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Interactions between two sheets of a bilayer membrane and its internal lateral pressure*

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Abstract. We have modelled a phospholipid bilayer as two monolayer sheets which interact with each other by a coupling which depends upon the states of the lipid hydrocarbon chains in each sheet. We make use of a model (Georgallas and Pink 1982a) and its parameters, already used to study monolayer phase changes at the LC-LE transition, in order to study the lipid main transition. Although the monolayer coexistence curve can be calculated exactly, we have made use of high-temperature series expansions to calculate the critical point of the bilayer. We also present the results of computer simulations on triangular lattices for the pressure-area isotherms. We find: (*i*) the interaction between the sheets of a DPPC bilayer is about 1.5–2% of the maximum interaction within the plane of each sheet; (*ii*) the internal lateral pressure of a DPPC bilayer is about 30.5 dyne/cm; (*iii*) the bilayer transition enthalpy depends sensitively upon the coupling between the sheets. Should this coupling vary from sample to sample (due, possibly, to its preparation) then very different values of transition enthalpy may be measured. (*iv*) We present a rough rule-of-thumb for estimating the internal lateral pressure of a bilayer from a knowledge of the corresponding monolayer pressure-area isotherms.

Key words: Bilayers, monolayers, theoretical models, thermodynamics, internal pressure

Introduction

It is generally held that the liquid expanded to liquid condensed (LE/LC) transition of a phospholipid monolayer at the air-water interface (Gaines 1966; Cadenhead et al. 1980) has its analogue in the "main" melting transition of the corresponding phospholipid bilayer in excess water and that this transition proceeds predominantly through a "melting" of the hydrocarbon chains (e.g., Chapman 1980).

A number of theoretical models have been developed to study these transitions (e.g., Baret 1981; Bell et al. 1981; Pink 1984a; Marčelja 1974). These models have several features in common. They all specify a set of lipid hydrocarbon chain states which they consider to describe adequately the chain conformations of importance. They either specify as a parameter a lateral pressure acting in the plane of the monolayer or bilayer (Marčelja 1974; Georgallas and Pink 1982a, b), or else they specify a surface density as a parameter (Dill and Flory 1980). In the case of a monolayer this lateral pressure is an externally-controlled variable. These models also specify interactions between hydrocarbon chains, either as attractive van der Waals forces or hard core steric repulsions.

All models of lipid bilayers assume that the interaction between the two sheets of the bilayer is sufficiently weak that it can be ignored. It is the intention here to show that even if this interaction is only a few percent of the maximum interaction within a sheet, it is nevertheless not negligible when calculating certain properties of bilayers. Here we show that in order to deduce the properties of bilayers from monolayer studies a knowledge of this interaction is essential.

The related question of what is the internal lateral pressure, Π, of a bilayer has been considered in a number of studies. Estimates for its value have been (in dyne/cm*) 12.5 (Albrecht et al.1978), 14.7 (Meraldi and Schlitter 1981), 20 (Marčelja 1974), 30 (Blume 1979; Pink and Chapman 1979), and 50

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Abbreviations: LC-LE liquid condensed – liquid expanded; DPPC dipalmitoylphosphatidylcholine; ΔQ transition enthalpy

* Lateral pressures are expressed throughout in dyne/cm = 0.001 $N \cdot m^{-1}$

(Nagle 1976). Fulford and Peel (1980) analysed the motion of the fluorescent probe 1,6-diphenyl-1,3,5-hexatriene in dipalimitoylphosphatidylcholine (DPPC) bilayers and deduced that this pressure ranged from ~ 92 dyne/cm at 5° C to ~ 20 dyne/cm at 51° C.

Monolayer studies at an air-water interface have been used to deduce the internal lateral pressure of the corresponding bilayer. This approach, however, is not without its difficulties. In the case of DPPC, for example, the bilayer has a main transition at ~ 41° C with a transition enthalpy, ΔQ, of ~ 8.7 kcal/mole (Chapman 1975). If one asks what is the transition enthalpy of a DPPC monolayer at 41° C and at what lateral pressure does it occur, then one finds $\Pi \approx 30$ dyne/cm but $\Delta Q \approx 0$. On the other hand if one asks at what temperature and pressure does one find a DPPC monolayer transition with $\Delta Q \approx 8.7$ kcal/mol, then one finds $\Pi \approx 20$ dyne/cm but $T \approx 30°$ C.

In addressing this difficulty, Albrecht et al. (1978) suggested that an interaction between the two halves of a bilayer could be regarded as an effective lateral pressure acting in each sheet of the bilayer. Each sheet could then be regarded as an independent monolayer. In this way it is seen that the question of an interaction between the two sheets of a bilayer is closely related to the question of the internal lateral pressure of a bilayer and its counterpart in the corresponding monolayer.

