STABILITY AND PHASE BEHAVIOR OF MIXED SURFACTANT VESICLES

S. A. Safran [†] and F. C. MacKintosh

Exxon Research and Engineering
Rt. 22 E. Clinton Township
Annandale, NJ 08801

P. A. Pincus

Materials Department
University of California, Santa Barbara, CA 93106

D. A. Andelman

Raymond and Beverly Sackler Faculty of Exact Sciences
School of Physics and Astronomy
Tel Aviv University
Ramat Aviv, Israel 69978

†Current address:
Department of Polymer Research
Weizmann Institute, Rehovot, Israel, 76100

Recent experiments have shown that 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 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.

INTRODUCTION

Applications of vesicles, 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. 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 re-equilibrate back into the multilamellar, liquid crystalline structure. Recently, however, Kaler[1] et al. 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[2,3,4,5]. Using the charge as a control parameter has both chemical and physical advantages since a wide variety of head groups, counterions, 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. This is because the bilayer is composed of two amphiphilic monolayers which, in the single surfactant case, have the same spontaneous curvature[6]. 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 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 radius is 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 Ref. 7,8,9,10. 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[11]. We find that the stabilization of the 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.

CURVATURE ELASTICITY

We consider a single monolayer at a water/oil interface. 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[6]

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

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.

The spontaneous curvature[12] describes the tendency of the surfactant film to be either water external ($c_s' < 0$ by convention) or oil external($c_s' > 0$). It is taken — in the absence of long-range interactions — to arise from the competition between the packing areas of the polar head and hydrocarbon tail 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 moduli are mostly sensitive to the surfactant chain length[12,13,14].

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

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

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.

SINGLE SURFACTANT VESICLES

We now show that from an energetic point of view, large vesicles, composed of a single surfactant, are always of higher curvature energy than a flat lamellar phase. By large vesicles, we mean that the thickness of the bilayer, δ, is negligible compared with the vesicle radius, R. Thus, to first order in the small quantity $c\delta = \delta/R$, the curvatures of the inner and outer layers are equal and opposite. The total bending energy per unit area is:

$$f_c = 2K\left[(c + c_o)^2 + (c - c_i)^2\right], \qquad (3)$$

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. 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 which 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[7,9]. 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 $\succeq 500\text{Å}$, much greater than $\delta \sim 10\text{Å}$. In Ref. 15 we show that these large, energetically unfavorable, vesicles can be stabilized by entropy in the extreme dilute limit. The resulting vesicles, however, are very polydisperse; their typical size increases with the bending energy as $\exp(K/T)$, where temperature is measured in units where the Boltzmann constant is unity.

MIXED VESICLES

Effective Spontaneous Curvatures

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. 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 $\psi = \frac{1}{2}(\psi_o + \psi_i)$.

Since the physical origin of the spontaneous curvature is the mismatch in the packing areas of the polar heads and hydrocarbon chains[12], the nearest-neighbor bond distances are linearly related to the spontaneous curvatures. In a mean-field approximation, one can 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[9,15]

$$c_i = (1 - \psi_i)^2 c_1 + \psi_i^2 c_2 + (c_1 + c_2 + \Delta c)\psi_i(1 - \psi_i). \tag{4}$$

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. (4) dictates that the spontaneous curvature of a "1-2" pair is the concentration- dependent, weighted 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. We can then write:

$$c_i = \bar{c}(\psi) + \alpha(\psi)\phi - \beta(\psi)\phi^2 \tag{5}$$

$$c_o = \bar{c}(\psi) - \alpha(\psi)\phi - \beta(\psi)\phi^2 \tag{6}$$

where

$$\bar{c} = c_1(1 - \psi) + c_2\psi + \beta\psi(1 - \psi), \tag{7a}$$

$$\alpha = (c_1 - c_2) - \beta(1 - 2\psi), \tag{7b}$$

$$\beta = \Delta c. \tag{7c}$$

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, but different head groups. A random mixing approximation for the average distance a_i between polar heads in the inner layers yields:

$$a_i = a_1(1 - \psi_i)^2 + a_2\psi_i^2 + (1 - \gamma)(a_1 + a_2)\psi_i(1 - \psi_i) \tag{8}$$

with a similar equation for the average distance between polar heads in the outer layer. In Eq. (8), 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 [16] 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 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. (4)-(6), 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 are equal and opposite, 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 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 $c = c_i = -c_o$, the system is at its lowest curvature energy state and the frustration is relieved.

This is seen quantitatively from Eqs. (4) and (5) where the choice

$$\phi = \pm (\bar{c}/\beta)^{1/2} \qquad (9)$$

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. (9). 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 ($\phi = 0$), bilayers.

Free Energy

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 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 Ref. 9 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.

In the remainder of this section, we consider two surfactants which have identical spontaneous curvatures: $c_1 = c_2$. 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:

$$H = \sum_{<ij>} JS_iS_j, \qquad (10)$$

where the sum over $< ij >$ includes only nearest neighbor pairs. The constituents are labeled by i, and $S_i = +1 (-1)$ denotes the presence of surfactant A (B). 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}, 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:

$$H = \sum_{<ij>} \left(JS_iS_j - B(1 - S_iS_j)\Delta_{ij} + \frac{k}{2}\Delta_{ij}^2 \right). \qquad (11)$$

Here, B represents the strength of the coupling between the spin and elastic degrees of freedom. Equation (11) represents the compressible Ising model.

