ if there is no orientational order of the surfactant in the surface of the film, one finds[8]

$$f_c=\tfrac{1}{2}K'(c_\parallel+c_\perp-2c_s')^2+\bar{K}'c_\parallel c_\perp \ . \tag{1}$$

This expression accounts for the energy cost for bending a surface; deviations of the average curvature from the spontaneous curvature, c_s', raise the energy of the system by an amount proportional to K'. The second term in Eq. (1) accounts for the energy cost for creating saddle-type deformations (e.g., $c_\parallel>0$, $c_\perp<0$), and the modulus $\bar{K}'$ is termed the saddle-splay modulus. If the interactions between surfactant molecules are short ranged, K', $\bar{K}'$, and c_s' are all independent of the concentrations of water, oil, and surfactant. They are, however, dependent upon the chemistry of the surfactant molecules, the oil chain length, the salinity, and temperature in a manner that is not included in the phenomenological curvature expansion. Thus, chemical trends are not predicted by the interfacial theory except by the dependence of the properties of the system on the "lumped" quantities, K', $\bar{K}'$, and c_s'. The microscopic origins of the modulii K' and $\bar{K}'$, and the spontaneous curvature c_s', have been discussed in Ref. 16.

The spontaneous curvature describes the tendency of the surfactant film to bend towards either the water ($c_s'<0$ by convention) or the oil ($c_s'>0$). It is taken—in the absence of long-range interactions—to arise from the competition between the packing areas of the polar heads and hydrocarbon tails of the surfactant molecules. If the interactions between the polar heads (as mediated through the intervening water and electrolyte) favor a smaller packing area than that dictated by the tail-oil-tail interactions, the surfactant film will tend to curve so that the heads (and the water) are on the "inside" of the interface. The bending moduli, K' and $\bar{K}'$, arise from the elastic constants determined by the head-head and tail-tail interactions. It is expected that these modulii are mostly sensitive to the surfactant chain length.[16–18].

Since we limit our discussion to spherical and lamellar structures, where $c=c_\parallel=c_\perp$, it is convenient to rewrite the curvature energy as

$$f_c=\tfrac{1}{2}K(c_\parallel+c_\perp-2c_s)^2+\bar{K}(c_\parallel-c_\perp)^2 \ , \tag{2}$$

where K, $\bar{K}$, and c_s are related to the standard K' by $K'=K+2\bar{K}$, $\bar{K}'=-4\bar{K}$, $c_s'=(K/K')c_s$. In this form for f_c, the term proportional to the saddle splay, $\bar{K}$, vanishes for spherical and lamellar structures and c_s is the curvature of the minimum energy sphere. We note that the two forms of the curvature energy [Eqs. (1) and (2)] differ by a constant term that is independent of curvature.

B. Vesicle stability

We consider the curvature energy of spherical vesicles. Neglecting terms in the small quantity $c\delta=\delta/R$, the curvatures of the inner and outer layers have the same magnitude but opposite signs. The total bending energy per unit area of the midplane between the two monolayers which comprise the bilayer is

$$f_c=2K[(c+c_o)^2+(c-c_i)^2] \ , \tag{3}$$

where c_o and c_i are the spontaneous curvatures of the inner and outer monolayers and c is the actual curvature of the inner layer. We use the convention that the inner monolayer of the vesicle has positive curvature and the outer monolayer, negative curvature. For the case of single surfactant systems, in the limit of small curvatures, $c_o = c_i$. In this case, the minimum of f_c with respect to c implies that $c=0$, or flat bilayers, are the lowest bending energy state.