In this paper we review a model of a monolayer for which a number of exact results have already been obtained (Georgallas and Pink 1982a). The advantage of a model for which exact results are known is that any defects of the model are known in advance and thus cannot be ascribed to an approximation scheme which may be used to calculate properties of the model. We shall extend the model to describe a bilayer by explicitly including in the Hamiltonian terms due to the interaction between lipid chains in opposite halves of the bilayer. We show that this model is isomorphic to a spin-½ Ising model on a honeycomb lattice which has nearest and next-nearest neighbour interactions, and an external magnetic field. An unusual feature of the isomorphism is that the interactions between next-nearest neighbours are stronger than those between nearest neighbours. The model is solved for the second order critical point using standard series expansion techniques. Computer simulation methods are then used to calculate isotherms for the bilayer. From these Monte Carlo simulations, the lateral pressure is deduced, at which the bilayer displays a first-order phase transition at the desired temperature with the correct value of the enthalpy. We show that a very weak interaction between the sheets of a bilayer (of the order of 2% of the maximum interaction within a sheet) can successfully account for the higher transition temperature of a bilayer compared to that of a monolayer possessing the same transition enthalpy. We thus find, in effect, that the correct criterion for determining the internal lateral pressure of a bilayer from monolayer studies is to identify the pressure at which the monolayer has a transition at the main transition temperature of the corresponding bilayer. For the case of DPPC bilayers in excess water we find that the internal lateral pressure is 30.5 dyne/cm.

Theory

We shall make use of a model previously used in a study of monolayers (Georgallas and Pink 1982a, b). Each site of a triangular lattice is occupied by a hydrocarbon chain which can be in one of 10 conformational states, with state n characterized by an internal enery, E_n, a cross-sectional area, A_n, and a degeneracy, D_n ($n = g, 2, \ldots, 9, e$). Van der Waals forces between nearest neighbour chains are represented by interaction energies, $-J_0\, J(n,m)$ where n and m denote the states of the chains. The states g,2,. . . .9 describe chains containing 0 (g), 1 (2, 3, 4), 2 (5, 6, 7) or 3 (8, 9) gauche bonds, while e is a high energy, highly-degenerate "melted" chain state. Transitions between the low-energy states and e have a characteristic time of ~ 10^{-6}–10^{-7} s, while those between low-energy states have a characteristic time of ~ 10^{-10}–10^{-11} s. Because we are interested in the main melting transition, viz. the 10^{-6}–10^{-7} s transitions, then we can perform an average over the nine low-lying states to obtain a single effective ground state, G, with a temperature-dependent energy, $\mathcal{E}_G$, area, $\mathcal{A}_G$ and degeneracy, $\mathcal{D}_G$ (Pink et al. 1980). The interactions between two different chains now become $-J_0\mathcal{J}(G,G)$, $-J_0\mathcal{J}(G,e)$ and $-J_0 J(e,e)$. In practice, the averaging performed is a mean field approximation (Pink 1984a).

The Hamiltonian function for a monolayer is then

$$\mathcal{H}_M = -\frac{J_0}{2}\sum_{\langle ij\rangle}\sum_{nm}\mathcal{J}(n,m)\mathcal{L}_{in}\mathcal{L}_{jm} + \sum_{i}\sum_{n}(\Pi_{\mathrm{ext}}\mathcal{A}_n + \mathcal{E}_n)\mathcal{L}_{in} \qquad (1)$$

where $\mathcal{A}_e = A_e$, $\mathcal{E}_e = E_e$, $\mathcal{D}_e = D_e$ and $\mathcal{J}(e,e) = J(e,e)$. Here $\mathcal{L}_{in}$ is a projection operator for chain state n at site i and $<ij>$ indicates that the sum is taken over nearest neighbours only. Π_{ext} is the externally-applied lateral pressure and is an independent variable.

In order to model a bilayer we make the following two assumptions:

(*i*) The Hamiltonian for each sheet of the bilayer is given by (1) with Π_{ext} replaced by Π_{int}, the effective lateral pressure set up in the hydrocarbon chain region due to the polar region interactions which bring about the formation of the bilayer.
(*ii*) Each hydrocarbon chain interacts with its nearest neighbours in the other sheet with an energy $-J_0K(n,m)$ where n and m are the states of the nearest neighbour chains in the two sheets.

If we denote sites and states in the two sheets by primed and unprimed labels, with (ij') denoting nearest neighbour sites in different sheets and $\langle ij\rangle$ and $\langle i'j'\rangle$ denoting nearest neighbour sites in the same sheet, the numbers being q and $z = 6$ respectively, then the bilayer Hamiltonian is

$$\begin{aligned}\mathcal{H}_B = &-\frac{J_0}{2}\sum_{\langle ij\rangle}\sum_{nm}\mathcal{J}(n,m)\mathcal{L}_{in}\mathcal{L}_{jm}\\ &+\sum_{i}\sum_{n}(\Pi_{\text{int}}\mathcal{A}_n+\mathcal{E}_n)\mathcal{L}_{in}\\ &-\frac{J_0}{2}\sum_{\langle i'j'\rangle}\sum_{n'm'}\mathcal{J}(n',m')\mathcal{L}_{i'n'}\mathcal{L}_{j'm'}\\ &+\sum_{i'}\sum_{n'}(\Pi_{\text{int}}\mathcal{A}_{n'}+\mathcal{E}_{n'})\mathcal{L}_{i'n'}\\ &-J_0\sum_{(ij')}\sum_{nm'}\mathcal{K}(n,m')\mathcal{L}_{in}\mathcal{L}_{j'm'}\\ &n,m,n',m' = G,e \qquad (2)\end{aligned}$$

