

Fractional order phase transition in lipid bilayer: dipalmitoyllecithin

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Abstract. Dipalmitoyllecithin (DPL) shows an order \leftrightarrow disorder pressure transition which is neither of first order nor of second order but can be treated as a fractional order ($3/2$ order) transition. The Ising model formalism is adopted for the study of such a system. A suitable equilibrium constant is defined which generates a $3/2$ order transition. Transition curves are obtained and compared with the experimental curves of Liu and Kay. Reverse transition curves are also obtained and the system exhibits hysteresis effect. An approximate expression connecting transition pressures at different temperatures is obtained and the calculated and the experimental values are in good agreement.

Keywords. Pressure phase transition; dipalmitoyllecithin; lipid bilayer; gel; liquid crystalline.

1. Introduction

Biophysical studies of phospholipids play a significant role in elucidating structure and function relation in biological membranes, which are the systems with lipid and globular proteins as main constituents. These proteins, ranging in molecular weight from 15,000 to 20,000 and in size from a few Å to a few hundred Å, are interspersed in the lipid matrix (Singer 1972; Fox 1972; Singer and Nicolson 1972). The lipid assumes a mechanically stable bilayer structure with headgroup on outer and hydrocarbon chains on the inner side (Singer 1972, Singer and Nicolson 1972). Various studies (Lee 1975, 1976; Cronan and Gelmann 1975; Stier and Sackmann 1973; Chapman *et al* 1967) have shown that membrane proteins have precise environmental requirements for optimum activity, some requiring a fluid environment (liquid crystal phase), whereas others require much more rigid surrounding (gel phase) provided by phospholipid molecules.

The present paper deals with the pressure-induced phase transition in DPL, a lipid bilayer. The system goes from ordered (gel) to disordered phase (liquid crystalline) as a function of pressure. The main transition which follows the pretransition (orientational ordering of entire hydrocarbon chain) is the *trans-gauche* rotation about C-C bond in hydrocarbon chain. The experimental and theoretical evidence suggests these transitions to be order \leftrightarrow disorder transitions. The presence of the headgroup interaction introduces an element of asymmetry in the overall interaction and this interaction-asymmetry is reflected in the

order \leftrightarrow disorder transition profile. This is unlike other polypeptides such as (polybenzyl-L-glutamate) PBLG. The ΔV vs P curves for DPL are, therefore, asymmetric about mid-point, and as such the mid-point cannot be taken as a transition point. The specific heat behaviour observed by Nagle (1973) indicates that the phase transition is neither of the first, nor of the second order type. The experimental data are better fitted to a 3/2-order temperature phase transition. For such a transition the lowest derivative of the free energy to be discontinuous is the third derivative with respect to $(T - T_c)^{1/2}$, where T_c is the transition temperature. The discussion of the mathematical model for a system showing fractional order phase transition may be found in Kasteleyn (1963).

This idea of a fractional-order (3/2 order) pressure transition has been incorporated in our theory based on the Ising model formalism (Zimm and Bragg 1959; Mehrotra et al 1979, Agnihotri et al 1981) by suitably defining the equilibrium constant in such a manner that the lowest derivative of Gibbs free energy that is discontinuous is the third derivative with respect to $(P_T - P)^{1/2}$ where P_T is the transition pressure. Following the matrix method the partition function and hence the fraction of segments in ordered (gel) state is obtained. Change in volume (ΔV) can then be computed if the volume per gram of liquid crystalline and gel states are known. Theoretical ΔV vs P curves thus computed can be compared with the experimental ones (Liu and Kay 1977).

2. Theory

The basic theoretical approach based on the Ising model formalism is well-known and a transition matrix is written for the main transition, in terms of segment partition functions, as follows:

$$M = \begin{matrix} & \begin{matrix} g & & tg & & t \end{matrix} \\ \begin{matrix} g \\ tg \\ t \end{matrix} & \begin{array}{|cc|cc|cc} \hline f_g^{1/2} & f_g^{1/2} & f_a^{1/2} & f_{tg}^{1/2} & 0 & \\ \hline f_{tg}^{1/2} & f_a^{1/2} & 0 & & f_{tg}^{1/2} & f_t^{1/2} \\ \hline f_t^{1/2} & f_g^{1/2} & 0 & & f_t^{1/2} & f_t^{1/2} \\ \hline \end{array} \end{matrix} \quad (1)$$

where t , g and tg represent the low energy trans (ordered or gel), higher energy gauche (disordered or liquid crystalline) states and first gel residue in the sequence of gel segments respectively.

