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Application of finite-size scaling to the Pink model for lipid bilayers

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We present a Monte Carlo finite-size scaling analysis of the Pink model with the fitted parameters appropriate for dipalmitoyl phosphatidylcholine and disteroyl phosphatidylcholine lipid-bilayer systems. The numerical simulations were performed in conjunction with the extrapolation method of Ferrenberg and Swendsen [Phys. Rev. Lett. **61**, 2635 (1988)] and the finite-size scaling method of Lee and Kosterlitz [Phys. Rev. Lett. **65**, 137 (1990)]. In contrast to previous work, we found that there is no first-order phase transition and that the abrupt jump in the order parameter and the enhancement of the response functions found by previous numerical simulations are due to the presence of strong lateral density fluctuations which give rise to a large correlation length.

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I. INTRODUCTION

Fully hydrated lipid bilayers have been the subject of both experimental and theoretical studies due to their role as models for biological membranes [1]. Furthermore, a study of their phase behavior leads to an understanding of the fundamental interactions between membrane components. Here we concentrate on the main phase transition of pure lipid bilayers, in which the system passes from a gel (quasi-two-dimensional solid) phase to a liquid crystalline (quasi-two-dimensional fluid) phase. This transition has been characterized experimentally by the occurrence of a sharp peak in the specific heat and by abrupt changes in the order parameter which describes the acyl chain conformations in each phase. This transition is usually considered as a *sharp* first-order phase transition with a latent heat which depends on the chain length of the lipid molecules [1]. However, a recent interpretation of experimental thermodynamic data for the main phase transition by Biltonen [2] leads to the conclusion that this transition is not a phase transition. Theoretical work by Ipsen, Jørgensen, and Mouritsen [3] on the Pink model [4] predicts the occurrence of strong lateral density fluctuations in the neighborhood of the main phase transition and the concomitant scaling behavior suggests that the main phase transition could be weakly first order close to a critical point. In this paper we use numerical simulations in conjunction with powerful new finite size scaling methods to show that that there is *no* phase transition in the thermodynamic limit for the Pink model with the parameters used in [3].

Two-dimensional interacting lattice models are extremely useful tools for the study of critical behavior, particularly in conjunction with modern computer simulation techniques. One such model, the multistate Pink model, has proved extremely useful in the study of the main phase transition of pure lipid bilayers [4] and its extensions have been used to examine the phase behavior of lipid-protein mixtures, lipid-cholesterol mixtures, and lipid bilayers containing foreign molecules [5]. It was first analyzed in the mean-field approximation from which the parameters of the model were found for saturated lecithin bilayers by fitting to the available thermodynamic data [4]. This analysis led to the prediction of sharp first-order phase transitions for saturated lecithin bilayers with acyl chain lengths from 12 to 22 carbons per chain and the results were used to understand data from Raman spectra for dipalmitoyl phosphatidylcholine (DPPC), which is a saturated lecithin with 16 carbons per chain. Note that lecithins are lipid molecules with two acyl chains connected to each other and to a PC zwitterionic (dipolar) polar head via a glycerol backbone. Mouritsen *et al.* [6] performed numerical simulations for the Pink model with the fitted parameters found for DPPC using the Metropolis Monte Carlo method. They found abrupt but continuous changes in physical quantities such as the internal energy and the cross-sectional area per lipid chain at the transition. Sharp peaks at T_m were observed in the response functions (specific heat and lateral compressibility) of the system at a temperature T_m which was taken to be the transition temperature of the main phase transition. Furthermore, the response function data predicted the occurrence of strong lateral density fluctuations away from the transition region, which decreased in strength as a function of increasing chain length, resulting in a sharpening of the transition. Mouritsen [7] and later Ipsen, Jørgensen, and Mouritsen [3] showed that these fluctuations give rise to the appearance of fluctuating clusters of the minority phase in the majority phase in the region of T_m. The interfaces between the clusters and the bulk were considered as packing faults and this led to a novel interpretation for the behavior of the passive ionic permeability of pure lipid bilayers at T_m [8, 9].

The question therefore arises: what is the nature of the phase transition predicted by the Monte Carlo results for the Pink model with the fitted parameters appropriate for saturated lecithin bilayers? No detailed analysis of this question has as yet been made, even though it was thought that the system was close to a critical point. Such an analysis is undertaken in this paper. In an earlier paper, Ipsen, Jørgensen, and Mouritsen [3] suggested that the pseudocritical behavior of the system could well be indicative of a weak first-order phase transition close to a critical point. In this paper, we use recently developed numerical methods due to Ferrenberg and Swendsen [10] and Lee and Kosterlitz [11] to examine the nature of this transition. By using finite-size scaling analysis, we find that, contrary to what was previously thought, the transition observed for the Pink model with the fitted parameters in numerical simulations is not a phase transition. Furthermore, this conclusion applies to lecithin bilayers with chain lengths of up to 18 carbon atoms.

