

Coupled Modulated Bilayers: A Phenomenological Model

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Dedicated to Erich Sackmann on the occasion of his 75th birthday

We propose a model addressing the coupling mechanism between two spatially modulated monolayers. We obtain the mean-field phase diagrams of coupled bilayers when the two monolayers have the same preferred modulation wavelength. Various combinations of the monolayer modulated phases are obtained and their relative stability is calculated. Due to the

coupling, a spatial modulation in one of the monolayers induces a similar periodic structure in the second one. We have also performed numerical simulations for the case when the two monolayers have different modulation wavelengths. Complex patterns may arise from the frustration between the two incommensurate but annealed structures.

1. Introduction

Quite a number of physical, chemical, and biological systems manifest some type of modulation in their spatial ordering.^[1–3] Such structures are stripes and bubbles in two-dimensional (2D) systems, or lamellae, hexagonally packed cylinders, and cubic arrays of spheres in three-dimensional (3D) cases, as well as more complex structures such as gyroids. Examples of such systems include ferromagnetic layers,^[4] magnetic garnet films,^[5] ferrofluids,^[2,3,6] dipolar Langmuir films,^[7] rippled phases in lipid bilayers,^[8] and block copolymers.^[9,10] Modulated phases may also occur in systems described by two (or more) coupled order parameters, each favoring a different equilibrium state.^[11] The observed spatial patterns exhibit striking similarity even for systems that are very different in their nature. It is generally understood that the modulated structures are formed spontaneously due to the competition between short- and long-range interactions.

In the case of 2D ferromagnetic layers, for example, the short-range interaction arises from magnetic domain wall energy, while the long-range interaction is due to magnetic dipole–dipole interaction which induces a demagnetizing field.^[2,3] Adding both contributions and minimizing the total free energy with respect to the wavenumber q , one obtains the most stable mode $q^* \neq 0$. This description is valid in the weak segregation limit (close to a critical point), where the equilibrium domain size is given by $d^* = 2\pi/q^*$. In general, this quantity depends on temperature and/or other external fields.

Herein, we consider two modulated monolayers that are jointly coupled. Our motivation is related to recent experiments by Collins and Keller^[12] who investigated Montal–Müller planar bilayer membranes^[13] composed of lipids and cholesterol. With this technique, a bilayer is constructed by separately preparing two independent monolayers and then combining them into one joint bilayer across a hole at the air/water interface. The experiments specifically addressed the question of liquid domains in the two leaflets, and the mutual influence of the monolayers in terms of their domain phases. In the experi-

ment, asymmetric bilayers were prepared in such a way that one leaflet's composition would phase-separate in a symmetric bilayer and the other's would not. In some cases, one leaflet may induce phase separation in the other leaflet, whereas in other cases, the second leaflet suppresses domain formation in the original leaflet. These results imply that two-leaflet coupling is an important ingredient in determining the bilayer phase state.

Motivated by these experiments, the coupled bilayer system was investigated theoretically. The coupling mechanism arises through interactions between lipid tails across the bilayer mid-plane, and the phase behavior of such a bilayer membrane was computed using either regular solution theory^[14] or Landau theory.^[15] The theoretical results are in accord with several of the experimental observations. It should be noted that all previous models dealt with the coupling between two *macro-phase-separated* leaflets, while it is also of interest to investigate the coupling between two *micro-phase-separated* (modulated) leaflets. Furthermore, one might also consider the interplay between a macro- and a micro-phase separation.

Herein, we suggest a model describing the coupling between two modulated systems, and, in particular, we analyze the influence of this coupling on the phase behavior of two coupled 2D monolayers. When the two monolayers have the same preferred periodicity of modulation, we obtain mean-field phase diagrams that exhibit various combinations of micro-phase-separated structures. In some cases, the periodic structure in one of the monolayers induces a modulation in the other monolayer. Interesting situations take place when

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the two monolayers have different preferred wavelengths of modulation. Here the frustrations between the two competing modulated structures need to be optimized. These structures and their dynamical behavior are examined using numerical simulations. We note that modulated patterns of compositions are indeed found in the experiments using giant unilamellar vesicles formed from a ternary mixture of the lipids dioleoyl-phosphatidylcholine (DOPC), sphingomyelin, and cholesterol.^[16,17] In these bilayer vesicles, a micro-phase separation occurs between a liquid-disordered phase rich in DOPC and a liquid-ordered phase rich in sphingomyelin and cholesterol. In ref. [17], even a dynamical sequence of the striped-to-hexagonal morphological transition was observed. Although there has been no experiment so far which directly corresponds to the proposed model, our predictions may be verified, for example, by constructing Montal–Mueller bilayers^[13] consisting of two lipid monolayers that exhibit a striped phase near the miscibility critical point.^[18,19]

In the next section, we present a phenomenological model describing the coupling between two modulated lipid monolayers. In Section 3, we discuss the case when the two monolayers have the same preferred wavelength of modulation. Monolayers having different preferred wavelengths are considered in Section 4, and some related situations are further discussed in Section 5. Although we limit our present analysis to 2D systems, the suggested model can be generalized to 3D systems as well.

2. Model

In order to illustrate the coupling effect between two modulated systems, we imagine a pair of lipid monolayers forming a coupled bilayer. Each of the monolayers can separately undergo a micro-phase separation. As shown in Figure 1, we assume that each monolayer is a mixture of two lipid species, say lipid A and lipid B. Their area fractions are defined by $\phi_A(\mathbf{r})$ and

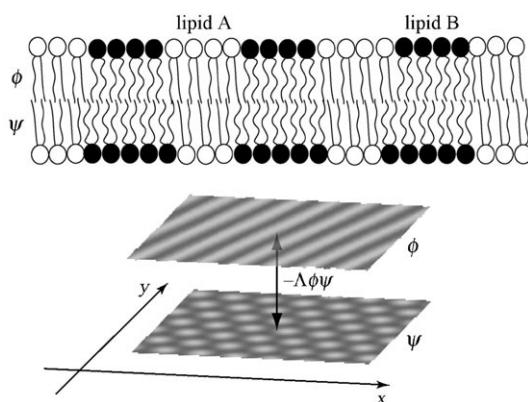


Figure 1. Schematic illustration of two coupled modulated monolayers forming a bilayer membrane. Each monolayer is composed of a binary A/B lipid mixture, which can have a spatial modulation. The relative composition of the two lipids in the upper and the lower leaflets are defined by ϕ and ψ , respectively. In general, the average composition in the two monolayers can be different. The lipid tails interact across the bilayer midplane. The phenomenological coupling term between these two variables are assumed to be bilinear of the form $-\Lambda\phi\psi$ in the free-energy Equation (1).