Of course, the two layers do not have curvatures that are exactly equal and opposite. Such corrections, which scale as δc are of the same order as the higher-order terms in the curvature expansion that are neglected here. They can, however, be important for vesicles whose size is comparable with the surfactant size, δ and their study depends on a microscopic model for the bilayers.[10,19] Qualitatively, one can imagine a vesicle where the outer layer has a curvature $c=-c_o$ so that it has a minimum (zero) value of its curvature energy. The inner layer, with spontaneous curvature $c_i = c_o$ is, however, frustrated and $f_c = 8Kc_o^2$. A flat bilayer, with $c=0$, has an energy $f_c = 4Kc_o^2$ and is thus energetically preferred. In this approximation, we compare the energy per unit area, since we assume that the inner and outer layers have the same numbers of surfactant molecules. If, however, the outer layer had a significantly large number of molecules than the inner layer, we would have to compare the free energy per molecule. For small enough vesicles, it can happen that the lowering of the free energy by the outer layer matching its curvature to the spontaneous curvature can compensate the gain in f_c due to the frustration of the inner layer and the vesicle can have a lower bending energy than the lamellar phase. However, these differences between the inner and outer layers can be significant only when the vesicle size is comparable to the surfactant size. In that case, a microscopic model is needed, since the curvature expansion breaks down.[10,19] In addition, the stability of these small vesicles has to be compared with that of a phase of micelles. This regime is outside the scope of the present work and appears unrelated to the recent experiments on mixed systems, where typical vesicle sizes are ≥ 500 Å, much greater than $\delta \sim 10$ Å.

Thus, for large vesicles composed of a single amphiphile, the lamellar phase has lower curvature energy than the vesicle. However, the vesicles have an entropy of mixing that is much larger than that of the lamellar phase.[20] As a bound on the stability of the vesicle phase, we consider the dilute limit where the excluded volume interactions of the vesicles can be neglected. We thus include the translational entropy and calculate the distribution of vesicle sizes obtained by minimizing the total free energy per unit volume in units of $k_B T$, which is

$$\sum_N n_N[\ln(n_N v)-1]+n_N\kappa+n_N N\mu \ . \tag{4a}$$

Here, v is the surfactant molecular volume, n_N is the number of vesicles per unit volume of aggregation number N $(N\sim c^{-2})$, $\kappa = 32\pi K/k_B T$ is the energy per vesicle, and μ is a Lagrange multiplier that accounts for the conservation of surfactant and is determined from

$$\sum_N v n_N N = \phi_s \ , \tag{4b}$$

where ϕ_s is the surfactant volume fraction.

Minimizing the free energy of Eq. (4a) with respect to n_N yields the vesicle distribution

$$n_N = \frac{1}{v} e^{-\kappa-\mu N} \ . \tag{5}$$

The Lagrange multiplier, μ is proportional to $(\phi_s e^{\kappa})^{-1/2}$. This distribution, previously discussed in Refs. 9 and 10 is *not* a Gaussian about some average size (usually determined by the energetics), since the minimum energy state is a vesicle with curvature $c=0$ corresponding to the infinite aggregation number of a flat bilayer. The average vesicle size $\bar{N}$ is proportional to $1/\mu$ and diverges exponentially as the bending stiffness increases. Of course, at finite surfactant volume fraction, the average size is finite. However, the value of ϕ_s at which these vesicles can still remain dilute is exponentially small. To see this, we determine the volume fraction enclosed by the vesicles Φ, which scales as

$$\Phi \sim \sum_N N^{3/2} n_N \sim \phi_s \bar{N} \ . \tag{6}$$

Since $\bar{N} \sim (\phi_s e^{\kappa})^{1/2}$, we see that the vesicles are overpacked, i.e., $\Phi > 1$, unless ϕ_s is exponentially small. For stiff membranes, where $\kappa \gg 1$, this implies that the vesicles can only exist as a dilute solution for surfactant volume fractions, $\phi_s < e^{-\kappa}$; for larger volume fractions, the lowest free-energy state is probably lamellar.

We therefore conclude that for single surfactants the lamellar phase is usually more stable than the spherical vesicle phase. Exceptions to this behavior can occur for (i) the case of small[11] vesicles, comparable to the surfactant size, where the energetics may stablize the system—although the micellar phase may ultimately be even more stable—or for (ii) the case of extremely small surfactant volume fractions, where the entropy of mixing can stabilize a polydisperse distribution of large vesicles. In contrast with the trend for single surfactants, mixed surfactants can form a phase of large vesicles with a well-defined average size which is determined by the curvature energy of the interacting system.

