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Short Communication

Frustration-induced ripple phase in bilayer membranes

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Abstract. — A model describing the phase transition from the L_α or L_β phase to the modulated P_β (“rippled”) phase in a bilayer membrane is considered within mean-field approximation. The coupling between the curvature and the asymmetry in the area per molecule can destabilize the flat phase by releasing its frustration energy. We obtain the pressure-temperature phase diagram which qualitatively accounts for part of the pressure experiment of DPPC in excess water. The existence of the modulated structure within our model is also confirmed by a cell dynamical simulation.

Properties of membranes with high flexibility are of current interest in connection with the statistical physics of fluctuating surfaces and biophysics of organic membranes [1]. Lipid bilayers constitute a rich set of physical and biological systems, exhibiting a wide variety of behavior under varying circumstances. One well-known fact about such systems is the presence of a first-order phase transition associated with the melting of the hydrocarbon chains, separating a high-temperature disordered fluid phase called the L_α and a low-temperature ordered gel phase called the L_β phase. Between these two flat phases, an intermediate structurally modulated (“rippled”) phase has been detected in a few phospholipids. This phase is termed the P_β phase and has stimulated considerable theoretical interest [2-5] as well as several related experimental investigations [6].

In this article, we shall present a simple but physically clear explanation of the ripple formation mechanism by considering the combined effect of a curvature instability [7-9] and a frustrated flat bilayer [10-13]. The former accounts for the possible destabilization of the membrane shape by introducing coupling between the curvature and the internal degrees of freedom, such as, the local composition. On the other hand, a flat bilayer composed of two identical amphiphilic monolayers with finite spontaneous curvature is always energetically frustrated and can be also destabilized. In the case that the bilayer is composed of a mixture of two surfactants, for instance, the allowed asymmetries in the local composition can lead to a

spontaneous vesicle formation [14].

As far as the P_β phase is concerned, both of these aspects are expected to play an important role. In the physical picture we consider, the local curvature and the asymmetry in the area per molecule are coupled. The area per unit molecule represents the order parameter describing the main transition. We obtain a pressure-temperature phase diagram within the mean-field theory. Our results qualitatively reproduce part of the phase diagram obtained in recent pressure study on water-rich compositions of DPPC [15]. In order to confirm the existence of the modulated structure in the expected region of the phase diagram, we have also performed a cell dynamical simulation of the present model [16].

We shall first discuss the main transition between the L_α and L_β phases, in which the discontinuous jump in the area per molecule S can be typically observed. According to the pressure-area phase diagram of monolayers of phospholipids determined by the film balance technique [17], typical values of the critical temperature, lateral pressure, and area per molecule are $T_c = 42 \sim 44$ °C, $\Pi_c = 47 \sim 50$ dyn/cm, and $S_c = 40 \sim 50$ Å², respectively. Although this critical point has been identified as a tricritical point forming a junction between a first order and a second order transition curve [17], we assume here, for simplicity, that the main transition can be represented within the framework of the van der Waals theory of ordinary gas-liquid phase transitions near the critical point. As a convenient set of independent variables, we use the temperature T and n , where $n = 1/S$ is the number of molecules per unit area. The dimensionless molecular density, $\phi = (n - n_c)/n_c$, is taken here as the order parameter. By using the notation $\pi = (\Pi - \Pi_c)/\Pi_c$ and $t = (T - T_c)/T_c$, the equation of state near the critical point can be written as

$$\pi = bt + at\phi + B\phi^3, \quad (1)$$

with dimensionless constants $b > 0$, $a > 0$ and $B > 0$ [18]. When $t < 0$ and $\pi = bt$, the L_α ($\phi = -(-at/B)^{1/2}$) and L_β ($\phi = (-at/B)^{1/2}$) phases coexist. Equation (1) can be obtained by minimizing the thermodynamic potential per molecule $\Phi = \epsilon \left\{ -(\pi - bt)\phi + \frac{1}{2}at\phi^2 + \frac{1}{4}B\phi^4 \right\}$ with respect to ϕ , where ϵ is some molecular energy of order $S_c\Pi_c$. The inhomogeneity in the monolayer can be conveniently taken into account by another potential which relates to some chosen and specified area A in the monolayer, consisting of a variable number of molecules. Upon keeping in mind that π is then a function of temperature and chemical potential, we consider the following Ginzburg-Landau type Hamiltonian in the unit of energy scale ϵ/S ;

$$H_{GL} = \int dA \left\{ -(\pi - bt)\phi + \frac{1}{2}at\phi^2 + \frac{1}{4}B\phi^4 + \frac{1}{2}g(\nabla\phi)^2 \right\}, \quad (2)$$

with $g > 0$.