The mean-field value of $\langle \Delta_{ij} \rangle$ is found by minimizing Eq. (11) with respect to $\langle \Delta_{ij} \rangle$:

$$\langle \Delta_{ij} \rangle = B(1 - \langle S_i S_j \rangle)/k, \tag{12}$$

The resulting expression for the free energy per surfactant, h, is

$$h = J \langle S_i S_j \rangle - \frac{B^2}{2k}(1 - \langle S_i S_j \rangle)^2. \tag{13}$$

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 A or B at each site:

$$\langle S_i S_j \rangle = (1 - \psi)^2 + \psi^2 - 2\psi(1 - \psi) = (1 - 2\psi)^2. \tag{14}$$

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 $\langle S_i S_j \rangle$:

$$c(\psi) - c(0) = \frac{\beta}{4}(1 - \langle S_i S_j \rangle) = \beta\psi(1 - \psi). \tag{15}$$

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.

Considering now the properties of a bilayer, we use this model to derive expressions for the effective spontaneous curvatures, given by Eqs. (5)-(7). The curvature free energy of Eq. (3) then becomes

$$f_c = 4K \left[(c - \alpha\phi)^2 + \left(\bar{c}(\psi) - \beta\phi^2 \right)^2 \right]. \tag{16}$$

Thus, the spontaneous curvature of the bilayer is $c = \alpha\phi$. This describes a flat bilayer, unless $\phi \neq 0$. We must now determine the value, ϕ^*, which minimizes the free energy as a function of ϕ. When $c = \alpha\phi$, the free energy per surfactant, F_c is

$$F_c = 2K\sigma \left(c(\psi) - \beta\phi^2 \right)^2 = 2K\sigma \left[c(\psi)^2 - 2\beta c(\psi)\phi^2 + \beta^2\phi^4 \right]. \tag{17}$$

where σ is the area per polar head group. The contribution of the interaction terms of Eq. (13) to the free energy per surfactant is

$$F_i = J(1 - 2\psi)^2 - \frac{8B^2}{k}\psi^2(1 - \psi)^2 + \left[4J - 8\frac{B^2}{k}(1 - 6\psi(1 - \psi)) \right]\phi^2 - 8\frac{B^2}{k}\phi^4. \tag{18}$$

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

$$F_m = T \left[\psi \log \psi + (1 - \psi)\log(1 - \psi) + \frac{1}{2}\left(\frac{1}{\psi(1 - \psi)} \right)\phi^2 + \frac{1}{12}\left(\frac{1}{\psi^3} + \frac{1}{(1 - \psi)^3} \right)\phi^4 \right] \tag{19}$$

The total free energy per surfactant can be written as

$$F = F_0 - \epsilon\phi^2 + A\phi^4, \tag{20a}$$

where

$$\epsilon = 4K\sigma\beta c(\psi) - 4J + \frac{8}{k}B^2\left(1 - 6\psi(1-\psi)\right) - \frac{T}{2}\left(\frac{1}{\psi(1-\psi)}\right), \qquad (20b)$$

$$A = \frac{T}{12}\left(\frac{1}{\psi^3} + \frac{1}{(1-\psi)^3}\right) - 8\frac{B^2}{k}, \qquad (20c)$$

and F_0 is independent of ϕ. Equations (19) and (20) are valid in the high "temperature" limit. This corresponds to interaction terms, J and B/k, which are small compared with T. In this limit, $\epsilon \sim (T_c - T)$ and $B \sim T$, where $T_c \simeq K\sigma\beta c(\psi)$. Then, a spontaneous vesicle phase, characterized by $\phi \neq 0$, 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[9].

STABILITY OF MIXED VESICLES

For $\epsilon < 0$, the minimum free energy state is composed of flat bilayers where the two monolayers have identical compositions ($\phi = c = 0$). When $\epsilon > 0$, the free energy is minimized by a non-zero value of ϕ and hence a non zero curvature. However, for this to happen for values of $B < J$, the product $\beta\bar{c}$ should be positive. 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 $\epsilon > 0$, 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. The allowed range of interaction strengths has $\beta < 0$ in agreement with the previous discussion. In addition, the interaction strength is bounded from above.

In addition to these constraints on the allowed values of the interactions, packing constraints on the (unilamellar) 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

$$\Phi = \frac{4\pi}{3}nR^3, \qquad (21)$$

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

$$\phi_s = 8\pi n\delta R^2. \qquad (22)$$

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

$$\phi_s = 6\delta c^*(\psi), \qquad (23)$$

where
$$c^* = \alpha(\psi)\phi^*, \qquad\qquad (24)$$
and $\phi^*(\psi)$ is the value of ϕ that minimizes Eq. (20). The resulting phase diagram is shown in Fig. 1. It indicates that the vesicle phase is only stable within a finite range of compositions, ψ. In particular, when $\psi = 1/2$, the vesicle phase is unstable to a lamellar phase.