Because of the averaging to give an effective ground state, G, we now have only three interactions between the two sheets, $\mathcal{K}(G,G)$, $\mathcal{K}(G,e) = \mathcal{K}(e,G)$ and $\mathcal{K}(e,e) = K(e,e)$.

In the fluid phase the ends of the hydrocarbon chains are disordered and the lipid lateral diffusion coefficient is at least three orders of magnitude greater in the fluid phase than in a gel phase. It is therefore reasonable to assume that $\mathcal{K}(n,m')$ is zero unless both chains are in their predominantly extended state, G:

$$\mathcal{K}(G,e) = \mathcal{K}(e,e) = 0\,. \qquad (3)$$

The monolayer Hamiltonian can be simplified by the following transformation

$$\mathcal{L}_{iG} = \tfrac{1}{2}(1+\sigma_i),\quad \mathcal{L}_{ie} = \tfrac{1}{2}(1-\sigma_i)\ \sigma_i = \pm 1 \qquad (4)$$

to give

$$\mathcal{H}_M = -\frac{J}{2}\sum_{\langle ij\rangle}\sigma_i\sigma_j - h_M\sum_i\sigma_i + \text{constant}$$

$$J = \frac{J_0}{4}[\mathcal{J}(G,G) - 2\,\mathcal{J}(G,e) + \mathcal{J}(e,e)]$$

$$h_M(\Pi_{\text{ext}},T) = \frac{3\,J_0}{2}[\mathcal{J}(G,G) - \mathcal{J}(e,e)]$$

$$+\ \tfrac{1}{2}\Pi_{\text{ext}}(\mathcal{A}_e - \mathcal{A}_G) + \tfrac{1}{2}(\mathcal{E}_e - \mathcal{E}_G)\,. \qquad (5)$$

This Hamiltonian has a critical point (Π_M^*, T_M^*) determined by J. There is a temperature T_f determined by (e.g., Pink 1984b).

$$T_f(\Pi_{\text{ext}}) = 2\,h_M(\Pi_{\text{ext}},T_f)/k_B\ln(\mathcal{D}_e/\mathcal{D}_G) \qquad (6)$$

where k_B is Boltzmann's constant. If $T_f < T_M^*$ then the monolayer exhibits a discontinuous phase transition. If $T_f > T_M^*$ the monolayer will display a continuous phase change.

For the bilayer Hamiltonian, Eq. (4) for one sheet can be supplemented with the transformations $\mathcal{L}_{i'G} = \tfrac{1}{2}(1+\sigma_{i'})$ and $\mathcal{L}_{i'e} = \tfrac{1}{2}(1-\sigma_{i'})$ for the other sheet to give

$$\begin{aligned}\mathcal{H}_B = &-\frac{J}{2}\sum_{\langle ij\rangle}\sigma_i\sigma_j - h_B\sum_i\sigma_i - \frac{J}{2}\sum_{\langle i'j'\rangle}\sigma_{i'}\sigma_{j'}\Sigma_j,\\ &- h_B\sum_{i'}\sigma_{i'} - K\sum_{(ij')}\sigma_i\sigma_{j'} + \text{constant}\end{aligned}$$

$$h_B(\Pi_{\text{int}},T) = h_M(\Pi_{\text{int}},T) + \frac{qJ_0}{4}\mathcal{K}(G,G),$$

$$K(\Pi_{\text{int}},T) = \frac{J_0}{4}\mathcal{K}(G,G) \qquad (7)$$

As in the case of (5), $\mathcal{H}_B$ has a critical point (Π_B^*, T_B^*) determined by J and K, and a temperature T_c given by

$$T_c(\Pi_{\text{int}}) = 2\,h_B(\Pi_{\text{int}},T_c)/k_B\ln(\mathcal{D}_e/\mathcal{D}_G) \qquad (8)$$

If $T_c < T_B^*$ then the bilayer will display a discontinuous (first-order) phase transition at $T = T_c$. If $T_c > T_B^*$ it displays a continuous phase change at T_c.