Section II gives a brief but reasonably detailed description of the Pink model. In particular the role of the intermediate conformational states is discussed in terms of interfacial activity at the cluster boundaries. The methods of Lee and Kosterlitz, and Ferrenberg and Swendsen are described in Sec. III together with the manner in which they can be applied to the Pink model. The finite-size scaling results for the Pink model are presented and discussed in Sec. IV. Section V concludes the paper and contains a discussion on the nature of the transition.

II. THE PINK MODEL

The Pink model [4, 12] is a multistate lattice model which is based on the assumption that the two monolayers forming the lipid bilayer do not interact and that the two acyl chains forming a lipid molecule can be treated independently. Each monolayer is modeled by a two-dimensional triangular lattice with a saturated lipid chain in one of several different conformational states at each of its sites. The parameters characterizing these states are obtained by examining the rotational isomerism of lipids chains in three dimensions. Therefore, even though the model is two dimensional, it contains information relating to three dimensions.

In the Pink model, the continuous rotational spectrum for each saturated carbon-carbon (C–C) bond is replaced by the three conformational states at the energy minima which correspond to one *trans* and two *gauche* bonds. There are ten different conformational states for the lipid chains in the Pink model, which were selected as follows on the basis of steric compatibility in the monolayer. The ground state of the chain is taken to be the conformation for which all the C–C bonds are *trans* bonds. The eight intermediate energy states are low-energy excitations of the all-*trans* configuration and are selected according to the following rules: the first two chain segments are kept fixed in a *trans* configuration, the chains have at most three *gauche* bonds, the length of the chains is at most three units shorter than that of the all-*trans* configuration, and the chains do not fold back upon themselves. All lipid chain conformations with the same energy and the same length are considered to be in the same conformational state. The tenth state is a high-energy state characteristic of the liquid crystalline or fluid phase and is a combination of many disordered states.

An important limitation of the Pink model is that the problem of chain packing in each monolayer of the bilayer has not been correctly addressed. Rather the chain conformations on neighboring sites are treated independently in a mean-field manner and are therefore uncorrelated from the point of view of chain packing. This problem has been addressed by several authors [13], who explicitly incorporate the statistics of the acyl chains in the analysis of phase transitions in Langmuir monolayers using a mean-field approach.

The original supposition [4] was that the low-energy intermediate states can be present in the gel phase and this allowed an interpretation of the Raman data for DPPC. However, Mouritsen [7] found that the intermediate states were also present in the interfaces between the clusters of different phases close to T_m. Cruzeiro-Hansen and Mouritsen [8] interpreted these states as packing defects at the cluster boundaries and based their theory of the ionic permeability close to T_m on this interpretation. The intermediate states have another important role in the phase behavior of the system. They stabilize the clusters by reducing the interfacial tension at their boundaries [5]. This can be considered as a "surfactant like" action which has a considerable influence on the nature of the transition at T_m.

Implementation of the Pink model requires a knowledge of the internal energy, the cross-sectional area, and the degeneracy associated with each conformational state. The internal energy of the all-*trans* state is taken as the reference energy and therefore this state has zero internal energy, its cross-sectional area is determined from experimental data [14] as $A_1 = 20.4$ Å^2, and it is nondegenerate. The internal energies of the intermediate states are determined by the number of *gauche* bonds, the energy required to form a *gauche* bond from a *trans* configuration being $E_g = 0.45 \times 10^{-13}$ erg. The cross-sectional areas are obtained from the assumption that the volume of the chain remains constant [15, 16]. The degeneracies are obtained by counting the number of possible configurations with the same energy and the same length. Table I gives a summary of the properties of the ground and intermediate conformational states. For the high-energy state, the cross-sectional area is assumed to be independent of chain length and is set to $A_{10} = 34$ Å^2. The degeneracy is assumed to be proportional to 3^m, where m is the number of carbon atoms forming the chain and is given by $D_{10} = 6 \times 3^{m-6}$. The energy is taken to be linear in chain length and is given by $E_{10} = (0.42m - 3.94) \times 10^{-13}$ erg.

Nearest-neighbor acyl chains are assumed to interact via anisotropic van der Waals interactions which are products of the isotropic interaction between two long parallel chains as calculated by Salem [17] and an orientational interaction between individual C–C bonds. The total anisotropic interaction between two neighboring chains in states α and β is

$$\mathcal{H}_{\text{int}} = -J_0 V_{\alpha\beta} S_\alpha S_\beta, \tag{1}$$

where J_0 is an interaction constant that depends on the

TABLE I. Energies, lengths and degeneracies of the ground and the intermediate states.