III. 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 of the vesicle is given by Eq. (3) supplemented by constitutive relations for the effective spontaneous curvatures of the inner and outer layers, c_i and c_o, respectively. We denote the spontaneous curvatures of films composed of each single surfactant as c_1 and c_2, and define ψ as the volume fraction of surfactant type "2" in the system. As a first approximation we neglect the polydispersity in the system (see Sec. V). In addition, we define ψ_i and ψ_o as the volume fraction of surfactant "2" in the inner and outer layers, respectively. The composition difference between these two layers is $\phi = \frac{1}{2}(\psi_o - \psi_i)$, with the constraint $\psi = \frac{1}{2}(\psi_o + \psi_i)$ being fixed.

With these definitions, we can phenomologically write the effective spontaneous curvatures as a power series in the composition difference ϕ, assumed to be small. Keeping terms to second order in ϕ, one has

$$c_i=\bar{c}(\psi)+\alpha(\psi)\phi-\beta(\psi)\phi^2 \ , \tag{7}$$

$$c_o=\bar{c}(\psi)-\alpha(\psi)\phi-\beta(\psi)\phi^2 \ . \tag{8}$$

The signs of the terms involving ϕ are chosen so that $c_i \rightarrow c_o$ when ϕ changes sign; this is required by symmetry since ϕ represents the composition asymmetry of the inner and outer layers. In a phenomenological theory, the coefficients $\bar{c},\alpha,\beta$ are unknown functions of ψ. To obtain physical insight into these functions, we consider a slightly more detailed model.

We assume that the spontaneous curvatures are determined by the local bond distances and thus the local compositions of the interface. We then use a mean-field approximation to write that the effective spontaneous curvature in a given layer is related to the probabilities that a nearest-neighbor pair consists of two surfactants of type "1" ("1-1"), or of type "2" ("2-2"), or a mixed pair "1-2." One then finds

$$c_i=(1-\psi_i)^2c_1+\psi_i^2c_2+(c_1+c_2+\Delta c)\psi_i(1-\psi_i) \ , \tag{9}$$

with a similar equation for c_o. The first two terms indicate that "1-1" or "2-2" pairs have the same spontaneous curvatures as films composed of the single amphiphiles. If $\Delta c=0$, the last term in Eq. (9) dictates that the spontaneous curvature of a "1-2" pair is the average of the two spontaneous curvatures. The term proportional to Δc represents the effects of interactions between the two surfactants and the fact that the effective spontaneous curvature is not simply the average. With this model, the coefficients $\bar{c},\beta,\alpha$ of Eqs. (7) and (8) are identified as

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

$$\alpha=(c_1-c_2)-\beta(1-2\psi) \ , \tag{10b}$$

$$\beta=\Delta c \ . \tag{10c}$$

With this model, we find that β is the two-body interaction parameter that is independent of ψ.

Further insight into the meaning of these expressions is obtained by considering the specific case of two surfactants with identical chains,[21] but different head groups. The spontaneous curvature is proportional to the difference in local head spacing compared to the tail packing.[16] If there were only steric interactions between the head groups, the polar bond distances in a mixed film would be a simple average of the bond distances in the pure monolayers. As shown below, this would result in vesicles that had a larger value of the bending energy than flat, lamellar structures. We therefore consider more generally the case where interactions between the polar groups result in a bond distance (and hence a local spontaneous curvature) whose value is not simply given by the average of the "1-1" and "2-2" bond distances. For short-range interactions,[22] a random mixing[23] approximation for the average distance a_i between polar heads in the inner layers yields

$$a_i=a_1(1-\psi_i)^2+a_2\psi_i^2+(1-\gamma)(a_1+a_2)\psi_i(1-\psi_i) \ , \tag{11}$$

with a similar equation for the average distance between polar heads in the outer layer. In Eq. (11), a_1 and a_2 are the distances between polar heads in monolayers composed of only surfactant "1" or "2," respectively. The term proportional to γ represents the effects of interactions of the two surfactants,[24] which can either increase ($\gamma<0$) or decrease ($\gamma>0$) the distance between a molecule of type "1" and one of type "2," compared to the average bond distance $(a_1+a_2)/2$. The case $\gamma=0$ represents an ideal mixing where the bond distances follow the average, e.g., for the inner layer, $a_i=a_1(1-\psi_i)+a_2\psi_i$. With the convention that the curvature of the inner layer (heads on the inside, tails on the outside) is positive, the spontaneous curvature is proportional[16] to the product of a positive constant and the difference between the chain packing distances (which are the same for both surfactants and hence are composition independent) and a_i. This leads to Eqs. (7)–(9), with β proportional to γ with a positive constant of proportionality. If the bond distance between the polar heads in a "1-2" pair is smaller than the average of the "1-1" and "2-2" bond distances, $\beta>0$ and the interaction term ($\sim\phi^2$) in the expression for the spontaneous curvature tends to reduce the values of c_i and c_o.