Up to this point, we have described the properties of a monolayer membrane. We now turn our attention to bilayer. By introducing the suffices 1 and 2 associated with each monolayer, we assume that the main transition of the bilayer is simply represented by

$$H_1 = \int dA \sum_{i=1,2} \left\{ -(\pi - bt)\phi_i + \frac{1}{2}at\phi_i^2 + \frac{1}{4}B\phi_i^4 + \frac{1}{2}g(\nabla\phi_i)^2 \right\}. \quad (3)$$

In general, when considering a particular such bilayer, one must take into account its interaction with neighboring bilayers [3]. In this paper, however, we consider water-rich systems for which such interactions are negligible [4, 5].

The total curvature bending energy per unit area of the two monolayers comprising the bilayer is [11, 12]

$$H_b = \frac{1}{2}\kappa \sum_{i=1,2} \left(c^{(i)} - c_0^{(i)} \right)^2, \quad (4)$$

where κ is the bending rigidity, and $c^{(i)}$ and $c_0^{(i)}$ denote the mean curvature multiplied by 2 and the spontaneous curvature of the i -th monolayer, respectively. If two monolayers are set apart, the curvature energy (4) takes its minimum value 0 by adopting their curvatures to $c^{(i)} = c_0^{(i)}$ independently. In the case of bilayer, however, the curvatures of each monolayer have the same magnitude but opposite signs, $c^{(1)} = -c^{(2)} (\equiv c)$, due to the fact that they are stuck together [12, 13]. Suppose both monolayers are characterized by the same spontaneous curvature c_0 . Then the curvature energy (4) can be minimized at $c = 0$, but this flat bilayer still has an energy κc_0^2 . This frustration energy can be decreased if an asymmetry in the spontaneous curvature exists, and turns out to vanish when $c = c_0^{(1)} = -c_0^{(2)}$. The reason why mixed vesicles can be energetically stabilized follows from the above argument [11-13]. As was considered by MacKintosh and Safran [13], we assume here the following simple linear dependence of the spontaneous curvature on the order parameter: $c_0^{(i)} = \bar{c}_0 - \gamma\phi_i$, where γ is a constant, and \bar{c}_0 is the spontaneous curvature when $\phi_i = 0$.

The shape energy of the bilayer integrated over the total area A is then

$$H_2 = \int dA \left\{ 2\sigma + \frac{1}{2}\kappa \left[(c - c_0^{(1)})^2 + (c + c_0^{(2)})^2 \right] \right\}, \quad (5)$$

in the energy scale ϵ/S as before. In the above, a non-zero constant surface tension σ has been included by assuming that the Shulman condition is not satisfied for the area per molecule under consideration [19].

While allowing the bilayer to curve, we consider the case in which its shape is close to planer without any overhangs or discontinuities. If we use a single valued function $\ell(x, y)$ which measures the displacement of the bilayer from a flat reference xy -plane (Monge representation), the total Hamiltonian H is

$$\begin{aligned} H &= H_1 + H_2 \\ &= \int dx dy \left[\sigma (\nabla \ell)^2 + \kappa (\nabla^2 \ell)^2 + 2\kappa \gamma \phi_- (\nabla^2 \ell) \right. \\ &\quad \left. + g \left\{ (\nabla \phi_+)^2 + (\nabla \phi_-)^2 \right\} + f(\phi_+, \phi_-) \right], \end{aligned} \quad (6)$$

with

$$f(\phi_+, \phi_-) = -2(\pi - bt)\phi_+ + at(\phi_+^2 + \phi_-^2) + B \left(\frac{1}{2}\phi_+^4 + 3\phi_+^2\phi_-^2 + \frac{1}{2}\phi_-^4 \right), \quad (7)$$