Now, given a model of a monolayer displaying a discontinuous phase transition at Π_{ext} and $T_f < T_M^*$ with a transition enthalpy ΔQ we ask what must we choose $\mathcal{K}(G,G)$ to be such that the bilayer model exhibits a discontinuous phase transition at $T_c > T_f$ and possesses the same value of ΔQ. Because the transition enthalpy is given by (Pink et al. 1980)

$$\Delta Q_M = 2\,h(\Pi_{\text{ext}},T_f)\,|\langle\sigma\rangle|$$

$$\Delta Q_B = 2\,h(\Pi_{\text{int}},T_c)\,|\langle\sigma\rangle|\,, \qquad (9)$$

we must choose $\mathcal{K}(G,G)$ so that $T_B^* - T_c \approx T_M^* - T_f$. In Eq. (9) $2\,|\langle\sigma\rangle|$ is the discontinuity in $\langle\sigma\rangle$ at the transition. Once the value of $\mathcal{K}(G,G)$ has been chosen we can calculate at what value of Π_{int} does the phase transition at T_c occur. In order to get an idea of the value of Π_{int} we recall (e.g., Pink 1984a) that Eq. (6) and (8) arise from the requirements that the effective "fields"

$$H_M(\Pi_{\text{ext}},T_f) = h_M(\Pi_{\text{ext}},T_f) - \tfrac{1}{2}k_B T_f\ln(\mathcal{D}_e/\mathcal{D}_G)$$

$$H_B(\Pi_{\text{int}},T_c) = h_B(\Pi_{\text{int}},T_c) - \tfrac{1}{2}k_B T_c\ln(\mathcal{D}_e/\mathcal{D}_G) \qquad (10)$$

are zero at the phase transitions or phase changes. Now, because $\mathcal{T}(n,m)$ $\mathcal{E}_G$, $\mathcal{A}_G$, and $\mathcal{D}_G$ do not change much in the temperature and pressure ranges of interest we can put

$$H_B(\Pi_{\text{int}}, T_c) \approx H_M(\Pi_{\text{ext}}, T_c) + \tfrac{1}{2}(\Pi_{\text{int}} - \Pi_{\text{ext}})(\mathcal{A}_e - \mathcal{A}_G) + qK. \quad (11)$$

From previous work (Georgallas and Pink 1982a, Fig. 1) we see that for $T_c = 41°$ C, $\Pi_{\text{ext}} \approx 31.5$ dyne/cm. From below we will find that $qK \approx 0.004 \times 10^{-13}$ ergs. Using values of $\mathcal{A}_e \approx 34\text{Å}^2$ and $\mathcal{A}_G \approx 21\text{Å}^2$, we immediately see that the requirement $H_B(\Pi_{\text{int}}, T_c) = 0$ (making use of the fact that $H_M(\Pi_{\text{ext}}, T_c) = 0$) gives $\Pi_{\text{ext}} - \Pi_{\text{int}} \approx 4$ dyne/cm. This gives us the result that $\Pi_{\text{int}} \approx 27.5$ dyne/cm.

In the next section we shall describe how we go about calculating $\mathcal{H}(G,G)$ and then show the results of calculations as well as computer simulations to deduce a more exact value for Π_{int}.

Results

(i) Calculation of $\mathcal{H}(G,G)$

The model of a monolayer used by Georgallas and Pink (1982a) possesses a critical point at $\Pi_M^* = 18.9$ dyne/cm and $T_M^* = 30.55°$ C. The values of Π_{ext} and T_f at which this model displays a first-order phase transition with $\Delta Q_M \approx 8.7$ kcal/mole are $\Pi_{\text{ext}} = 15.2$ dyne/cm and $T_f = 27.5°$ C. Thus, in order to have the same value for ΔQ_B at $T_c = 41°$ C we should choose $T_B^* \approx 44°$ C.

The critical temperature of the monolayer Hamiltonian (5) on a triangular lattice is known exactly (Syozi 1972). The same cannot be said of that of the bilayer Hamiltonian (7) where two monolayers are coupled through the term in K. In order to calculate T_B^* we assumed that each site in one sheet has three nearest neighbours in the other sheet, or $q = 3$. The result of this assumption is shown in Fig. 1. Fig. 1A shows the two triangular lattices superimposed. Figure 1B shows the sites superimposed with the interactions between nearest neighbours within the same lattice represented by solid lines and those between nearest neighbours on different lattices represented by dashed lines. We can now consider this superposition as one lattice. All sites are now considered to belong to the same lattice outlined by dashed lines, and it can be seen that this is a honeycomb lattice. However, in reducing the two triangular lattices, with nearest neighbour interactions within and between the two lattices, to one honeycomb lattice, we have admitted interactions between nearest neighbours (the term in (7) involving K) and between next nearest neighbours (the term in (7) involving J). These are shown in Fig. 1B as dashed and solid lines respectively. We thus wish to calculate the critical point of the following Ising Hamiltonian on a honeycomb lattice

$$\mathcal{H} = -\frac{K}{2}\sum_{nn} \sigma_i\sigma_j - \frac{J}{2}\sum_{nnn} \sigma_i\sigma_k, \ \sigma_i = \pm 1 \quad (12)$$

where *nn* and *nnn* indicate a sum over nearest and next nearest neighbours respectively and the factors of ½ allow for double counting of interactions.

At this point it is worthwhile remarking that, because we expect the interaction between sheets to be weaker than the interaction within the sheets, we are interested in the case $K < J$. We shall obtain values of T_B^* as a function of K/J by using the techniques of high-temperature series analysis.