$\phi_B(\mathbf{r})$, where $\mathbf{r}=(x,y)$ is the 2D positional vector. By assuming that the monolayer is incompressible, $\phi_A(\mathbf{r}) + \phi_B(\mathbf{r}) = 1$, the monolayer composition can be characterized by a single-order parameter defined by the relative A/B composition $\phi(\mathbf{r}) = \phi_A(\mathbf{r}) - \phi_B(\mathbf{r})$. Let us denote this local order parameter of the upper and lower monolayers by $\phi(\mathbf{r})$ and $\psi(\mathbf{r})$, respectively. The coarse-grained free-energy functional for the coupled modulated bilayer is written as Equation (1):

$$\begin{aligned} F[\phi, \psi] = & F_u[\phi] + F_\ell[\psi] - \Lambda \int d\mathbf{r} \phi \psi \\ = & \int d\mathbf{r} \left[2(\nabla^2 \phi)^2 - 2(\nabla \phi)^2 + \frac{\tau}{2} \phi^2 + \frac{1}{4} \phi^4 - \mu_\phi \phi \right. \\ & \left. + 2D(\nabla^2 \psi)^2 - 2C(\nabla \psi)^2 + \frac{\tau}{2} \psi^2 + \frac{1}{4} \psi^4 - \mu_\psi \psi - \Lambda \phi \psi \right] \end{aligned} \quad (1)$$

This is a modified Ginzburg–Landau free energy expanded in powers of the order parameters ϕ and ψ and their derivatives. The $F_u[\phi]$ free energy has five terms depending only on ϕ and its derivatives. It describes the upper monolayer and its possible modulations, while the coefficients of the Laplacian squared, the gradient squared and the ϕ^4 terms are taken to be numbers, for simplicity. Similarly, $F_\ell[\psi]$ describing the lower monolayer contains the next five terms that are only functions of ψ and its derivatives. The last term represents the coupling between the two leaflets. The coefficients of the two gradient squared terms are both negative ($C>0$), favoring spatial modulations, whereas the coefficients of the Laplacian squared terms are positive ($D>0$) to have a stable modulation at finite wavenumbers. The ϕ^2 , ϕ^4 , ψ^2 and ψ^4 terms in F are the usual Landau expansion terms with $\tau = (T - T_c)/T_c$ being the reduced temperature (T_c is the critical temperature). For simplicity, the two leaflets are taken to have the same critical temperature T_c (and hence the same τ). Finally, the linear term coefficients, μ_ϕ and μ_ψ , are the chemical potentials which regulate the average values of ϕ and ψ , respectively.

In the absence of the coupling term ($\Lambda=0$), each of the two leaflets can have its own modulated phase. Free-energy functionals such as F_u have been used successfully in the past to describe a variety of modulated systems: magnetic garnet films,^[5] Langmuir films,^[7] diblock copolymers,^[9,20] and amphiphilic systems.^[21] Furthermore, interfacial properties between different coexisting phases have been investigated using a similar model.^[22–24] In the above expression for the free energy F , the ϕ -leaflet has a dominant wavenumber $q_\phi^* = 1/\sqrt{2}$, and so has the ψ -leaflet with $q_\psi^* = \sqrt{C/2D}$. The modulation wavenumbers and amplitudes of the two monolayers coincide when $D=C=1$ and the average compositions are the same.

Next we address the physical origin of the coupling term $-\Lambda\phi\psi$. We first note that this quadratic term is invariant under the exchange of $\phi \leftrightarrow \psi$. When $\Lambda>0$, this term can be obtained from a $(\phi - \psi)^2$ term,^[14,15] which represents a local energy penalty when the upper and lower monolayers have different compositions. In the case of mixed lipid bilayers, such a coupling may result from the conformational confinement of the lipid chains, and hence would have entropic origin.^[14] By estimating the degree of the lipid chain interdigititation, the

magnitude of the coupling parameter Λ was recently estimated by May.^[25] In general, the coupling constant Λ can also be negative depending on the specific coupling mechanism.^[25] However, it is explained later that the phase diagram for $\Lambda < 0$ can easily be obtained from the $\Lambda > 0$ one. Hence, it is sufficient to consider only the $\Lambda > 0$ case without loss of generality. Although the microscopic origin of the coupling may differ between systems, we will regard Λ as a phenomenological parameter and investigate its role on the structure, phase behavior and dynamics of coupled modulated bilayers.

The phase behavior for uncoupled case, $\Lambda = 0$, can be obtained from the analysis of $F_u[\phi]$ ^[11] and is only briefly reviewed here (see also Figure 2). For a 2D system, the mean-field phase diagram can be constructed by comparing the free energies of striped (S) and hexagonal (H) phases. In terms of the ϕ order parameter, the stripe phase is described by Equation (2):

$$\phi_S(\mathbf{r}) = \phi_0 + 2\phi_q \cos(q^*x) \quad (2)$$

where $\phi_0 = \langle \phi \rangle$ is the spatially averaged composition (imposed by the chemical potential μ_ϕ), and ϕ_q is the amplitude of the q^* -mode in the x -direction. Similarly, the composition of the hexagonal phase is given by a superposition of three 2D modes of equal magnitude, $|\mathbf{q}_i| = q^*$ as shown in Equation (3):

$$\phi_H(\mathbf{r}) = \phi_0 + \frac{2\phi_q}{\sqrt{3}} \sum_{i=1}^3 \cos(\mathbf{q}_i \cdot \mathbf{r}) \quad (3)$$

where [Eq. (4)]:

$$\begin{aligned} \mathbf{q}_1 &= q^* \hat{\mathbf{x}}, \\ \mathbf{q}_2 &= \frac{q^*}{2} (-\hat{\mathbf{x}} + \sqrt{3}\hat{\mathbf{y}}), \\ \mathbf{q}_3 &= \frac{q^*}{2} (-\hat{\mathbf{x}} - \sqrt{3}\hat{\mathbf{y}}) \end{aligned} \quad (4)$$