where $\phi_{\pm} = (\phi_2 \pm \phi_1)/2$. Here we have eliminated the terms which merely shift the critical point. The degree of freedom $\{\ell\}$ can be traced out by performing a Gaussian integral $\int \mathcal{D}\{\ell\} \exp(-H/k_B T)$ [8]. If we expand up to the forth order in the wave number, the effective Hamiltonian becomes

$$H_{\text{eff}} = \int dx dy \left[\frac{1}{2}\Sigma (\nabla \phi_-)^2 + \frac{1}{2}K (\nabla^2 \phi_-)^2 + g (\nabla \phi_+)^2 + f(\phi_+, \phi_-) \right], \quad (8)$$

where $\Sigma = 2(g - \kappa^2\gamma^2/\sigma)$, and $K = 2(\kappa^3\gamma^2/\sigma^2)$. The necessary condition for the presence of the modulated phase is $\Sigma < 0$ [3].

Hereafter we shall use the reduced notations; $\pi' = (1/B)(2BK/\Sigma^2)^{3/2}\pi$, $\tau = (2K/\Sigma^2)at$, $m_{\pm} = (2BK/\Sigma^2)^{1/2}\phi_{\pm}$, $b' = (1/a)(2BK/\Sigma^2)^{1/2}b$, $g' = (-2/\Sigma)g$ and $\nabla' = (-K/\Sigma)^{1/2}\nabla$. The effective Hamiltonian (8) is minimized with respect to the reduced order parameters at $m_{\pm} = m_{\pm}^*$;

$$0 = (\pi' - b'\tau) + (g'\nabla'^2 - \tau - 3m_-^{*2})m_+^* - m_+^{*3}, \quad (9a)$$

$$0 = (-\nabla'^2 - \nabla'^4 - \tau - 3m_+^{*2}) m_-^* - m_-^{*3} \quad (9b)$$

The constant solution $m_-^* = 0$ is linearly stable when

$$|\pi' - b'\tau| > \left(\frac{1-4\tau}{12}\right)^{1/2} \left(\frac{1+8\tau}{12}\right). \quad (10)$$

In particular, if $\tau < -1/8$, the main transition between the L_α and L_β phases occurs by changing π' . At $\pi' = b'\tau$, the reduced mean order parameter m_+ takes the uniform values $m_+^* = \pm(-\tau)^{1/2}$, being of equal energy, and the L_α and L_β phases coexist.

Let us consider the parameter region where $m_-^* = 0$ is unstable, namely, when (10) is not satisfied. If we assume that $|m_+^*|$ is sufficiently small, or more precisely, $3|m_+^*|^2 \ll 1/4 - \tau$, (9b) now has a stable modulated solution for which orientational symmetry is broken. Close to the critical point of the homogeneous system $\tau = 0$, the above condition is well satisfied. To first order in $(1-4\tau)^{1/2}$, this solution is given by [20]

$$m_-^* \approx \frac{1}{2}(1-4\tau)^{1/2} \cos(x'/\sqrt{2}), \quad (11)$$

where x' is chosen along the axis parallel to the wave vector of the modulation. The modulation of m_-^* will induce a modulation of the local curvature corresponding to the rippled P_β phase. When g is sufficiently small, m_+^* is also periodic along x' with approximately half the wave length of m_-^* .

Accordingly, after taking the spacial average, we obtain the isotherm as a function of $\langle m_+^* \rangle$ for a given τ as

$$\pi' = \begin{cases} b'\tau + \tau \langle m_+^* \rangle + \langle m_+^* \rangle^3 & |\pi' - b'\tau| \geq \left(\frac{1-4\tau}{12}\right)^{1/2} \left(\frac{1+8\tau}{12}\right), \\ b'\tau + \frac{3-4\tau}{8} \langle m_+^* \rangle + \langle m_+^* \rangle^3 & \text{otherwise.} \end{cases} \quad (12)$$