There have been many studies of Ising models with nearest and next nearest neighbour interactions. To our knowledge, however, no one has examined the honeycomb lattice, and in particular, no one has investigated the dependence of critical point on the ratio of the interactions in the regime where the next nearest neighbour interaction dominates, such a situation being apparently so unphysical! The recent work of Oitmaa (1981) could easily be applied to the case here and would yield much longer series than we will use and more refined estimates of critical point variation. However, for our purposes which require accuracy of ~ 1% in T_B^*, it has been sufficient for us to use the general expansion to sixth order of Dalton and Wood (1969) for the high temperature susceptibility expressed in terms of the contributing lattice constants (see Appendix).

We calculated the required lattice constants on the honeycomb lattice and obtained for the susceptibility χ the series

$$\begin{aligned} k_B T X_0 = 1 + 2 \Bigg\{ & \left[\frac{3\nu_1}{2} + 3\nu_2\right] + [3\nu_1^2 + 18\nu_1\nu_2 \\ & + 15\nu_2^2] + [6\nu_1^3 + 54\nu_1^2\nu_2 + 144\nu_1\nu_2^2 \\ & + 69\nu_2^3] + [12\nu_1^4 + 138\nu_1^3\nu_2 + 591\nu_1^2\nu_2^2 \\ & + 954\nu_1\nu_2^3 + 303\nu_2^4] + [24\nu_1^5 + 324\nu_1^4\nu_2 \\ & + 1872\nu_1^3\nu_2^2 + 5088\nu_1^2\nu_2^3 + 5652\nu_1\nu_2^4 \\ & + 1293\nu_2^5] + [45\nu_1^6 + 738\nu_1^5\nu_2 \\ & + 5181\nu_1^4\nu_2^2 + 19506\nu_1^3\nu_2^3 + 37815\nu_1^2\nu_2^4 \\ & + 31086\nu_1\nu_2^5 + 5409\nu_2^6] + \cdots \end{aligned} \quad (13)$$

where $\nu_1 = \tanh(K/k_BT)$ and $\nu_2 = \tanh(J/k_BT)$. We analyzed (13) in $x_2 = J/k_BT$ and $x_1 = K/k_BT \equiv \beta x_2$,

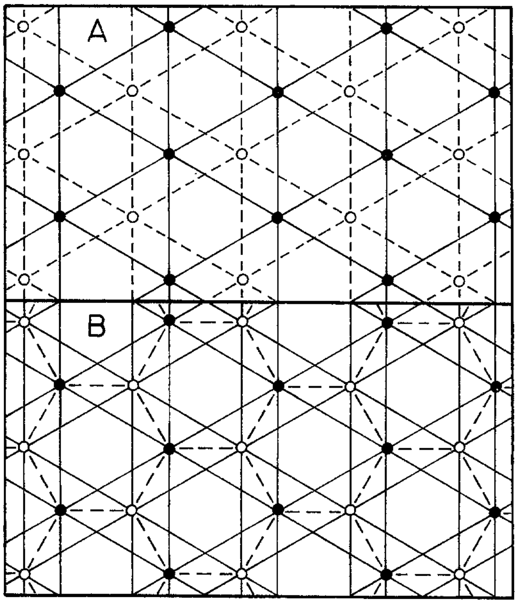

Fig. 1. A The two monolayer triangular lattices. Solid circles and solid lines indicate one lattice; open circles and dashed lines indicate the other lattice. **B** The two lattices showing the interactions. Solid lines indicate the interaction, J, within the sheets; dashed lines indicate the interaction, K, between sheets. The honeycomb lattice (dashed lines) is formed from the superposition of the two triangular lattices. The dashed lines indicate the nearest neighbour interactions K; solid lines indicate the next nearest neighbour interactions J

Table 1. Critical values of x for the triangular and honeycomb lattices as functions of $\beta = K/J$

	$1/\beta$	$x_{c\ \mathrm{tri}} = J/k_BT$	$x_{c\ \mathrm{hon}} = \beta x_{c\ \mathrm{tri}}$
Triangular limit	∞	0.274653 . . .	–
	100	0.2664	0.0027
	50	0.2603	0.0052
	25	0.2503	0.0100
	20	0.2452	0.0123
	10	0.2317	0.0232
	$6^2/_3$	0.2221	0.0333
	5	0.2149	0.0430
	1	0.1612	0.1612
Honeycomb limit	0	–	0.6585