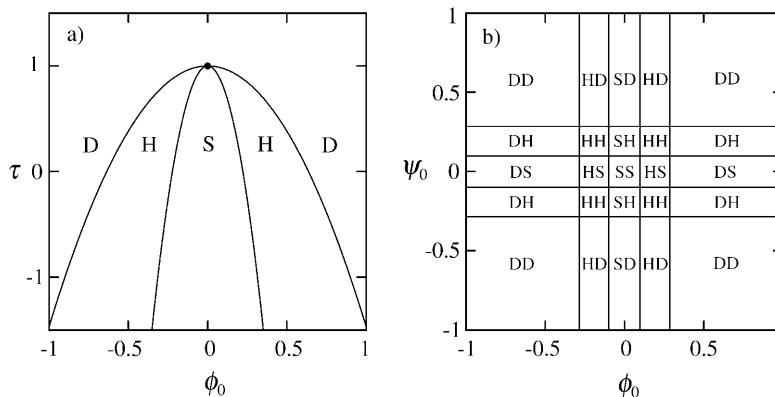


Figure 2. a) Mean-field phase diagram of a single monolayer with a modulated structure in the vicinity of the critical temperature, computed using a model as in Equations (5)–(7). ϕ_0 is the average composition and τ is the reduced temperature. The three phases are: striped (S), hexagonal (H), and disordered (D). These phases are separated by first-order transition lines, while for clarity we omit showing coexistence regions. (●) located at $(\phi_0, \tau) = (0, 1)$ indicates the critical point. Note the shift of the critical temperature from zero to unity when the modulated phases are considered. b) Mean-field phase diagram of decoupled ($\Lambda = 0$) modulated monolayers at $\tau = 0.8$. ϕ_0 and ψ_0 are the average compositions in the two leaflets. The notations of the different phases are described in Section 3.1. All the phases are separated by first-order transition lines.

and $\sum_{i=1}^3 \mathbf{q}_i = 0$. In the above, only the most stable wavenumber q^* is used within the single-mode approximation. This can be justified for the weak segregation region close to the critical point.^[5]

Averaging over one spatial period, we obtain the free energy densities of the striped, hexagonal, and disordered phases, respectively, shown in Equations (5)–(7):

$$f_S(\phi_0, \phi_q) = \frac{\tau}{2} \phi_0^2 + \frac{1}{4} \phi_q^4 + (\tau - 1 + 3\phi_0^2) \phi_q^2 + \frac{3}{2} \phi_q^4 \quad (5)$$

$$f_H(\phi_0, \phi_q) = \frac{\tau}{2} \phi_0^2 + \frac{1}{4} \phi_q^4 + (\tau - 1 + 3\phi_0^2) \phi_q^2 + \frac{4}{\sqrt{3}} \phi_0 \phi_q^3 + \frac{5}{2} \phi_q^4 \quad (6)$$

$$f_D(\phi_0) = \frac{\tau}{2} \phi_0^2 + \frac{1}{4} \phi_0^4 \quad (7)$$

In Figure 2a, we reproduce the original phase diagram of refs. [7, 11]. The striped, hexagonal, and disordered phases are separated by first-order phase-transition lines. Regions of two-phase coexistence do exist, but are omitted from the Figure for clarity's sake.^[26] Thus, the transition lines indicate the locus of points at which the free energies of two different phases cross each other, and are not the proper phase boundaries (binodals). The critical point (●) is located at $(\phi_0, \tau) = (0, 1)$.

3. Two Coupled Leaflets with the Same q^*

Having introduced the free energy and explained the phase behavior of the uncoupled case, we now explore the equilibrium and non-equilibrium properties of two coupled modulated monolayers, $\Lambda \neq 0$.

3.1. Free-Energy Densities

First we consider the case when $D = C = 1$ so that the preferred wavenumbers are the same for both monolayers, $q_\phi^* = q_\psi^* = q^* = 1/\sqrt{2}$. The mean-field phase diagram is calculated within the single-mode approximation. Various combinations of 2D modulated structures appearing in the two monolayers are possible. The first example is the striped-striped (SS) phase, in which both monolayers exhibit the striped phase. This can be expressed by Equations (8) and (9):

$$\phi_S(\mathbf{r}) = \phi_0 + 2\phi_q \cos(q^*x) \quad (8)$$

$$\psi_S(\mathbf{r}) = \psi_0 + 2\psi_q \cos(q^*x) \quad (9)$$

where $\phi_0 = \langle \phi \rangle$ and $\psi_0 = \langle \psi \rangle$ are the average compositions, ϕ_q

and ψ_q are the respective amplitudes. These composition profiles are substituted into the free energy of Equation (1). Averaging over one spatial period, we obtain the free-energy density of the SS phase, given by Equation (10):

$$f_{SS} = f_S(\phi_0, \phi_q) + f_S(\psi_0, \psi_q) - \Lambda(\phi_0\psi_0 + 2\phi_q\psi_q) \quad (10)$$

where f_S is defined in Equation (5). We then minimize f_{SS} with respect to both ϕ_q and ψ_q for given ϕ_0 , ψ_0 , τ and Λ . When either ϕ_q or ψ_q vanishes, the corresponding monolayer is in its disordered phase and the mixed bilayer state will be called the striped-disordered (SD) or the disordered-striped (DS) phase. Note that we use the convention that the first index is of the ϕ -leaflet and the second of the ψ -one. When both ϕ_q and ψ_q are zero, the free energy density of the disordered-disordered (DD) phase is given by Equation (11):

$$f_{DD} = f_D(\phi_0) + f_D(\psi_0) - \Lambda\phi_0\psi_0 \quad (11)$$

where f_D is defined in Equation (7). This free energy f_{DD} was analyzed in ref. [15] in order to investigate the macro-phase separation of a bilayer membrane with coupled monolayers. It was shown that the bilayer can exist in four different phases, and can also exhibit a three-phase coexistence.