This reduction is just what is necessary to stabilize the vesicle so that the effective spontaneous curvatures of the inner and outer layers have the same magnitude but are of opposite sign, thus relieving the frustration present in the single surfactant case. Imagine, for example, that both surfactants "1" and "2" tend to form monolayers that tend to bend with the water on the outside ($c_1,c_2<0$ by our convention that the inner layer is water internal and has positive curvature). For ideally mixed, or noninteracting, 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 $c=c_i=-c_o$, the system is at its lowest curvature enegy state and the frustration is relieved.

This is seen quantitatively from Eqs. (7) and (8) where the choice

$$\phi=\pm(\bar{c}/\beta)^{1/2} \tag{12}$$

results in $c_i=-c_o$. Note that this stabilization is only possible if the interaction terms are considered. Thus, vesicles of curvature $c=c_i=\phi\alpha$ minimize the curvature energy when the composition asymmetry is chosen as indicated by Eq. (12). Within this model, the curvature free energy of Eq. (3) is zero for such vesicles and is lower than the curvature free energy $4K\bar{c}(\psi)^2$ of flat ($c=0$), mixed[25] ($\phi=0$) bilayers.

A more complete accounting of the free energy of the mixed vesicles must consider curvature-independent terms. Such contributions, which can be both ψ and ϕ dependent, arise from the statistical mechanics of a layer of surfactant molecules and exist even in the absence of curvature.[19] One part of this additional free energy comes from the entropy of mixing, f_m, which resists the composition asymmetry responsible for the stability of the vesicles with respect to the flat, mixed bilayers. In a mean-field approximation, the entropy of mixing of a single layer with composition ψ is proportional to

$$\psi \log\psi + (1-\psi)\log(1-\psi) \ .$$

Expanding this expression with respect to the composition asymmetry ϕ, one writes the ϕ-dependent part of the entropy of mixing, f_m, as

$$f_m = K\tau \left[\frac{\phi^2}{\psi(1-\psi)} + \tfrac{1}{6}\phi^4 \left[\frac{1}{\psi^3} + \frac{1}{(1-\psi)^3} \right] \right] , \tag{13a}$$

where $\bar{a}$ is a molecular size, related to the area per molecule on the interface, and $\tau = T/(\pi K \bar{a}^2)$.

Another contribution to the additional free energy is the direct interaction between surfactant molecules in a single layer. An attraction between the two different surfactants, for example, results in a contribution to the free energy per unit area, f_i, of the vesicle of the form

$$f_i = -2J\psi(1-\psi) + 2J\phi^2 , \tag{13b}$$

where J is proportional to the strength of the interaction as discussed in detail in Ref. 19. Including the contributions from the curvature free energy f_c, the entropy f_m, and the interactions f_i enables the determination of both the curvature and composition asymmetry by minimizing the total free energy per unit area with respect to ϕ and c.

Minimizing first with respect to the curvature determines the minimum energy curvature c^* as $c^* = \alpha\phi$. With this value of c^*, the free energy f is

$$f = 2K\left(-\tfrac{1}{2}\varepsilon\phi^2 + \tfrac{1}{4}A\phi^4\right) , \tag{14}$$

where

$$\varepsilon = 8\beta\bar{c} - \tilde{\tau}/[\psi(1-\psi)] , \tag{15a}$$

$$A = 8\beta^2 + \frac{\tau}{3}[1/\psi^3 + 1/(1-\psi)^3] , \tag{15b}$$

where $\tilde{\tau}$ includes both the interactions and entropy terms and is defined by

$$\tilde{\tau} = [T + J\psi(1-\psi)]/(\pi K \bar{a}^2) . \tag{15c}$$

Equation (15) indicates that the sign of ε dictates the vesicle stability; when $\varepsilon > 0$, the vesicle phase is stable with respect to the lamellar phase. Considering the case where ψ is a number of order unity and similarly neglecting the numerical factors in Eq. (15), one sees that $\varepsilon > 0$ when