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" sur-factant 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 cur-vature 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 asymme-try of the two layers is such that the effective spontaneous curvatures of the inner and outer layers 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[9]. 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 parameter β can be related to charge and salinity.
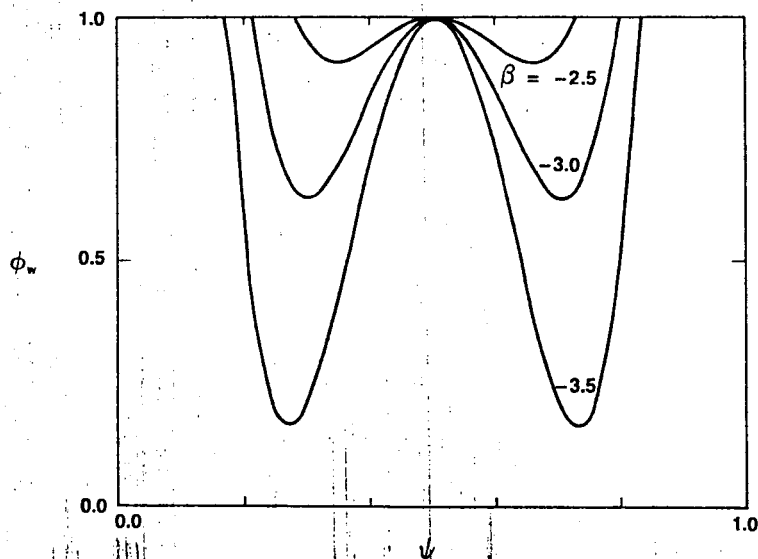

Fig. 1. Stability boundary for the vesicle phase as a function of the composition asymmetry ψ and the water volume fraction ϕ_w. Curves are shown for three values of the interaction parameter β. For simplicity, we have taken $J = B = T = 0$. The figure is drawn for the case where the spontaneous curvatures of the two surfactants are positive (tending to make micelles in oil), $c_1 = c_2 = 1/2\delta$, where δ is of the order of the surfactant size.

REFERENCES

1. E. W. Kaler, A. K. Murthy, B. E. Rodriguez and J. A. N. Zasadzinski, Science 245, 1371 (1989).

2. S. Carnie, J. N. Israelachvili, and B. A. Pailthorpe, Biochim. Biophys. Acta 554, 340 (1979).

3. N. E. Gabriel and M. F. Roberts, Biochemistry 23, 4011 (1984); W. R. Hargreaves and D. W. Deamer, Biochemistry 17, 3759 (1978).

4. D. D. Miller, J. R. Bellare, T. Kaneko and D. F. Evans, Langmuir 4, 1363 (1988) and J. Phys. Chem., in press.

5. M. K Jain and G. H. de Hass, Biochim. et Biophys. Acta 642, 203 (1981); S. Almog, T. Kushnir, S. Nir, and D. Lichtenberg, Biochemistry 25, 6597 (1986).

6. W. Helfrich, Z. Naturforsch. 28a, 693 (1973) and in J. de Phys. (Paris) 47, 321 (1986).

7. J. N. Israelachvili, D. J. Mitchell, and B. W. Ninham, Trans. Faraday Soc.II 72, 1525 (1972).

8. J. Israelachvili, D. J. Mitchell, and B. W. Ninham, Biochim. Biophys. Acta 470, 185 (1977).

9. A unified theory which accounts for both the curvature energy and the in-plane interactions is given in F. C. MacKintosh, S. A. Safran, P. Pincus, to be published.

10. Z. G. Wang, to be published.

11. E. W. Kaler, unpublished, 1990.

12. E.A. Evans and R. Sklak, CRC Critical Reviews Bioeng. 3, 181 (1979); A.G. Petrov and A. Derzhanski, J. Phys. Coll. 37, C3-155 (1976); L.A. Turkevich, S. A. Safran and P.A. Pincus, in "Surfactants in Solution", K. Mittal and P. Bothorel editors, Vol. 6, pp. 1177-1191, (Plenum, New York, 1986); I. Szleifer, D. Kramer, A. Ben-Shaul, D. Roux and M. Gelbart, Phys. Rev. Lett. 60, 1966 (1988).

13. R. S. Cantor, Macromolecules 14, 1186 (1981); L. Leibler, Makromol. Chem. Macromol. Symp. 16, 1 (1988); Z. G. Wang and S. A. Safran, J. de Phys. 51, 185 (1990).

14. S. T. Milner and T. A. Witten, J. de Phys. 49, 1951 (1988).

15. S. A. Safran, P. Pincus, D. Andelman, Science 248, 354 (1990); S. A. Safran, P. Pincus, D. Andelman, and F. C. MacKintosh, Phys. Rev. 43, 1071 (1991).

16. Non-ideality in another context has been discussed by B. G. Tenchov and R. D. Koynova, Biochim. Biophys. Acta 815, 380 (1985).