Similar to the stripe case, the order parameters of the hexagonal-hexagonal (HH) phase can be represented by Equations (12) and (13):

$$\phi_H(\mathbf{r}) = \phi_0 + \frac{2\phi_q}{\sqrt{3}} \sum_{i=1}^3 \cos(\mathbf{q}_i \cdot \mathbf{r}) \quad (12)$$

$$\psi_H(\mathbf{r}) = \psi_0 + \frac{2\psi_q}{\sqrt{3}} \sum_{i=1}^3 \cos(\mathbf{q}_i \cdot \mathbf{r}) \quad (13)$$

where the basis of the three \mathbf{q}_i is defined in Equation (4). By repeating the same procedure as for the SS phase, the free-energy density of the HH phase is obtained as Equation (14):

$$f_{HH} = f_H(\phi_0, \phi_q) + f_H(\psi_0, \psi_q) - \Lambda(\phi_0\psi_0 + 2\phi_q\psi_q) \quad (14)$$

where f_H is defined in Equation (6). When either ϕ_q or ψ_q vanishes, one of the monolayers is in the disordered phase and the bilayer will be called the hexagonal-disordered (HD) phase or the disordered-hexagonal (DH) phase.

When the normal hexagonal phase in one leaflet is coupled to the inverted hexagonal phase in the other leaflet, it is energetically favorable to have a particular phase shift of $2\pi/3$ between the two hexagonal structures. The order parameters which represent such a different type of hexagonal-hexagonal (HH*) phase can be written as Equations (15) and (16):

$$\phi_H(\mathbf{r}) = \phi_0 + \frac{2\phi_q}{\sqrt{3}} \sum_{i=1}^3 \cos(\mathbf{q}_i \cdot \mathbf{r}) \quad (15)$$

$$\psi_{H^*}(\mathbf{r}) = \psi_0 + \frac{2\psi_q}{\sqrt{3}} \sum_{i=1}^3 \cos\left(\mathbf{q}_i \cdot \mathbf{r} + \frac{2\pi}{3}\right) \quad (16)$$

The free energy density of the HH* phase is then obtained as Equation (17):

$$f_{HH^*} = f_H(\phi_0, \phi_q) + f_H(\psi_0, \psi_q) - \Lambda(\phi_0\psi_0 - \phi_q\psi_q) \quad (17)$$

Another combination which should be considered in the present model is the asymmetric case where one monolayer exhibits the striped phase and the other the hexagonal phase. This striped-hexagonal (SH) phase is expressed as Equations (18) and (19):

$$\phi_S(\mathbf{r}) = \phi_0 + 2\phi_q \cos(q^*x) \quad (18)$$

$$\psi_H(\mathbf{r}) = \psi_0 + \frac{2\psi_q}{\sqrt{3}} \sum_{i=1}^3 \cos(\mathbf{q}_i \cdot \mathbf{r}) \quad (19)$$

The free energy density of this SH phase is calculated to be [Eq. (20)]:

$$f_{SH} = f_S(\phi_0, \phi_q) + f_H(\psi_0, \psi_q) - \Lambda\left(\phi_0\psi_0 + \frac{2}{\sqrt{3}}\phi_q\psi_q\right) \quad (20)$$

The phase in which ϕ_S and ψ_H in Equations (18) and (19) are interchanged with ϕ_H , ψ_S is called the hexagonal-striped (HS) phase, and its free energy is obtained from the SH phase by noting the $\phi \leftrightarrow \psi$ symmetry. In addition to these phases, we have also taken into account the square-square (QQ) phase expressed by Equations (21) and (22):

$$\phi_Q(\mathbf{r}) = \phi_0 + \frac{2\phi_q}{\sqrt{2}} [\cos(q^*x) + \cos(q^*y)] \quad (21)$$

$$\psi_Q(\mathbf{r}) = \psi_0 + \frac{2\psi_q}{\sqrt{2}} [\cos(q^*x) + \cos(q^*y)] \quad (22)$$

Then its free energy density is given by Equation (23):

$$f_{QQ} = f_Q(\phi_0, \phi_q) + f_Q(\psi_0, \psi_q) - \Lambda(\phi_0\psi_0 + 2\phi_q\psi_q) \quad (23)$$

where [Eq. (24)]:

$$f_Q(\phi_0, \phi_q) = \frac{\tau}{2}\phi_0^2 + \frac{1}{4}\phi_0^4 + (\tau - 1 + 3\phi_0^2)\phi_q^2 + \frac{9}{4}\phi_q^4 \quad (24)$$

However, we show below that this QQ phase cannot be more stable than the other phases.

3.2. Bilayer Phase Diagrams

Minimizing Equations (10), (14), (17), (20) and (23) with respect to both ϕ_q and ψ_q , we obtain the phase diagram for the coupled bilayer. As a reference, we first show in Figure 2b the phase diagram in the decoupled case ($\Lambda=0$) for $\tau=0.8$. This can easily be obtained from Figure 2a by combining its two cross-sections (one for ϕ_0 and one for ψ_0) at $\tau=0.8$. Figure 3

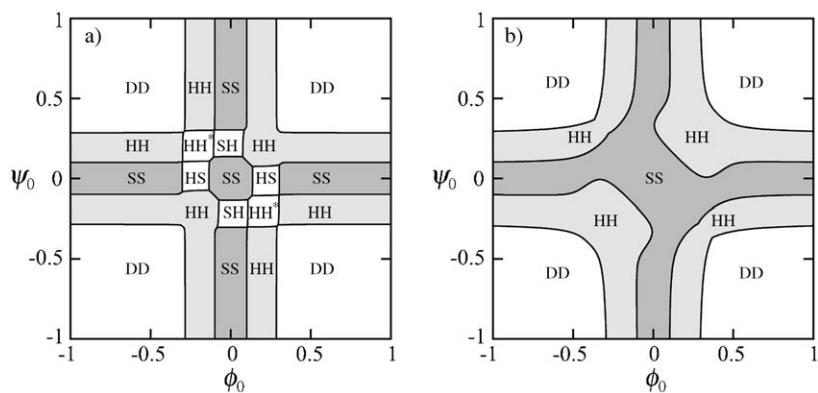


Figure 3. Mean-field phase diagram of coupled modulated bilayers for $\tau=0.8$. ϕ_0 and ψ_0 are the average compositions in the two leaflets. The coupling parameter is chosen to be a) $\Lambda=0.02$ and b) $\Lambda=0.2$. The notations of the different phases are described in Section 3.1. All the phases are separated by first-order transition lines. The phase diagram is symmetric with respect to the two principal diagonals $\phi_0=\psi_0$ and $\phi_0=-\psi_0$.