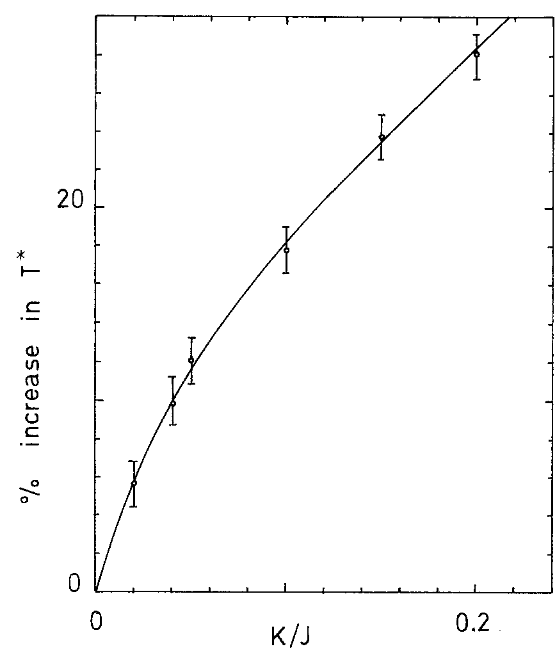

Fig. 2. Percentage increase in the critical temperature for the Ising model on a honeycomb lattice, T^*, as a function of the ratio of nearest neighbour, K, to next nearest neighbour, J, interactions

where $\beta = K/J$. We used values of $\beta = 0.01$, 0.02, 0.04, 0.05, 0.10, 0.15, 0.20, and 1.00, as described in the Appendix where we comment on the confidence limits of our analysis. The results of the analysis are shown in Table 1. Figure 2 shows the percentage increase in T_B^* as a function of K/J. When $K/J = 0$, $T_B^* = T_M^*$.

The first point to notice from this figure is that the critical temperature, T_B^*, is not a linear function of K/J and that its maximum rate of increase is at $K/J = 0$. This means that a small coupling between the sheets of the bilayer will have a relatively large effect upon T_B^*. In the previous section we mentioned that we wish to choose $\mathcal{H}(G,G)$ so that $T_B^* \approx 44°$ C, where J is such that $T_M^* = 30.55°$ C. This represents a 4.4% increase in the critical temperature, and we see from Fig. 2 that a choice of $K/J \approx 0.015$ will achieve this. $\mathcal{H}(G,G)$ is then calculated from

$$\mathcal{H}(G,G) = K[\mathcal{I}(G,G) - 2\,\mathcal{I}(G,e) + \mathcal{I}(e,e)]/J \quad (14)$$

We chose $K/J = 0.02$ which gives $T_B^* \approx 45.5°$ C in order to ensure that the bilayer main transition at $T_c \approx 41°$ C is sufficiently far from our critical point so that we do not have problems with fluctuations when we perform computer simulations.

(ii) Computer simulation

We have performed a Monte Carlo simulation using the Metropolis algorithm (e.g., Binder 1979; Pink 1984b) in order to obtain a value for Π_{int} when $T = 41°$ C and to compare a monolayer with the corresponding bilayer. We made use to two independent triangular lattices of 900 sites each, with periodic boundary conditions for monolayer calculations and with two such lattices coupled as described above for the bilayer. We equilibrated the system for 50 Monte Carlo steps and calculated thermodynamic averages over a subsequent 100 steps. In the simulation of the monolayer, where we can calculate $\langle\sigma\rangle$ exactly at a phase transition, we have found no evidence of non-equilibrium behaviour. The isotherms are shown in Fig. 3 together with the coexistence curves. We see that the effect of the coupling between the sheets of the bilayer is to reduce the lateral pressure at which the monolayer exhibits a phase transition at the same temperature. Thus, at 27.5° C, the monolayer has a phase transition at 15.24 dyne/cm while the bilayer has it at 14.25 dyne/cm. At 34.1° C, the monolayer has a continuous phase change at 23.2 dyne/cm while the bilayer has a discontinuous phase transition at 22.2 dyne/cm.

At 41° C, because of our choice of $\mathcal{H}(G,G)$, the bilayer has a phase transition with $\Delta Q \approx 8.9$ kcal/mole at a value of internal lateral pressure $\Pi_{\text{int}} \approx$ 30.5 dyne/cm, while the monolayer has a continuous phase change at $\Pi_{\text{ext}} \simeq 31.5$ dyne/cm.

The existence of hysteresis, as shown, confirms the nature of the computer-simulated first-order phase transitions. The coexistence curve for the monolayer is an exact calculation while that for the bilayer is essentially exact. The pressures at which the phase transitions occur are all exact calculations and the fact that they coincide with the centres of the hysteresis curves supports the accuracy of the simulations. The simulations for the monolayer cases where no phase transition occurs were run for both increasing and decreasing pressures and, as required, show no hysteresis. In Fig. 3 the results for one sheet are indicated by × and for the other by +.

Summary and conclusions

We have modelled a bilayer of DPPC as two triangular lattices each site of which is occupied by a lipid hydrocarbon chain. For hydrocarbon chains in each sheet of the bilayer we used a ten-state model, which was reduced to a two-state model by a time-scale argument. This was used before to study the thermodynamic properties of monolayers (Georgallas and Pink 1982a, b). The parameters here are those used in the former work. The two questions that we have tried to answer are: (*a*) What is the strength of the interaction between the two sheets of the bilayer, and (*b*) What is the internal lateral pressure of a PC bilayer. In the second case the internal lateral pressure is understood to arise from the polar group interactions which bring the bilayer into existence and is the analogue of the externally-applied lateral pressure in the case of monolayers at an air-water interface. Connected with these is the question of how to deduce the internal lateral pressure of a bilayer from the pressure-area isotherms of the corresponding monolayer, together with a knowledge of the bilayer main transition temperature and transition enthalpy.