State 1	State 2	State 3
$E = 0$	$E = E_g$	$E = E_g$
$L = m - 1$	$L = m - 2$	$L = m - 3$
$D = 1$	$D = 4$	$D = 4$
State 4	State 5	State 6
$E = E_g$	$E = 2E_g$	$E = 2E_g$
$L = m - 4$	$L = m - 2$	$L = m - 3$
$D = 4$	$D = 2(m - 6)$	$D = 2(m - 8)$
State 7	State 8	State 9
$E = 2E_g$	$E = 3E_g$	$E = 3E_g$
$L = m - 4$	$L = m - 3$	$L = m - 4$
$D = 2(m - 10)$	$D = 8(m - 8)$	$D = 16(m - 10)$

number of C–C bonds. S_α and S_β are the nematic acyl chain order parameters for the two molecules and are given by

$$S_\alpha = \frac{8}{5}\frac{1}{(m-1)}\sum_{n=1}^{m-1}\frac{(3\cos^2\theta_{\alpha n}-1)}{2}, \tag{2}$$

where the summation is over all chain segments and $\theta_{\alpha n}$ is the angle between the nth chain segment and the bilayer normal. $V_{\alpha\beta}$ can be written in terms of the cross sectional areas as

$$V_{\alpha\beta} = V_\alpha V_\beta = \left(\frac{A_1}{A_\alpha}\right)^{5/4}\left(\frac{A_1}{A_\beta}\right)^{5/4}. \tag{3}$$

This form of the interaction is not valid for the tenth state because the chains are far from being parallel to each other. A weakening factor is therefore introduced such that $V_{10} = \omega(\frac{A_1}{A_{10}})^{5/4}$ [6].

A geometrical relationship between the nematic order parameter and the chain length was derived by Seelig and Seelig [18]. This relationship together with the assumption of constant volume allows us to write the interaction Hamiltonian in terms of the cross-sectional areas A_β ($\beta = 1, 2, \ldots, 10$).

Repulsive forces due to electrostatic interactions between the polar head groups and steric interactions from both the polar head groups and the lipid chains are taken into account in an approximate manner by the inclusion of an energy proportional to the total area in the Hamiltonian [4, 12, 16]. The constant of proportionality can be regarded as an effective lateral pressure Π.

The Hamiltonian for the Pink model is given by

$$\mathcal{H} = \sum_i\sum_\alpha E_\alpha\mathcal{L}_{\alpha,i} - \frac{J_0}{2}\sum_{<i,j>}\sum_{\alpha,\beta} I_\alpha I_\beta\mathcal{L}_{\alpha,i}\mathcal{L}_{\beta,j} + \Pi\sum_i\sum_\alpha A_\alpha\mathcal{L}_{\alpha,i}, \tag{4}$$

where the first term is the single chain contribution, the second term represents the van der Waals interaction between lipid chains, and the third term accounts approximately for steric interactions and interactions between polar heads. The indices i and j refer to lattice sites and the indices α and β refer to conformational states. $\mathcal{L}_{\alpha,i}$ is an occupation variable which is defined as

$$\mathcal{L}_{\alpha,i} = \begin{cases} 1 & \text{if the state of the lipid at site } i \text{ is } \alpha \\ 0 & \text{otherwise.} \end{cases} \tag{5}$$

I_α is defined as $I_\alpha = \omega_\alpha V_\alpha S_\alpha$. I_α can be written in terms of the areas as follows:

$$I_\alpha = \omega_\alpha\left(\frac{9}{5}\frac{A_1}{A_\alpha} - \frac{4}{5}\right)\left(\frac{A_1}{A_\alpha}\right)^{5/4}, \tag{6}$$

where $\omega_\alpha = 1$ for states 1 to 9 and $\omega_{10} = 0.4$.

III. COMPUTATIONAL METHODS

The model Hamiltonian of Eq. (4) can be rewritten as a sum of two terms: a term comprising both the internal energy of the chains and the interaction term and a term proportional to the effective lateral pressure Π:

$$\mathcal{H} = U + \Pi A, \tag{7}$$

where the first term is given by

$$U = \sum_i\sum_\alpha E_\alpha\mathcal{L}_{\alpha,i} - \frac{J_0}{2}\sum_{<i,j>}\sum_{\alpha,\beta} I_\alpha I_\beta\mathcal{L}_{\alpha,i}\mathcal{L}_{\beta,j}. \tag{8}$$