gives the phase diagram for a coupled bilayer when a) $\Lambda=0.02$ and b) $\Lambda=0.2$, while the temperature is fixed to $\tau=0.8$ as before. On the (ϕ_0, ψ_0) -plane, we have identified the phase which has the lowest energy, whereas possible phase coexistence regions between different phases were ignored. All the boundary lines indicate first-order transitions. Since the free-energy Equation (1) is invariant under the exchange of $\phi \leftrightarrow \psi$, the phase diagrams are symmetric about the diagonal line $\phi_0=\psi_0$ as the upper and lower leaflets have been chosen arbitrarily. These phase diagrams are also symmetric under rotation of 180 degrees around the origin because Equation (1) is invariant (except for the linear terms) under the simultaneous transformations of $\phi \rightarrow -\phi$ and $\psi \rightarrow -\psi$. This is reasonable as the labels of "A" or "B" for the two lipids were assigned arbitrarily. As a consequence, the phase diagrams are also symmetric about the diagonal line $\phi_0=-\psi_0$. The symmetries with respect to both $\phi_0=0$ and $\psi_0=0$ in Figure 2b for $\Lambda=0$ are now broken because of the coupling between the two leaflets.

When the coupling parameter is small ($\Lambda=0.02$), the global topology of the phase diagram resembles that of the uncoupled case presented in Figure 2b. Close to the origin, $\phi_0=\psi_0=0$, there is a region of SS phase surrounded by eight other phases: two SH, two HS, two HH, and two HH* phases. The HH phase appearing in the region of $\phi_0 < 0$ and $\psi_0 < 0$ is a combination of the two inverted hexagonal structures on each monolayer. One sees that the HH* phase appears in the regions of $\phi_0\psi_0 < 0$, where the hexagonal and the inverted hexagonal structures are coupled to each other.

A remarkable feature of this phase diagram is the existence of the SS and HH phases in the regions where either $|\phi_0|$ or $|\psi_0|$ are large. These outer SS and HH phases extend up to the maximum or the minimum values of the compositions. These regions of the SS and HH phases with $\Lambda>0$ roughly correspond to those of the SD (DS) and HD (DH) phases, respectively, in Figure 2b with $\Lambda=0$. Hence, the modulated structure in one of the monolayers induces the same modulated phase in the other monolayer due to the coupling term. Notice that the SD (DS) phase and HD (DH) phase do not exist in Figure 3a. We further remark that the extent of the four DD phase re-

gions is almost unaffected by the coupling. Even when the temperature is lowered by decreasing τ , only the phases located close to the origin ($\phi_0=\psi_0=0$) would expand, and the global topology does not change substantially.

For a larger value of the coupling parameter ($\Lambda=0.2$), the five regions of the SS phase merge together forming one single continuous SS region. The four HH regions are still distinct and separate the SS region from four DD phase regions. Note that in Figure 3b, all phases have a symmetric combination

of phase modulation such as SS or HH. The asymmetric combination such as the SH phase does not appear, because the large coupling parameter strongly prefers symmetric phases of equal modulations in the two monolayers, although the ϕ_q and ψ_q amplitudes of the two modulated monolayers are not the same in the stripe SS phase (or the hexagonal HH phase). As the value of Λ increases from 0.02 to 0.2, first the SH phase disappears, followed by the disappearance of the HH* phase. When the value of Λ increases further, the regions of the SS and HH phases expand at the expense of the DD phase regions. This means that the coupling between the monolayers causes more structural order in the bilayer. Finally we remark that the QQ phase was never found to be more stable than any of the other phases considered above.

Although we have so far assumed that Λ is positive, the phase diagrams for $\Lambda<0$ can be easily obtained from those for $\Lambda>0$ by rotating them by 90 degrees around the origin. This is because the free-energy Equation (1) is invariant under the simultaneous transformations of either $\phi \rightarrow -\phi$ and $\Lambda \rightarrow -\Lambda$, or $\psi \rightarrow -\psi$ and $\Lambda \rightarrow -\Lambda$.

3.3. Modulated Bilayer Dynamics

In order to check the validity of the obtained phase diagram and to investigate the dynamics of coupled modulated bilayers, we consider now the time evolution of the coupled equations for ϕ and ψ , as shown in Equation (25):

$$\frac{\partial \phi}{\partial t} = L_\phi \nabla^2 \frac{\delta F}{\delta \phi}, \quad \frac{\partial \psi}{\partial t} = L_\psi \nabla^2 \frac{\delta F}{\delta \psi} \quad (25)$$

Here we have assumed that both ϕ and ψ are conserved order parameters in each of the monolayers (model B in the Hohenberg–Halperin classification^[27]). For simplicity, the kinetic coefficients L_ϕ and L_ψ are taken to be unity, and both the hydrodynamic effect and thermal fluctuations are neglected. We solve the above equations numerically in 2D using the periodic boundary condition. Each simulation starts from a disordered state with a small random noise around the average composi-

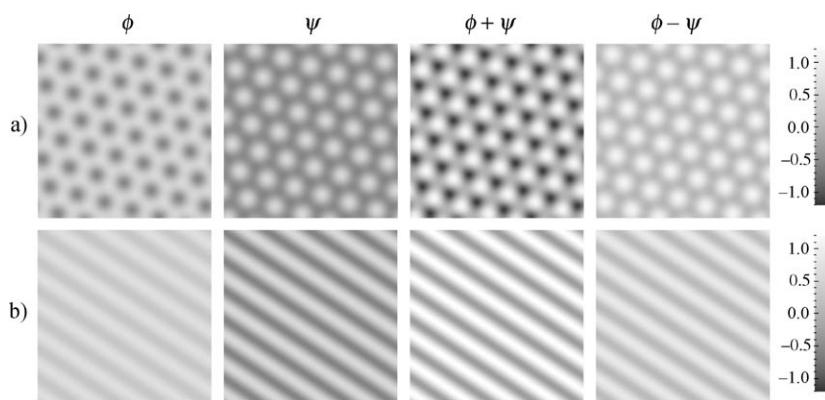


Figure 4. Equilibrium patterns of coupled modulated monolayers with $\tau=0.8$. Setting $D=C=1$ implies the same q^* in both monolayers. The patterns of ϕ , ψ , $\phi+\psi$, and $\phi-\psi$ at $t=5000$ are presented. The other parameters are chosen to be a) $\phi_0=0.2$, $\psi_0=-0.2$, $\Lambda=0.02$, and b) $\phi_0=0.5$, $\psi_0=0$, $\Lambda=0.2$.

tions ϕ_0 and ψ_0 . In Figure 4, we show typical equilibrium patterns of ϕ , ψ , $\phi+\psi$ and $\phi-\psi$ for two choices of parameters. The $\phi+\psi$ pattern is presented here because this quantity can be directly observed in the experiment on Montal–Mueller bilayers using fluorescence microscopy.^[12] The quantity $\phi-\psi$ measures the concentration contrast between the ϕ and ψ leaflets. Time is measured in discrete time steps, and $t=5000$ corresponds to a well-equilibrated system. In all the simulations below, the temperature is fixed to be $\tau=0.8$, corresponding to the weak segregation regime. Notice that all the patterns in Figure 4 are presented with the same gray scale.