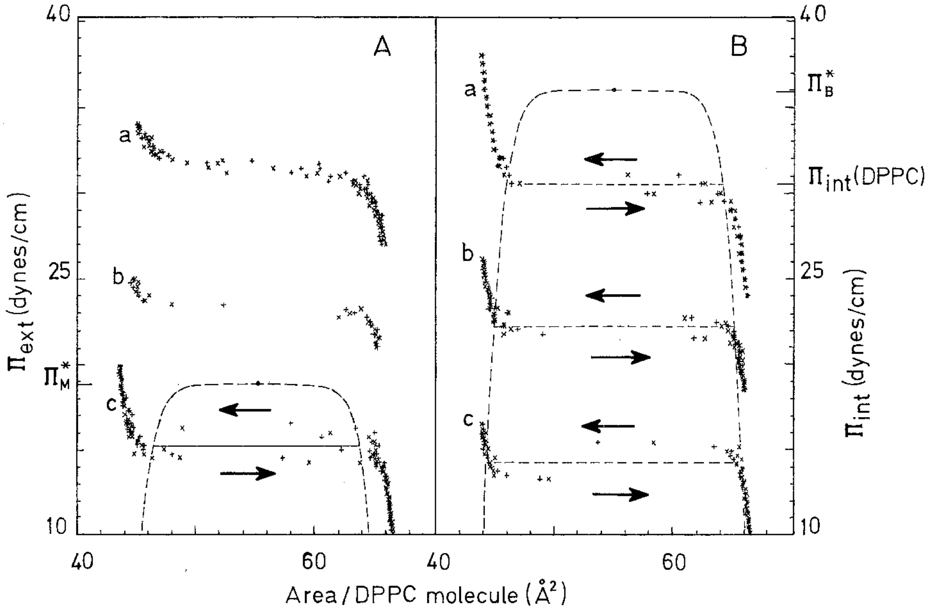

Fig. 3A and B. Pressure-area isotherms for the model of a DPPC monolayer and the corresponding bilayer used here. The dashed curves are the coexistence curves with the critical points shown as dots. The horizontal solid or dashed lines show the pressures at which first-order phase transitions occur. The monolayer coexistence curve and the transition pressures are exact calculations. The nature of the phase transitions is confirmed by the hysteresis displayed by the computer simulation results shown as × and + for the two sheets. **A** Monolayer ($K/J = 0$). The applied lateral pressure Π_{ext} is the independent variable. **B** Bilayer with $K/J = 0.02$. With this choice of K/J to give the desired transition enthalpy at $T_c = 41°$ C, the internal lateral pressure of a DPPC bilayer is 30.5 dyne/cm. The temperatures for the simulations are 41°C (a), 34.1° C (b), and 27.5° C (c).

We mapped each triangular lattice onto a spin-½ Ising model in a temperature-dependent magnetic field (see e.g., Doniach 1978; Pink et al. 1980 or, for a simple description, Pink 1984b). In the case of the bilayer model we reduced the problem involving two triangular lattices, each possessing a nearest neighbour interaction J, and interacting with each other via a coupling K, to one of a single honeycomb lattice with nearest neighbour interaction K and next nearest neighbour interaction J.

We calculated the critical temperature for the bilayer, T_B^*, as a function of K/J by performing a zero-field high temperature series expansion of the susceptibility to sixth order in J/k_BT and K/k_BT. We also performed Monte Carlo simulations to calculate pressure-area isotherms for the model of the bilayer and compared them with isotherms for the monolayer (Georgallas and Pink 1982a).

The results of our studies are:

(*1*) The interaction between the sheets of a DPPC bilayer is ~ 1.5–2% of the maximum interaction between two nearest neighbour *all-trans* chains within one of the sheets.

(*2*) From this result, we find that the internal lateral pressure of a DPPC bilayer is $\Pi_{\text{int}} = 30.5$ dyne/cm. This result provides some justification for the choice of 30 dyne/cm by Blume (1979) and Pink and Chapman (1979).

(*3*) We have pointed out that the critical temperature of a bilayer, T_B^*, is very sensitive to changes in $\mathcal{K}\ (G,G)$, the coupling between the sheets. In the model presented here and elsewhere (Doniach 1978), the main transition in the bilayer occurs at T_c, only a few degrees below T_B^*. From (4) and (9) it is easy to see that the transition enthalpy depends here upon $\Delta\mathcal{A}$, the change in cross-sectional area at the phase transition, through $\Delta Q = 2\,\text{h}\,\Delta\mathcal{A}/(\mathcal{A}_e - \mathcal{A}_G)$. We can see from Fig. 3, that a small decrease in T_B^* can lead to a large decrease in ΔQ. Thus, if bilayers are prepared under varying conditions so that the coupling between the sheets differ from preparation to preparation, it is possible that significantly different values of ΔQ may be observed.