Here A is the total area of the system

$$A = \sum_i\sum_\alpha A_\alpha\mathcal{L}_{\alpha,i}. \tag{9}$$

The probability of finding the system at a point (U, A) in phase space at temperature T and effective lateral pressure Π is

$$P_{T,\Pi}(U,A) = \frac{N(U,A)\exp(-\frac{U+\Pi A}{k_BT})}{Z(T,\Pi)}, \tag{10}$$

where $N(U, A)$ is the total number of states at these values of U and A and $Z(T, \Pi)$ is the partition function, i.e.,

$$Z(T,\Pi) = \sum_{U,A} N(U,A)\exp\left(-\frac{U+\Pi A}{k_BT}\right). \tag{11}$$

Ferrenberg and Swendsen [10] show that the probability distribution at any temperature T' and lateral pressure Π' can be written exactly in terms of the probability distribution at T and Π as follows:

$$P_{T',\Pi'}(U,A) = \frac{P_{T,\Pi}(U,A)\exp[-(\frac{1}{k_BT'} - \frac{1}{k_BT})U - (\frac{\Pi'}{k_BT'} - \frac{\Pi}{k_BT})A]}{\sum_{U,A} P_{T,\Pi}(U,A)\exp[-(\frac{1}{k_BT'} - \frac{1}{k_BT})U - (\frac{\Pi'}{k_BT'} - \frac{\Pi}{k_BT})A]}. \tag{12}$$

This equation shows that it is sufficient to know the probability distribution at a temperature T and a lateral pressure Π in order to find the probability distribution at a neighboring temperature and pressure. This allows us to calculate averaged quantities such as the internal energy and area and their fluctuations at (T', Π') from a knowledge of the probability distribution at (T, Π).

This method is implemented numerically by calculating the two-dimensional histogram of U and A, which is proportional to the probability distribution given in Eq. (10). This method was used successfully for several models such as the Ising model [10], the Potts model [10, 11], the Φ^4 model [19], and more recently a lattice-gas model for ternary water-oil-surfactant systems [20].

The method has, however, several numerical limitations. Consider, for example, the equilibrium probability distribution given by a Gaussian centered at the equilibrium energy density ϵ_0 [21, 22],

$$P_T(\epsilon) = \left(\frac{L^d}{2\pi k_B T^2 C}\right)^{1/2} \exp\left(-\frac{(\epsilon-\epsilon_0)^2 L^d}{2k_B T^2 C}\right), \tag{13}$$

where ϵ is the energy density, L is the linear system size, d is the spatial dimension, and C is the specific heat. We know that, far away from phase transitions, the specific heat is finite and independent of the size of the system. Therefore the width of the probability distribution, which is proportional to C/L^d, narrows as L increases and becomes a δ function in the thermodynamic limit. This implies that the width of the energy spectrum decreases as L^{-d} and therefore the extrapolation becomes more difficult as L increases. Near a continuous phase transition $C \sim L^{\alpha/\nu}$, where α and ν are the usual critical exponents [25]. The width of the distribution then decreases as $L^{-d+\alpha/\nu}$, implying that the distribution will sharpen, but at a slower rate. It is worth noting that in most two-dimensional systems α is small ($\alpha \approx 0$) [25], implying that extrapolation to other parameters will still be difficult. This clearly shows that the best extrapolations are those with a starting point at which the system exhibits strong fluctuations, particularly for small systems where the distribution is sufficiently wide.

In second-order phase transitions, the divergences in the specific heat and the compressibility are linked to the divergence in the correlation length. First-order transition are, on the other hand, characterized by discontinuities in the first derivatives of the free energy such as the energy and the area. This leads to singularities in the specific heat and the compressibility. The divergences and singularities are only observed in the thermodynamic limit. For example, in finite systems, the phase transitions are smeared out, leading to ambiguities in distinguishing first order from second order in numerical simulations. Even the occurrence of hysteresis is not always an indication that the transition is first order. Indeed, critical slowing down might lead to hysteresis. Therefore, in order to distinguish first-order transitions unambiguously from second-order ones, it is necessary to perform a finite-size scaling analysis. In a second-order transition, the smearing out of the transition is due to the fact that the correlation length ξ is now limited by the system size L. Finite-size scaling theory shows that the specific heat and the compressibility diverge as $L^{\alpha/\nu}$ and $L^{\gamma/\nu}$, respectively, at T_c. At a first-order phase transition, starting from the assumption that the probability distribution is a double Gaussian, it can be shown that both the specific heat and the compressibility scale as L^d, which is usually observed when the system size L is much larger than the correlation length. However, the correlation length might sometimes be very large at first-order transitions. In this case it becomes somewhat ambiguous to determine the type of the transition from simulations on finite systems.