Here we have defined $\langle m_+^* \rangle$ as the average of absolute maximum and absolute minimum values of m_+^* . Figure 1 shows the phase diagram in the $(\tau, \langle m_+^* \rangle)$ -plane obtained from (12). It is remarkable that the P_β phase appears as an intermediate phase in the temperature range $-1/8 < \tau < 1/4$. In figure 2, the same phase diagram is shown in the (π', τ) -plane with $b' = 1$. Three first order transition lines join together at the triple point $\pi' = \tau = -1/8$. Under the condition $3|m_+^*|^2 \ll 1/4 - \tau$, the isotherms (12) are discontinuous and cannot be precisely determined in the coexistence region. In the present phase diagrams, we have assumed that the coexistence of the P_β phase and the two flat phases occurs when the equality in (10) holds. Although we are confident that the transition should be continuous near the critical point ($\tau = 1/4$), and thus that there exists a tricritical point connecting the first and second order transition lines, it is difficult to determine the precise position of this point within the present approximation and it is hence omitted in figure 2.

In order to confirm the existence of the modulated structure as an equilibrium pattern, we performed a cell dynamical simulation [16]. We start from a random initial configuration and impose periodic boundary conditions. Figure 3 exhibits a typical fully developed profile of $m_-(x, y)$ for which the parameters are chosen from the P_β phase region in the phase diagram. If the parameters corresponding to either the L_α or L_β phase are used, m_+ simply reaches a finite uniform value, and no asymmetry appears ($m_- \approx 0$). Although we used the cell dynamical method only to obtain the stationary profiles of m_\pm , their time evolution might be also interesting to investigate. Detailed results of the simulation will be reported elsewhere.

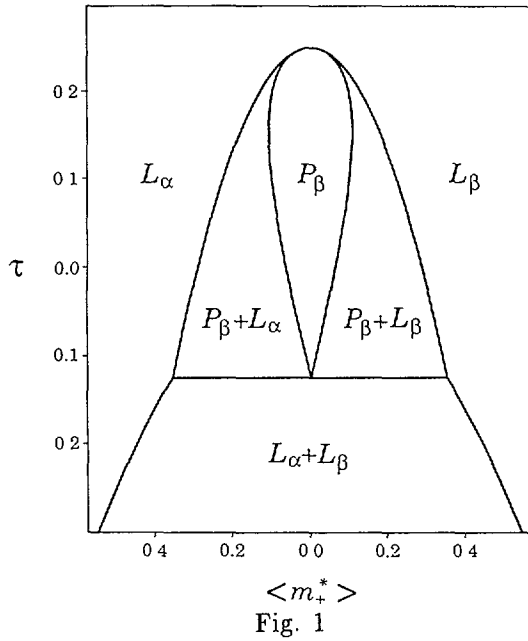


Fig. 1

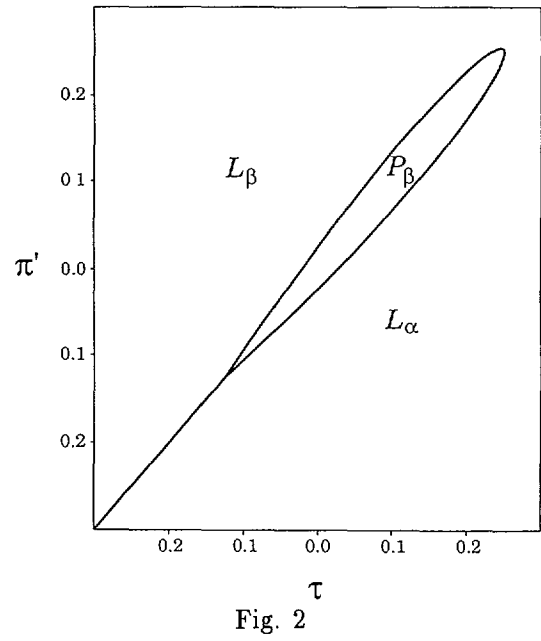


Fig. 2

Fig. 1. — Phase diagram in the $(\tau, \langle m_+^* \rangle)$ -plane where τ is the reduced temperature and $\langle m_+^* \rangle$ is the spatial average of the reduced mean molecular density. The P_β phase appears as an intermediate phase in the temperature range $-1/8 < \tau < 1/4$. The direct transition between the L_α and L_β phases is also seen for $\tau < -1/8$. Two-phase coexistence regions between the three single phases are indicated by $L_\alpha + P_\beta$ etc.