$$\frac{\tilde{\tau}}{\beta\bar{c}} < 1 . \tag{16}$$

In principle, this occurs for stiff systems, where K is large, as long as $\bar{c}\,\bar{a}$ is not too small. (For a discussion of a microscopic model and the relevant limits, see Ref. 19.) For simplicity, we consider the limit of small values of τ where the curvature energy dominates and $\varepsilon > 0$; the vesicle is then stable and the vlaue of ϕ that minimizes f is $\phi^* = \pm(\bar{c}/\beta)^{1/2}$, where the correct sign is obtained by the requirement that $c^* = \phi^*\alpha$ be positive by convention. In this case, the vesicle free energy is lower than the lamellar[25] free energy by an amount $f = -4K\bar{c}^2$. These values of ϕ^* and c^* are precisely what is needed so that $c^* = c_i = -c_0$; the compositions of the two surfactants in the two monolayers are such that the effective spontaneous curvatures of the inner and outer layers are equal and of opposite sign. If the complexing is absent (that is, $\beta = 0$), this can only occur for the special case of $\bar{c} = 0$, and flat bilayers and vesicles are energetically degenerate. However, the lowest free-energy state would be the flat bilayers ($\varepsilon < 0$) due to the entropy of mixing. When the terms arising from the in-plane entropy and interactions are non-negligible (finite τ), the value of ε can be positive and the vesicle phase is unstable with respect to a flat, mixed, lamellar phase.

IV. RANGE OF STABILITY AND PHASE DIAGRAM

For $\varepsilon < 0$, the minimum free-energy state is composed of flat bilayers where the two monolayers have identical compositions ($\phi = c = 0$). When $\varepsilon > 0$, the free energy is minimized by a nonzero value of ϕ and hence a nonzero curvature. However, for this to happen, the product $\beta\bar{c} > 0$. This condition, together with the requirement that the composition asymmetry not exceed the actual composition, $\phi^2 < \psi^2$, constrains the allowed ranges of the parameters c_1, c_2, β, and ψ. For example, if $c_1 \approx c_2 < 0$ (that is, the surfactants tend to form micelles in water), then β must be positive, implying that attractive interactions are necessary to stabilize vesicles. This occurs because the attractive interactions tend to decrease and even reverse the sign of the effective spontaneous curvature. For negative values of c_1 and c_2, putting more pairs on the inner layer would tend to relieve its frustration with respect to the bare spontaneous curvature, which prefers water-external monolayers.

The constraints for the stability of the vesicle phase, $\phi^{*2} < \psi^2$ and $\varepsilon > 0$, restrict the values of the parameters of the model. In addition to these constraints, one requires that the expansion for small curvatures be applicable—i.e., $c^* \ll 1/\delta$, where δ is a molecular size related to the thickness of the bilayer. Figure 1 shows the range of interaction strengths which obey these constraints. For illustrative purposes, we consider the case where the curvature elasticity dominates ($\tau \ll 1$) and where $c_1 = c_2 = 1/2\delta$ (which would tend to make small micelles for each individual surfactant). The allowed range of interaction strengths has $\beta < 0$ in agreement with the previous discussion. In addition, the interaction strength is bounded from above. For these graphs, we required that $c^*\delta < 0.2$. We note that we have chosen the case $\tau \ll 1$ for simplicity; a more realistic discussion is presented in Ref. 19.

In addition to these constraints on the allowed values of the interactions, packing constraints on the vesicles restrict the allowed values of both the relative (ψ) and total (ϕ_s) concentrations of the surfactants. 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

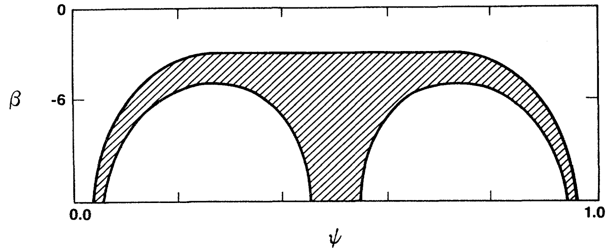

FIG. 1. Range of interaction strength where vesicles are stable (shaded area) as a function of the relative composition ψ. The figure is drawn for the case where the spontaneous curvatures of the two surfactants are positive (tending to make micelles in oil), $c_1=c_2=1/2\delta$, where δ is of order the surfactant size.