Lee and Kosterlitz [11] recently proposed a numerical finite-size scaling method which is able to discard a first-order transition even for small system sizes. This method consists of calculating the free energy as a function of energy or average area per lipid chain at the presumed transition point and then investigating how it scales with system size. To illustrate the method, let us suppose that our system is at a first-order transition. The lowest free energy then corresponds to the case when the system is in one of the two coexisting phases. The probability of occurrence of either of these phases is given by

$$P^{\max}_{T,\Pi} \propto \exp\left(-\frac{L^d f_B(T,\Pi)}{k_B T}\right), \tag{14}$$

where f_B is the free energy per unit volume. The phases can also coexist when separated by an interface. This state has a lower probability due to the cost of the interfacial free energy. The corresponding probability can be written as

$$P^{\min}_{T,\Pi} \propto \exp\left(-\frac{L^d f_B(T,\Pi) + L^{d-1} f_S(T,\Pi) + O(L^{d-2})}{k_B T}\right), \tag{15}$$

where f_S is the interfacial free energy density and is a positive quantity. Therefore the free energy difference between the state where the system consists only of one phase and the state consisting of the two coexisting phases is given by

$$\Delta\mathcal{F} = -k_B T \ln\left(\frac{P^{\max}}{P^{\min}}\right). \tag{16}$$

This gives the total interfacial free-energy $L^{d-1} f_S + O(L^{d-2})$, which increases with system size.

When there is no transition, it is quite possible that the free energy has a double minimum for system sizes smaller than the correlation length. However, as the system size is increased, the energy barrier decreases and the double well changes to a single well when the system size L is comparable to the correlation length. It is therefore concluded that for a first-order phase transition, the energy barrier of the double well increases with the system size, for a second-order phase transition it remains constant and if there is no phase transition, the energy barrier decreases with increasing the system size [11].

IV. RESULTS AND DISCUSSION

In this section we use the finite-size scaling analysis of Sec. III to examine the nature of the main phase transition as predicted by the Pink model for both DPPC and disteroyl phosphatidylcholine (DSPC, 18 carbons per chain) bilayers. The interaction constant J_0 depends on the chain length and is fitted for both systems in order to reproduce the experimental transition temperatures [23]. Table II gives the experimental transition temperatures [24] and the values of the interaction constant for the two systems studied. The value used for Π is 30 dyn/cm [4].

To this purpose, spin–flip Metropolis Monte Carlo simulations were performed on $L \times L$ triangular lattices for linear sizes from $L = 4$ to 50. In order to obtain good statistics, simulations were run for at least 320 000 Monte Carlo steps on each system size. The application of the Monte Carlo method to the Pink model has been described elsewhere [26]. Monte Carlo simulations were performed close to the experimental transition temperature and the method of Ferrenberg and Swendsen [10] was used to extrapolate to neighboring temperatures. We checked that the extrapolations were in good agreement with the direct Monte Carlo simulations of Corvera [27] by comparing quantities such as the internal energy, the specific heat, the area per lipid molecule, and the lateral compressibility calculated using standard Monte Carlo methods at different temperatures.

In order to apply the Lee-Kosterlitz method [11] we calculated the free energy as a function of area per lipid molecule. Figure 1 shows the free energy for DPPC bilayers as a function of area for three of the system sizes studied. For $L = 6$, the free energy exhibits two well-defined wells at areas A_1 and A_2, corresponding to the gel and fluid phases. However, when L increases, the free-energy barrier which separates these two states becomes smaller as shown for $L = 10$, implying that configurations in the region between A_1 and A_2 become more accessible as the system size increases. In other words, there is a lower cost in interfacial free energy for the coexistence of the two phases for larger systems. The barrier almost disappears for $L = 16$ and the double-well structure is no longer observed for $L = 24$. Only a single well is observed for larger system sizes. This leads to the conclusion that there is no first-order phase transition for the Pink model with the fitted parameters corresponding to DPPC bilayers.

We also conclude that the correlation length ξ is quite large, since the double-well structure disapears for a system of $L = 24$. Further, we calculated the specific heat corresponding to DPPC bilayers as a function of temperature for various system sizes. Figure 2 shows the

TABLE II. Experimental transition temperatures and interaction constants.