Figure 4a illustrates the coupling between a hexagonal phase with $\phi_0=0.2$ and an inverted hexagonal phase with $\psi_0=-0.2$ in the weak coupling regime ($\Lambda=0.02$). Being consistent with the phase diagram of Figure 3a, this parameter choice yields the HH* phase as seen from the pattern of $\phi+\psi$, where the two hexagonal structures are superimposed. We note that the difference in the order parameter $\phi-\psi$ also exhibits a hexagonal structure.

Figure 4b shows the equilibrium patterns for $\phi_0=0.5$ and $\psi_0=0$ in the strong coupling regime ($\Lambda=0.2$). If there were no coupling, the ϕ -monolayer would not exhibit any modulation (as it is in its own disordered phase), whereas the ψ -monolayer is in the striped phase. We clearly see that, due to the coupling effect, the stripe structure is induced in the pat-

tern of ϕ . This corresponds to the SS phase shown in Figure 3b. The periodicities of the two striped structures are the same, although their amplitudes differ. Notice that the modulation phase of $\phi+\psi$ is shifted by π relatively to that of $\phi-\psi$. Since the patterns in Figure 4 would correspond to the equilibrium configurations, they can be compared with the phase diagrams in Figure 3. We conclude that these simulation results indeed reproduce the predicted equilibrium modulated structures.

4. Coupled Monolayers with Two Different q^*

We consider next the more general case in which the preferred wavelengths of modulation in the two uncoupled leaflets are different, $q_\phi^* \neq q_\psi^*$. The free-energy densities cannot be obtained analytically as was done in Section 3.1, because there is not a single periodicity on which one can average $\phi(\mathbf{r})$ and $\psi(\mathbf{r})$. Due to such a difficulty in the analytical treatment, we present below the results of numerical simulations, relying on Equation (25) for the time evolution of the two coupled-order parameters.

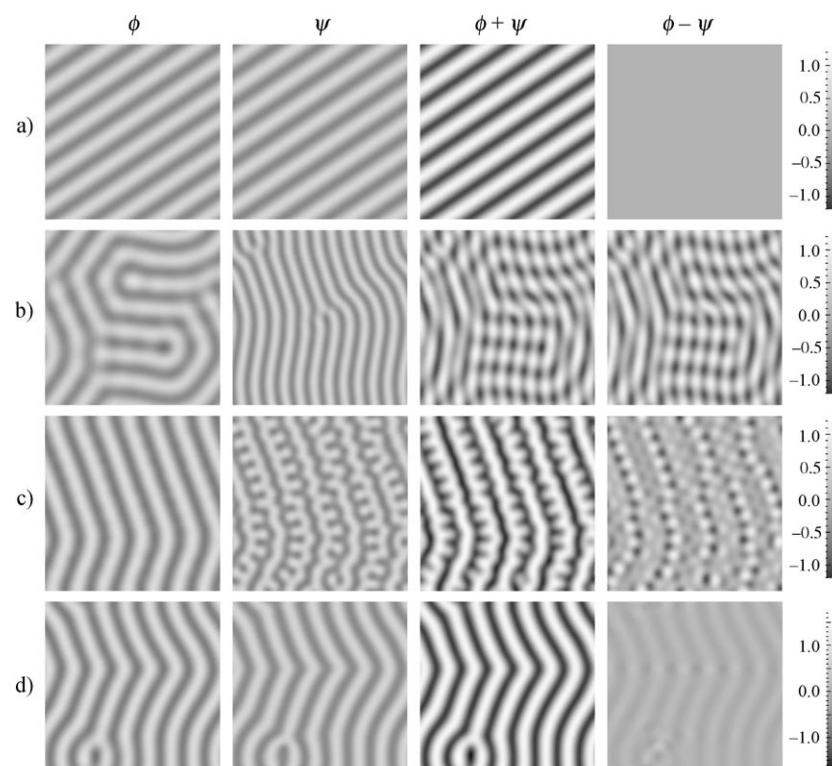


Figure 5. Patterns of coupled modulated monolayers with $\tau=0.8$. The patterns of ϕ , ψ , $\phi+\psi$, and $\phi-\psi$ are presented for simulation time, $t=5000$, and the average compositions are set to be $\phi_0=\psi_0=0$. The other parameters are chosen to be a) $D=C=1$, $\Lambda=0.02$, b) $D=0.1296$, $C=0.36$, $\Lambda=0.02$, c) $D=0.1296$, $C=0.36$, $\Lambda=0.2$, and d) $D=0.1296$, $C=0.36$, $\Lambda=0.4$. In all cases but (a), $D \neq C$ and the two periodicities are nonequal, $q_\phi^* \neq q_\psi^*$.

In Figure 5, we show the patterns for $\tau=0.8$ and $\phi_0 = \psi_0 = 0$, when both monolayers exhibit the striped phase without the coupling. As a reference, we show in Figure 5 a the case when $D=C=1$ and $\Lambda=0.02$ corresponding to the SS phase in Figure 3a. The patterns of ϕ and ψ match each other as the composition difference $\phi-\psi$ vanishes throughout the system. In Figure 5 b, the parameters are chosen to be $D=0.1296$, $C=0.36$ and $\Lambda=0.02$. The preferred wavenumbers of the two monolayers are different: $q_\psi^*=1.67q_\phi^*$ for uncoupled leaflets. The above set of parameters, especially D and C , is chosen in such a way that the amplitudes of the two stripes are nearly equal. As long as the coupling parameter is small, the two stripes of different periodicities are formed rather independently. The superposition of the two striped structures produces an interference pattern resulting in a new modulation as seen from the pattern of $\phi+\psi$. The striped modulations of ϕ and ψ are almost parallel or perpendicular to each other.