(4) From monolayer studies, the internal pressure of the corresponding bilayer can be deduced approximately as follows: Let T_c be the bilayer transition temperature. The lateral pressure at which the monolayer isotherm for $T = T_c$ exhibits a phase change or phase transition is approximately equal to the internal lateral pressure of the bilayer. This can be seen in Fig. 3. The role of the coupling between the sheets, $\mathcal{K}(G,G)$, is to drive the critical temperature T^* sufficiently high above T_c so that the transition enthalpy has the observed value.

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Appendix. High temperature series expansions

Zero-field high temperature susceptibilities are known to be among the easiest thermodynamic quantities to analyze (Hunter 1969). Very accurate estimates of the critical temperature and critical exponent γ were obtained from relatively short susceptibility series for the nearest neighbour Ising model (Domb and Sykes 1957). Given that estimates of the critical point, accurate to approximately 0.1%–1%, were sufficient for the present purpose, and that we were interested in values of J/K between 5 and 100, series to sixth order in $x_1 = K/k_BT$ and $x_2 = J/k_BT$ were thougth to be sufficient. For values of J/K close to zero (the honecomb lattice limit) six terms would be unlikely to yield sufficiently accurate estimates, because the lower the coordination number of the lattice the slower the convergence of the series. We know rigorously, however, that six terms for the nearest neighbour Ising model on a triangular lattice corresponds to twelve terms for it on a honeycomb lattice according to the star-triangle transformation (Syozi 1972).

We used only the well-known and straight-forward methods of series analysis: The ratio method with Neville extrapolation and the Padé approximant method. Both unbiased procedures and those biased by using the known exponent $\gamma = 1.75$ for 2-dimensional Ising systems with short-range forces, were used (see, e.g., Hunter and Baker 1973). More sophisticated methods of analysis have been devised recently (see, e.g., Fisher and Au-Yang 1979; Hunter and Baker 1979; Roskies 1981 and references therein) but these are simply not appropriate for such a straight-forward and crude calculation.

If the radius of convergence of the series is determined by the Curie singularity of the form $\chi \sim A(1 - x/x_c)^{-\gamma}$ then the coefficients, a_n, in the susceptibility series asymptotically tend to

$$a_n \sim (-1)^n A \binom{-\gamma}{n} x_c^{-n} \equiv A \binom{n+\gamma-1}{n} x_c^{-n} \qquad \text{(A1)}$$

Hence the ratios of successive coefficients

$$r_n = \frac{a_n}{a_{n-1}} \sim \left[1 + \frac{\gamma - 1}{n}\right] x_c^{-1} \qquad \text{(A2)}$$

must tend to x_c^{-1} as $n \to \infty$. The standard $1/n$ plot allows one to estimate x_c from the limit and γ from the slope. If γ is known, the modified or biased ratio sequence

$$\beta_n = \frac{n}{n + \gamma - 1} r_n \qquad \text{(A3)}$$

will approach the limit x_c^{-1} with zero slope.

The j-th order Neville extrapolants, $l_n^{(j)}$, to the sequences r_n or β_n are defined by the iterative process of linear extrapolation

$$l_n^{(j)} = \frac{1}{j}\,[n l_n^{(j-1)} - (n-j) l_{n-1}^{(j-1)}] \tag{A4}$$

where $l_n^{(0)} \equiv r_n$ (or β_n). The Padé approximant

$$[N/D] = P_N(x)/Q_D(x) \tag{A5}$$

to the function $f(x)$ is a rational polynomial expression of order N and D in numerator and denominator respectively, defined such that the Taylor series expansion of $f(x)$ and $[N/D]$ agree exactly to order $N + D$ in x. The Padé approximant is ideally suited to approximate simple-pole singularities in a function. If $\chi = A(1 - x/x_c)^{-\gamma}$ then

$$\frac{d}{dx} ln\chi \sim \frac{\gamma}{x_c - x} \tag{A6}$$

Hence, forming Padé approximants to the derivative of the logarithm of the susceptibility ("∂ log Padé") and looking for the root of the denominator closest to the origin in the complex x-plane should give good estimates of x_c.

We have used these methods of analysis on our series for the eight values of J/K quoted. The apparent degree of convergence of the estimates was about what we expected. The assignment of confidence limits to such estimates is a matter of judgment and experience. Our estimate of confidence limits based on all the evidence available was approximately 0.7% of the value quoted. As a test we then tried to estimate x_c for the nearest neighbour Ising model on a triangular lattice, where the value of $x_c = \frac{1}{4} \ln 3 = 0.273653\ldots$ is known exactly, from just six terms in the χ series. Our blind estimate was accurate to 0.75% suggesting that confidence limits of this order are entirely appropriate.

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