	T_m (K)	J_0 (10^{-13} erg)
DPPC	314.0	0.7099
DSPC	327.9	0.815

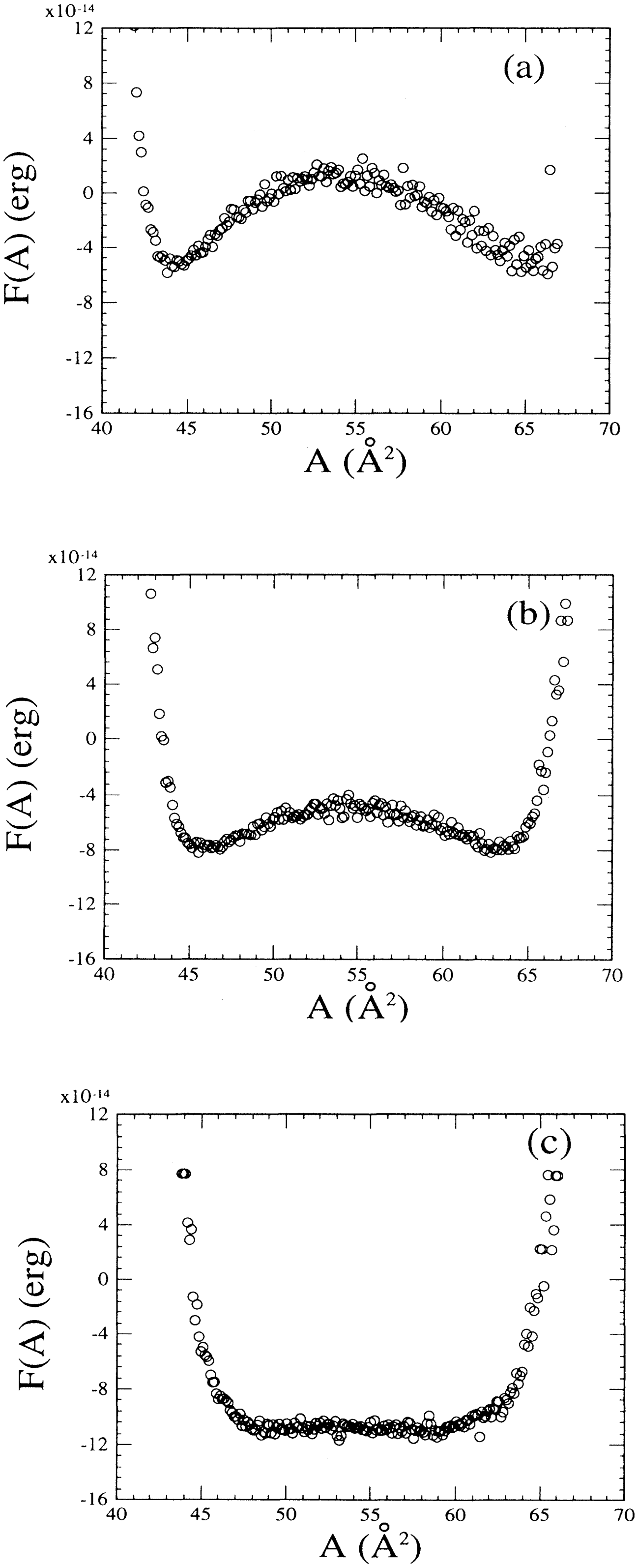

FIG. 1. Free energy $F(A)$ as a function of average area per molecule A corresponding to DPPC bilayers with a lateral pressure of $\Pi = 30$ dyn/cm for (a) $L = 6$, $T = 314.6$ K, (b) $L = 10$, $T = 314.2$ K, and (c) $L = 16$, $T = 314.1$ K.

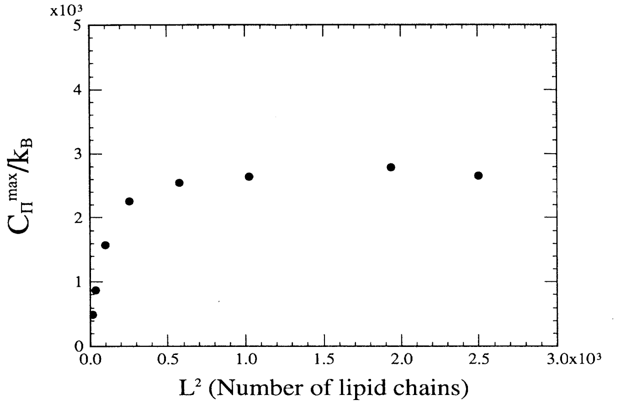

FIG. 2. Maximum of the specific heat as a function of the system size corresponding to DPPC bilayers with a lateral pressure of $\Pi = 30$ dyn/cm.

maximum of the specific heat as a function of the system size. The maximum of the peak increases with increasing system size for small L but begins to saturate at about $L = 24$. This behavior is consistent with the above findings that there is no phase transition at these system parameters. Therefore the presence of strong peaks in the response functions does not necessarily indicate the existence of any phase transition. Such peaks can be due to a large correlation length, as is the case when the system is close to a critical point. Indeed, similar behavior is observed in the Ising model for T slightly larger than T_c, where the specific heat and the susceptibility as a function of magnetic field exhibit a peak around zero field. It is important to note that a large correlation length does not necessarily imply that the system is close to a critical point.