When Λ increases, up to $\Lambda=0.2$ as in Figure 5 c, the ψ -field exhibits a complex pattern in which two different length scales coexist (reflecting q_ϕ^* and q_ψ^*), whereas the pattern of ϕ is characterized by a single mode (reflecting q_ϕ^*). The patterns of ϕ and ψ almost match each other when $\Lambda=0.4$, as seen in Figure 5 d. In this case, the modulation with a longer wavelength (q_ϕ^*) dominates both monolayers. Figures 5 b-d provide a typical sequence of morphological changes, that is, interference pattern → two-mode pattern → single-mode pattern, as the coupling constant Λ is increased.

To further analyze the temporal correlations of the two order parameters, ϕ and ψ , we have plotted in Figure 6 the time evolution of the quantity shown in Equation (26):

$$\Delta(t) = \frac{1}{L^2} \int d\mathbf{r} [\phi(\mathbf{r}, t) - \psi(\mathbf{r}, t)]^2 \quad (26)$$

where $L=128$ is the linear system size in the simulations. (—), (----), (.....) and (---) correspond to the time evolutions of $\Delta(t)$ in Figures 5 a, b, c, and d respectively. The (—, a)

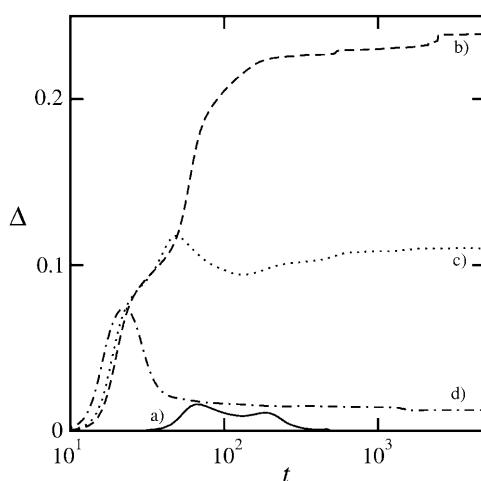


Figure 6. Time evolutions of Δ defined by Equation (26). (—), (----), (.....) and (---) correspond to the parameters of Figures 5a, b, c and d, respectively.

first increases and then approaches zero, as the patterns of the two stripes coincide in the late stage. In (b), (----) increases in two separate stages. At first it increases because the growth rate of the modulation with the smaller wavelength (corresponding to ψ) is faster than that with larger periodicity (corresponding to ϕ) as is also revealed from the linear stability analysis of Equation (25) which will be published elsewhere. Later, the value of Δ remains large for small coupling parameter ($\Lambda=0.02$). When the coupling becomes even stronger ($\Lambda=0.2$) as for (.....) in (c), the value of Δ is suppressed compared to (----, b), because ϕ and ψ tend to have more overlap for larger Λ . The same applies for (---, d) with $\Lambda=0.4$ as compared to (....., c).

5. Discussion and Conclusions

We propose a minimal model describing the coupling phenomena between two modulated bilayers. Considering 2D case, we obtain the mean-field phase diagram when the two coupled and spatially modulated monolayers have the same preferred periodicity. Various combinations of modulated phases can exist, such as the SS, HH, HH* and SH (HS) phases as described in Section 3. We have seen that modulations in one of the monolayers induce similar modulations in the other. The region of the induced modulated phase expands as the coupling parameter becomes larger.

When the two monolayers have different inherent wavelengths in the decoupled case, we have conducted numerical simulations to investigate the morphologies and dynamics of the coupled system. We obtain several complex patterns arising from the frustration induced by the two incommensurate structures. As the coupling constant Λ increases, the two different modes start to interfere with each other and eventually coincide. The time evolution of the striped structures can take place in two steps, reflecting the different growth rate of the two modulations.

It is instructive to rewrite the free-energy Equation (1) in terms of the sum and the difference of ϕ and ψ , that is, $\eta_{\pm} = \phi \pm \psi$. When $D=C=1$, we obtain Equation (27):

$$F[\eta_+, \eta_-] = \int d\mathbf{r} \left[(\nabla^2 \eta_+)^2 - (\nabla \eta_+)^2 + \frac{1}{4}(\tau - \Lambda)\eta_+^2 + \frac{1}{32}\eta_+^4 - \mu_+ \eta_+ + (\nabla^2 \eta_-)^2 - (\nabla \eta_-)^2 + \frac{1}{4}(\tau + \Lambda)\eta_-^2 + \frac{1}{32}\eta_-^4 - \mu_- \eta_- + \frac{3}{16}\eta_+^2 \eta_-^2 \right] \quad (27)$$

where $\mu_{\pm} = (\mu_\phi \pm \mu_\psi)/2$. Hence the coupling term between η_+ and η_- in the free energy takes the form of an $\eta_+^2 \eta_-^2$ term with a numerical positive coefficient. The original coupling parameter Λ enters in the coefficients of the η_+^2 and η_-^2 terms (but not in the $\eta_+^2 \eta_-^2$ coupling term). It shifts the respective transition temperatures of η_+ and η_- in opposite directions. When the gradient terms are absent and $\mu_- = 0$, a similar model was considered by MacKintosh and Safran, who studied transitions between lamellar and vesicle phases in two-component fluid bilayers.^[28]

The proposed free energy Equation (1) has some analogies to the previous model for the rippled phase in lipid bilayers.^[29] It was argued that the coupling between the membrane curvature and the asymmetry in the area per molecule between the two monolayers would induce a structural modulation of a bilayer. By considering a similar mechanism, Kumar et al.^[30] investigated various modulated phases in two-component bilayer membranes. They claimed that the phase behavior of two-component bilayers resembles that of three-component monolayer. This is because the three different local combinations of upper/lower composition in bilayers (A/B, B/A, and A/A for excess of A), would correspond to three different types of molecules for the monolayer. One of the new aspects in our model is that the preferred wavelengths of the two monolayers can, in general, be different from one another leading to a frustrated bilayer state.