Fig. 2. — The same phase diagram as in figure 1, in the (π', τ) -plane where π' is the reduced lateral pressure. Here we have set $b' = 1$. Three first order transition lines join together at the triple point $\pi' = \tau = -1/8$.

As regards the relevance to the previously existing theories, the mechanical origin of the periodic structure in the model by Honda and Kimura [4, 5] differs from that in ours since we have assumed that the membrane has a small but non-vanishing surface tension. Meanwhile our work corresponds to a natural extension of those of Leibler and Andelman [8], and MacKintosh and Safran [13] to the bilayer and non-local cases, respectively. In fact, Leibler and Andelman argued the P_β phase in terms of one scalar order parameter coupled to the local curvature [8], whereas our theory includes two order parameters, namely, ϕ_+ controlled by the lateral pressure and ϕ_- coupled to the curvature. The resulting main difference turns out that the regular 2-dimensional modulated structure having the symmetry of a hexagonal phase [8] does not show up in the whole parameter space, and hence only P_β phase appears just between the two flat phases. This can be interpreted as follows. The total Hamiltonian should be invariant under the exchange of the two monolayers or, in other words, $\phi_- \rightarrow -\phi_-$. Therefore the linear term in ϕ_- is absent in (6), corresponding to the vanishing chemical potential case in reference [8] so that only the stripe phase is relevant as a modulated phase. Although these aspects of the bilayer have been also discussed in the references [11-13], they only considered the transition between the homogeneous lamellar and vesicle phases.

As a generalization of our model, we could also introduce an external field conjugate to ϕ_- , for example, a uniform bending force that breaks the bilayer symmetry. Then it would be interesting to consider a phase diagram in a higher dimensional parameter space, such as the

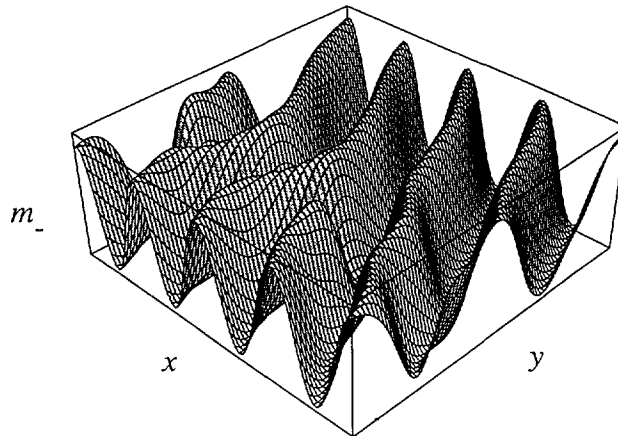


Fig. 3. — Typical fully developed ripple pattern of the reduced molecular density asymmetry $m_-(x, y)$ obtained by the cell dynamical simulation with periodic boundary conditions. The simulation has been started from a random initial configuration. The used parameters are chosen from the P_β phase region in the phase diagram.

temperature and two external fields coupled to ϕ_\pm . The phase diagram presented in figure 2 can be viewed as one particular cross section of such a generalized phase diagram. Another extension is to consider the coupling effect between the monolayers. This can be done by including additional terms in the Hamiltonian, such as $\phi_+\phi_-^2$, in accordance with the allowed symmetry. The addition of such terms may introduce an asymmetry, but is not expected to dramatically change the phase diagrams [13].

Figure 2 reproduces part of the phase diagram obtained in recent pressure study on water-rich compositions of DPPC by Krishna Prasad *et al.* [15]. From the experimental point of view, the lateral pressure in a bilayer system is not as easily controlled as that in a (Langmuir) monolayer system since bilayers are often formed in a solvent, while monolayers are formed at a liquid-air interface [17]. In reference [15], the hydrostatic pressure rather than the lateral pressure was changed. One possibility to control the lateral pressure in a bilayer may be found in the micropipet technique of Needham and Evans [21].