The Monte Carlo calculations of Ipsen, Jørgensen, and Mouritsen [3] show that the changes in internal energy, area per lipid molecule, and order parameter are more abrupt for DSPC bilayers at T_m than for DPPC bilayers. However, we find that there is again no first-order phase transition for the case of DSPC. As in the case of DPPC bilayers, the free-energy barrier which is large for small system sizes again decreases as L increases as is shown in Fig. 3 and then disappears at approximately $L = 50$. We therefore conclude that there is no phase transition for the Pink model with the fitted parameters corresponding to DSPC bilayers. Furthermore, since the energy barrier disappears at $L = 50$, the correlation length for DSPC is larger than for DPPC. Monte Carlo simulations were again performed at slightly lower pressures and the same behavior was observed.

The role of the intermediate states in preventing the occurrence of a first-order phase transition predicted by mean-field theory for DPPC and DSPC can be thought of as follows. From a kinetic point of view, first-order phase transitions can be described in terms of the nucleation and growth of a droplet of the stable phase in the unstable phase. In our case, this process is impeded by the intermediate conformational states which stabi-

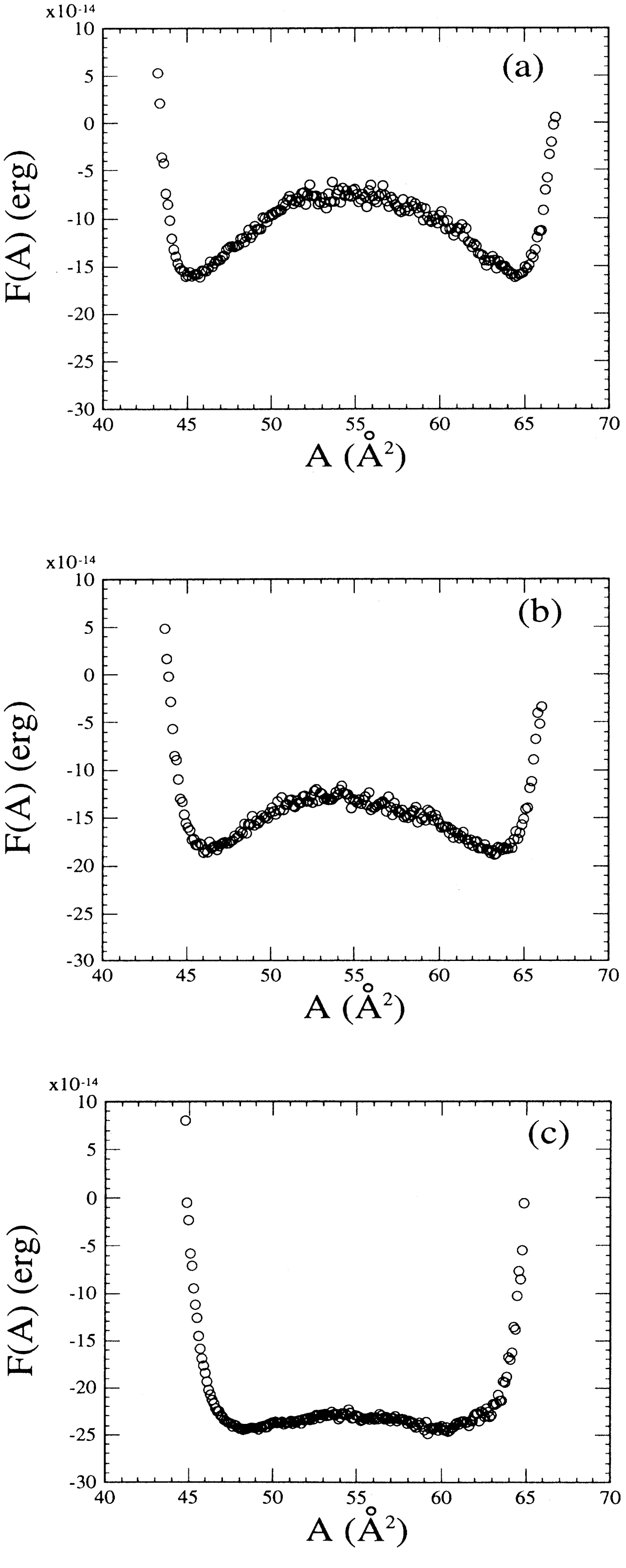

FIG. 3. Free energy $F(A)$ as a function of average area per molecule A corresponding to DSPC bilayers with a lateral pressure of $\Pi = 30$ dyn/cm for (a) $L = 16$, $T = 328.04$, (b) $L = 24$, $T = 327.96$, and (c) $L = 44$, $T = 327.95$.

lize the droplets by forming interfaces which are likely to exhibit low interfacial tension. This effect would destroy the phase transition in a manner analogous to the case of ternary mixtures of two immiscible fluids containing surfactants [20]. In our case, the intermediate states play the role of the surfactants, except that they are thermal excitations rather than molecules.