We also point out that there are some similarities between coupled modulated structures and the problem of atoms adsorbed on a periodic solid substrate. The latter topic has been extensively studied within the Frenkel–Kontorova (FK) model which provides a simple description of the commensurate–incommensurate transition.^[31] Our model and the FK model are analogous in the sense that there are two natural length scales whose ratio changes as a function of other model parameters. In the FK model, however, these length scales are quenched, whereas in our model they are annealed.

Another related experimental system can be seen for surface-induced ordering in thin film of diblock copolymers.^[32] When the surface is periodically patterned, a tilt of the lamellae is induced in order to match the surface periodicity. The situation becomes more complex if a copolymer melt is confined between two surfaces. An interesting case arises when the spacing between the two surfaces is incommensurate with the lamellar periodicity.^[32]

For systems out of equilibrium, spatial resonances and superposition patterns combining stripes and/or hexagons were investigated in a reaction–diffusion model with interacting Turing modes of different wavelengths.^[33] These models were successful in reproducing hexagonal superlattice patterns which are known as “black-eyes”. Although the mechanism of pattern formation is different than in our model, we observe similar superposition patterns as reported in ref. [33], such as hexagons on stripes or hexagons on hexagons (not shown herein).

A more detailed study of the present model and several interesting extensions will be published elsewhere. One possible extension is to consider vector order parameters describing, for example, the molecular tilt for coupled bilayers.^[34,35] When the two order parameters are vectors, the nature of the transitions between different phases can be different, and even the square phase may exist in thermodynamic equilibrium.^[36]

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- [1] M. Seul, D. Andelman, *Science* **1995**, *267*, 476–483.
- [2] D. Andelman, R. E. Rosensweig, *J. Phys. Chem. B* **2009**, *113*, 3785–3798.
- [3] D. Andelman, R. E. Rosensweig, *Polymers, Liquids and Colloids in Electric Fields: Interfacial Instabilities, Orientation and Phase Transitions* (Eds.: Y. Tsori, U. Steiner), World Scientific, Singapore, **2009**.
- [4] C. L. Dennis, R. P. Borges, L. D. Buda, U. Ebels, J. F. Gregg, M. Hehn, E. Jouguelet, K. Ounadjela, I. Petej, I. L. Prejbeanu, M. J. Thornton, *J. Phys. Condens. Matter* **2002**, *14*, R1175–R1262.
- [5] T. Garel, S. Doniach, *Phys. Rev. B* **1982**, *26*, 325–329.
- [6] R. E. Rosensweig, *Ferrohydrodynamics*, Cambridge University, New York, **1985**.
- [7] D. Andelman, F. Brochard, J.-F. Joanny, *J. Chem. Phys.* **1987**, *86*, 3673–3681.
- [8] E. Sackmann, *Structure and Dynamics of Membranes: From Cells to Vesicles* (Eds.: R. Lipowsky, E. Sackmann), Elsevier, Amsterdam, **1995**.
- [9] I. W. Hamley, *The Physics of Block Copolymers*, Oxford University, Oxford, **1998**.
- [10] G. H. Fredrickson, *The Equilibrium Theory of Inhomogeneous Polymers*, Oxford University, Oxford, **2005**.
- [11] S. Leibler, D. Andelman, *J. Phys. (France)* **1987**, *48*, 2013–2018.
- [12] M. D. Collins, S. L. Keller, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 124–128.
- [13] M. Montal, P. Mueller, *Proc. Natl. Acad. Sci. USA* **1972**, *69*, 3561–3566.
- [14] A. J. Wagner, S. Loew, S. May, *Biophys. J.* **2007**, *93*, 4268–4277.
- [15] G. G. Putzel, M. Schick, *Biophys. J.* **2008**, *94*, 869–877.
- [16] T. Baumgart, S. T. Hess, W. W. Webb, *Nature* **2003**, *425*, 821–824.
- [17] S. Rozovsky, Y. Kaizuka, J. T. Groves, *J. Am. Chem. Soc.* **2005**, *127*, 36–37.
- [18] S. L. Keller, W. H. Pitcher, W. H. Huestis, H. M. McConnell, *Phys. Rev. Lett.* **1998**, *81*, 5019–5022.
- [19] S. L. Keller, H. M. McConnell, *Phys. Rev. Lett.* **1999**, *82*, 1602–1605.
- [20] L. Leibler, *Macromolecules* **1980**, *13*, 1602–1617.
- [21] G. Gompper, M. Schick, *Phys. Rev. Lett.* **1990**, *65*, 1116–1119.
- [22] R. R. Netz, D. Andelman, M. Schick, *Phys. Rev. Lett.* **1997**, *79*, 1058–1061.
- [23] S. Villain-Guillot, D. Andelman, *Eur. Phys. J. B* **1998**, *4*, 95–101.
- [24] S. Villain-Guillot, R. R. Netz, D. Andelman, M. Schick, *Physica A* **1998**, *249*, 285–292.
- [25] S. May, *Soft Matter* **2009**, *5*, 3148–3156.
- [26] K. Yamada, S. Komura, *J. Phys. Condens. Matter* **2008**, *20*, 155107.
- [27] P. C. Hohenberg, B. I. Halperin, *Rev. Mod. Phys.* **1977**, *49*, 435–479.
- [28] F. C. MacKintosh, S. A. Safran, *Phys. Rev. E* **1993**, *47*, 1180–1183.
- [29] H. Kodama, S. Komura, *J. Phys. II* **1993**, *3*, 1305–1311.
- [30] P. B. S. Kumar, G. Gompper, R. Lipowsky, *Phys. Rev. E* **1999**, *60*, 4610–4618.
- [31] P. M. Chaikin, T. C. Lubensky, *Principles of Condensed Matter Physics*, Cambridge University, Cambridge, **1995**.
- [32] Y. Tsori, D. Andelman, *J. Chem. Phys.* **2001**, *115*, 1970–1978.
- [33] L. Yang, M. Dolnik, A. M. Zhabotinsky, I. R. Epstein, *Phys. Rev. Lett.* **2002**, *88*, 208303.
- [34] C.-M. Chen, T. C. Lubensky, F. C. MacKintosh, *Phys. Rev. E* **1995**, *51*, 504–513.
- [35] U. Seifert, J. Shillcock, P. Nelson, *Phys. Rev. Lett.* **1996**, *77*, 5237–5240.
- [36] C. Tang, E. M. Lennon, G. H. Fredrickson, E. J. Kramer, C. J. Hawker, *Science* **2008**, *322*, 429–432.

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