Finally, it should be mentioned that our model does not account for the orientational degree of freedom of lipid molecules with respect to the membrane surface in the rippled phase. This degree of freedom gives rise two possible phases. In addition to the P_β phase we have assumed throughout this paper in which the lipids are aligned orthogonally to the membrane, there may be a $P_{\beta'}$ phase in which the lipids are not so aligned. In fact, there are several experiments and models which suggest that the $P_{\beta'}$ phase does indeed exist [22-25]. From our point of view, however, the real molecular structure of the rippled phase is an open question [26, 27]. In this paper we have tried to suggest the minimal ripple formation mechanism in bilayers. Extending the model by considering a vector field order parameter, it should be possible to describe the tilting effect or defect structure.

In summary, we have discussed the phase transition from the L_α or L_β phase to the modulated P_β phase in a bilayer membrane within mean-field approximation. We obtained a pressure-temperature phase diagram which qualitatively reproduces part of the phase diagram obtained in recent pressure studies of bilayers. The cell dynamical simulation of our model

also demonstrates the existence of the modulated structure as an equilibrium pattern under certain conditions.

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References

- [1] Lipowsky R., *Nature* **349** (1991) 475.
- [2] Marder M., Frisch H.L., Langer J.S., McConnell H.M., *Proc. Natl. Acad. Sci.* **81** (1984) 6559.
- [3] Goldstein R.E., Leibler S., *Phys. Rev. Lett.* **61** (1988) 2213; *Phys. Rev. A* **40** (1989) 1025.
- [4] Honda K., Kimura H., *J. Phys. Soc. Jpn* **60** (1991) 1212.
- [5] Honda K., Kimura H., Kodama H., preprint.
- [6] Wack D.C., Webb W.W., *Phys. Rev. Lett.* **61** (1988) 1210; *Phys. Rev. A* **40** (1989) 2712, and references therein.
- [7] Leibler S., *J. Phys. France* **47** (1986) 507.
- [8] Leibler S., Andelman D., *J. Phys. France* **48** (1987) 2013.
- [9] Andelman D., Kawakatsu T., Kawasaki K., *Euro. Phys. Lett.* **19** (1992) 57.
- [10] Sadoc J.F., Charvolin J., *J. Phys. France* **47** (1986) 683.
- [11] Safran S.A., Pincus P.A., Andelman D., *Science* **248** (1990) 354.
- [12] Safran S.A., Pincus P.A., Andelman D., MacKintosh F.C., *Phys. Rev. A* **43** (1991) 1071.
- [13] MacKintosh F.C., Safran S.A., *Phys. Rev. E* **47** (1993) 1180.
- [14] Kaler E.W., Murthy A.K., Rodriguez J.A., Zasadzinsky N., *Science* **245** (1989) 1371.
- [15] Krishna Prasad S., Shashidhar R., Gaber B.P., Chandrasekhar S.C., *Chem. Phys. Lipids* **143** (1987) 227.
- [16] Oono Y., Puri S., *Phys. Rev. A* **38** (1988) 434.
- [17] Albrecht O., Gruler H., Sackmann E., *J. Phys. France* **39** (1978) 301.
- [18] Landau L.D., Lifshitz E.M., *Statistical Physics* (Pergamon Press, 1980).
- [19] de Gennes P.G., Taupin C., *J. Phys. Chem.* **86** (1982) 2294.
- [20] Manneville P., "Dissipative Structures and Weak Turbulence" (Academic Press Inc., 1990).
- [21] Needham D., Evans E., *Biochem.* **27** (1988) 8261.
- [22] Gebhardt C., Gruler H., Sackmann E., *Z. Naturforsch* **32c** (1977) 581.
- [23] Doniach S., *Chem. Phys.* **70** (1979) 4587.
- [24] Sackmann E., Ruppel D., Gebhardt C., Springer Series in Chemical Physics, W. Helfrich, G. Heppke Eds., Vol. 11 (1980) p. 309.
- [25] Belaya M.L., Feigel'man M.V., Levadny V.G., *J. Phys. II France* **1** (1991) 375.
- [26] Tsuchida K., Hatta I., *Biochim. Biophys. Acta* **945** (1988) 73.
- [27] Hentschel M.P., Rustichelli F., *Phys. Rev. Lett.* **66** (1991) 903.