The results discussed so far should not be regarded as implying that the Pink model never exhibits a phase transition. Indeed simulations of DSPC bilayers for considerably lower lateral pressures show that when $\Pi \approx 20$, the double-well structure becomes unchanged with increasing L to within numerical error. For a lateral pressure of $\Pi = 15$ we found that the free-energy barrier does indeed increase with system size as is shown in Fig. 4. This implies that $\Pi \approx 20$ is close to the critical pressure and that there is definitely a first-order phase transition for $\Pi = 15$.

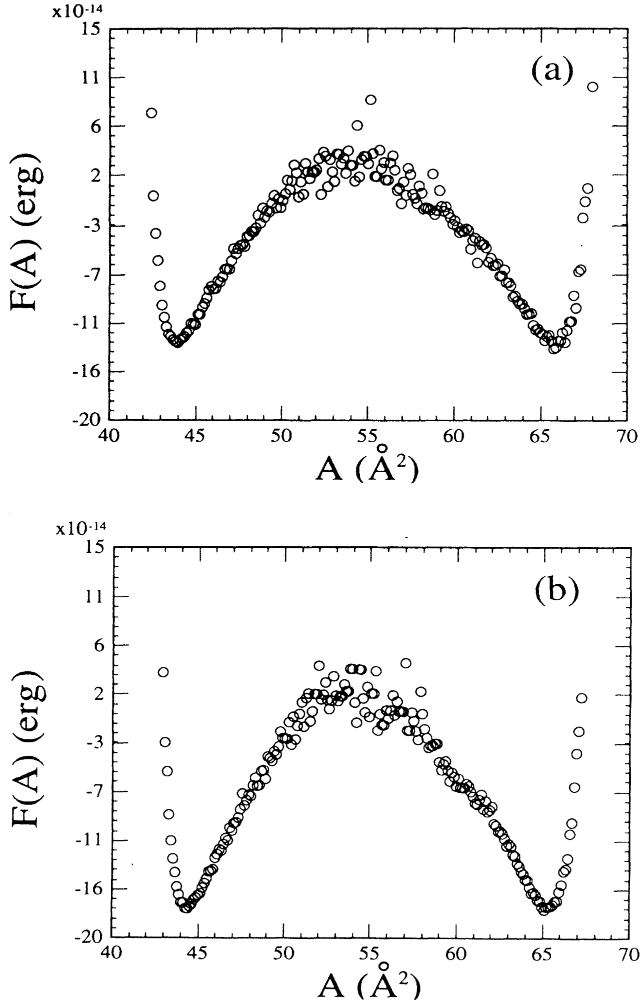

FIG. 4. Free energy $F(A)$ as a function of average area per molecule A corresponding to DSPC bilayers with a lateral pressure of $\Pi = 15$ dyn/cm for (a) $L = 10$, $T = 316.75$, and (b) $L = 44$, $T = 316.59$.

V. CONCLUSIONS

We have undertaken a finite-size scaling study of the Pink model with fitted parameters corresponding to both DPPC and DSPC bilayers using the extrapolation technique of Ferrenberg and Swendsen and the finite-size scaling method of Lee and Kosterlitz for calculating the free energy. We found that, in contrast to previous conclusions, there is no phase transition at T_m in the thermodynamic limit for the fitted parameters corresponding to DPPC and DSPC bilayers, even though a first-order phase transition is predicted by mean-field theory. However, it is important to realize that the calculations reported in this paper were performed for a single monolayer since it is assumed in the Pink model that the two monolayers of a bilayer are independent of each other. Furthermore, DPPC or DSPC monolayers spread on air-water interfaces do not exhibit phase transitions at lateral pressures of $\Pi = 30$ dyn/cm and temperatures equal to the values of T_m used here [29]. There are therefore two possible scenarios based on our results. The first is that our calculations are valid for bilayers as well as monolayers. The second is that, since it is difficult to distinguish between a weakly first-order transition and an apparent transition dominated by strong density fluctuations, it is reasonable to examine the critical region in more detail.

We took the second scenario. One way of accessing the critical region is to lower the effective lateral pressure Π. In fact we showed in Sec. IV that the Pink model can be made to exhibit a first order phase transition for DPPC by lowering Π considerably. However, the value of Π required to obtain a first-order transition is too small compared to the value used to fit experimental data. Another way is to extend the Pink model of Sec. II to include interactions which only exist in bilayers. To this purpose, Zhang *et al.* [30,31] extended the work of this paper by showing that either a mismatch interaction between lipids in different conformational states due to their unequal interfacial lengths of hydrophobic contact [28,30] or a weak attractive van der Waals interaction between the tails of the acyl chains belonging to lipid molecules in different bilayers [31] can bring the system across a critical point to a first-order phase transition region. Only quite small values of the interaction constants were required to achieve this and it causes a considerable reduction in the lateral density fluctuations. Further extensions of this work are discussed in [31].

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