$$\Phi=\frac{4\pi}{3}nR^3 , \tag{17}$$

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

$$\phi_s=8\pi n\delta R^2 . \tag{18}$$

Eliminating n, we find that $6\delta/R=\phi_s/\Phi$. 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

$$\phi_s=6\delta c^*(\psi) , \tag{19}$$

where

$$c^*=\alpha(\psi)(\bar{c}/\beta)^{1/2} , \tag{20}$$

and α, β, and $\bar{c}$ are defined above. The resulting phase diagram is shown in Fig. 2. Again, for illustrative purposes we consider the case where the curvature elasticity dominates, $\tau\ll 1$, and the two individual spontaneous curvatures are equal. As the magnitude of the interaction strength $|\beta|$ is decreased, the range of stability of the large vesicles decreases. The shape of the stability boundary is in qualitative agreement with recent experiments.[13] Also in agreement is the observation that for surfactants where $c_1\approx c_2$, the lamellar phase is more stable than the vesicular one in the neighborhood of $\psi=\frac{1}{2}$. Note that there is a value of ψ at which the vesicles are most stable (i.e., a minimum in the stability curve as a function of $\phi_w=1-\phi_s$). This minimum arises from the fact that the smallest vesicles occur at a finite value of ψ; at smaller ψ there is too little of the cosurfactant to stabilize a vesicle, while at values of $\psi\sim\frac{1}{2}$, the vesicles grow in size and are similar to lamellae.

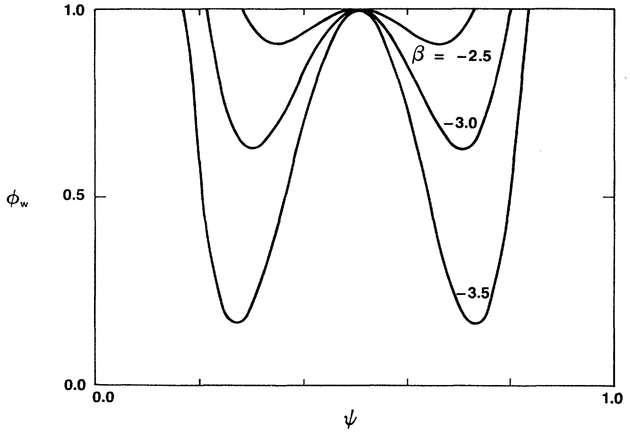

FIG. 2. Stability boundary for the vesicle phase as a function of the composition asymmetry ψ and the water volume fraction ϕ_ω. Curves are shown for three values of the interaction parameter β. The figure is drawn for the case where the spontaneous curvatures of the two surfactants are positive (tending to make micelles in oil), $c_1=c_2=1/2\delta$, where δ is of order the surfactant size.

V. POLYDISPERSITY

The preceding sections predicted the equilibrium vesicle radius in a mean-field approximation where all the vesicles have (i) the same size c^* and composition asymmetry ϕ^* and (ii) the same ratio of the two surfactants (i.e., the same value of ψ). We now consider fluctuations of these quantities which contribute to the polydispersity of the system. We consider an ensemble of vesicles each of which has the same value of ψ, but a distribution of sizes and composition asymmetries. We do not consider here the polydispersity in ψ—namely, fluctuations in the relative proportions of each surfactant in different vesicles. Such fluctuations are suppressed by the attractive in-layer interactions considered here. Repulsive interactions could lead to large fluctuations in ψ; they would also lead to phase separation of the two components within a single layer—even in the lamellar phase, a case that is outside the scope of the present work.[25]

Discussions of size distributions of vesicles for single surfactant systems can be found in (for single surfactant systems) Refs. 8–10; the most probable vesicle size is infinite, consistent with the fact that the minimum energy state is lamellar as discussed in Sec. II. The distribution has no sharp peak,[26] in contrast to the situation for mixed, interacting systems, where there is a well-defined size, $R=[c^*(\psi)]^{-1}$, which minimizes the curvature energy. Expanding the energy around c^* yields a distribution of vesicle sizes which is a Gaussian peaked at R.

To calculate the width of this distribution, we consider the case where the ratio of the two surfactants is identical in all the vesicles (each vesicle has the same value of ψ). We use Eqs. (3), (7), (8), and (10) for the effective free energy of the mixed, interacting system. The minima of the free energy are at values of $c^*=\alpha\phi^*$ and $\phi^*=(\bar{c}/\beta)^{1/2}$. We define dimensionless quantities: $x=c/c^*$, $y=\phi/\phi^*$, $g=f/(2Kc^{*2})$, $\bar{x}=\bar{c}/c^*$. We then have

$$x_i=\bar{x}(1-y^2)+y , \tag{21}$$

$$x_0=\bar{x}(1-y^2)-y , \tag{22}$$

and the reduced free energy is

$$g=(x+x_0)^2+(x-x_i)^2 , \tag{23}$$

with only one parameter, $\bar{x}=\bar{c}/c^*=(\beta\bar{c})^{1/2}/\alpha$. Expanding g about the minimum values of $x=y=1$ gives

$$g=g_0+(x-1)(y-1)g_{xy} + \tfrac{1}{2}[g_{xx}(x-1)^2+g_{yy}(y-1)^2]+\cdots , \qquad (24)$$

where $g_{xx}=4$, $g_{yy}=4(1+4\bar{x}^2)$, and $g_{xy}=-4$. In this case, the constraint of fixed total area determines the number of vesicles, so we can consider fluctuations of each vesicle at the unperturbed area (proportional to $1/c^{*2}$). Diagonalization of this quadratic form yields the mean-square values of the polydispersity, $\langle(x-1)^2\rangle$, and composition asymmetry fluctuations, $\langle(y-1)^2\rangle$:

$$\langle(x-1)^2\rangle=t\left[\frac{g_{yy}}{g_{xx}g_{yy}-g_{xy}^2}\right] , \qquad (25)$$

$$\langle(y-2)^2\rangle=t\left[\frac{g_{xx}}{g_{xx}g_{yy}-g_{xy}^2}\right] , \qquad (26)$$

where $t=T/8\pi K$. Using the expressions for the derivatives, we have

$$\langle(x-1)^2\rangle=\frac{t}{4}\frac{(1+4\bar{x}^2)}{\bar{x}^2} ,$$
$$\qquad (27)$$
$$\langle(y-1)^2\rangle=\frac{t}{4}\frac{1}{\bar{x}^2} .$$

When $\bar{x}$ is small, the polydispersity and composition asymmetry fluctuations can be large. Since

$$\bar{x}=\frac{\bar{c}}{c^*}=\frac{(\beta\bar{c})^{1/2}}{\alpha} , \qquad (28)$$

the fluctuations may become large near the onset of the vesicle instability, where $\beta\bar{c}$ is small. This can happen even if the spontaneous curvatures of each surfactant, c_1 and c_2, are order one in units of a molecular size, if the interaction is strong enough. Preliminary experimental evidence[13] indicates that the typical range of sizes has an rms deviation on the order of 10–40 %, so that fluctuations are not anomalously large.

VI. DISCUSSION

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 have the same magnitude but are of opposite sign; 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; the case of mixed amphiphiles of long and short chains should be studied. Next, the microscopic interactions that determine the different head spacings in ionic systems should be explored so that the interaction parameter β can be related to charge and salinity. Finally, a self-consistent theory that considers both the occupation energies as well as the curvature energies due to pairing interactions is important.[19] Such a treatment will indicate under what circumstances the various limits (large bending energy, large interaction strength, etc.) considered in our phenomenological treatment will apply.

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[20] We neglect the thermal undulation entropy which applies to both the lamellae and the vesicles.

[21] The effective bending modulus of the mixed system is also composition dependent. However, since the bending modulus is most sensitive to the chains, its composition dependence is not expected to be significant for the case considered here of identical chains. The effect of surfactant interactions on the spontaneous curvature is much more dramatic in stabilizing vesicles compared with the composition dependence of the bending modulus.

[22] We assume that the polar groups interact only at short distances. This can be due to screening from either added salt or from the action of the counterions which tend to screen the bare surfactant charges, especially in the case of a mixed charge system where one surfactant can result in additional screening of the other.

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