In writing the matrix (1) we have made use of the cell model for diffuse transition. In this model, two different phases (gel and liquid crystalline) of a long chain molecule coexist on a lattice. The two phases (t and g states) are dispersed in each other and each region of phase is assumed to be wholly enclosed by a boundary. If the coordination number for both the phases is z , the contribution to the total partition function of a segment (repeat unit) in t or g states is $f_t^{z/2}$ or $f_g^{z/2}$ whereas for a boundary segment it would be $f_{tg}^{z/4}$ or $f_g^{z/4}$. Generalization of this for a one-dimensional system with nearest neighbour interaction leads to the Ising matrix (1).

The transition matrix could as well have been written in terms of the segment pair partition function, but the transition matrix will then be of larger dimension although the results obtained are basically the same for either matrix and therefore it is better to opt for a simpler alternative. In the overall transition, the effect of saturation of hydrocarbon chain and head group interactions, is taken into account through the input parameters such as change in enthalpy, volume, etc, at the transition point.

The eigenvalues of M are determined by secular equation, $|M - \lambda I| = 0$, with I being a 3×3 unit matrix, and are found to be:

$$\lambda_1 = \frac{1}{2} \{ (f_g + f_t) + [(f_g - f_t)^2 + 4f_g f_{tg}]^{1/2} \},$$

$$\lambda_2 = \frac{1}{2} \{ (f_g + f_t) - [(f_g - f_t)^2 + 4f_g f_{tg}]^{1/2} \},$$

and $\lambda_3 = 0$. (3)

The matrices T and T^{-1} which diagonalize M are

$$T = \begin{array}{c} \left| \begin{array}{ccc} 1 & 1 & 1 \\ \lambda_1 - f_g & \lambda_2 - f_g & -f_g^{1/2} f_{tg}^{-1/2} \\ f_g^{1/2} f_{tg}^{1/2} & f_g^{1/2} f_{tg}^{1/2} & \\ f_t^{1/2} f_g^{1/2} & f_t^{1/2} f_g^{1/2} & -f_g^{1/2} f_t^{-1/2} \\ \lambda_1 - f_t & \lambda_2 - f_t & \end{array} \right. \end{array} \quad (4)$$

and

$$T^{-1} = \begin{array}{c} \left| \begin{array}{ccc} C_1 & C_1 f_g^{1/2} f_{tg}^{1/2} / \lambda_1 & C_1 f_g^{1/2} f_{tg} f_t^{1/2} / \lambda_1 (\lambda_1 - f_t) \\ C_2 & C_2 f_g^{1/2} f_{tg}^{1/2} / \lambda_2 & C_2 f_g^{1/2} f_{tg} f_t^{1/2} / \lambda_2 (\lambda_2 - f_t) \\ 0 & C_3 & -C_3 f_g^{1/2} f_t^{-1/2} \end{array} \right. \end{array} \quad (5)$$

where $C_1 = (\lambda_1 - f_t) / (\lambda_1 - \lambda_2)$, $C_2 = (\lambda_2 - f_t) / (\lambda_2 - \lambda_1)$, and

$$C_3 = (f_g^{1/2} f_{tg}^{1/2} f_t^{-1} - f_g^{1/2} f_{tg}^{-1/2})^{-1}.$$

Let the first segment be assumed in the liquid crystalline phase (gauche conformation). Its contribution to partition function is given by:

$$U = (f_g^{1/2}, 0, 0), \quad (6)$$

A column matrix V is defined as: $V = \begin{array}{c} \left| \begin{array}{c} f_g^{1/2} \\ f_g^{1/2} \\ f_t^{1/2} \end{array} \right| \end{array} \quad (7)$

The grand partition function Z of a macromolecule of N segments is then given by:

$$Z = U M^{N-1} V = U T T^{-1} M^{N-1} T T^{-1} V. \quad (8)$$

The right side is simplified by actual substitution of matrices and the partition function is obtained to be

$$Z = C_1 \lambda_1^N + C_2 \lambda_2^N = Z_1 + Z_2 \text{ (say)}. \quad (9)$$

The fraction of liquid crystalline (g) segments is then,

$$\begin{aligned} n_g &= \frac{1}{N} \frac{\partial \ln Z}{\partial \ln f_g}, \\ &= \frac{f_g}{NZ} \left(\frac{\partial Z_1}{\partial f_g} + \frac{\partial Z_2}{\partial f_g} \right). \end{aligned} \quad (10)$$

For a very long chain ($N \rightarrow \infty$) the value of $\langle n_g \rangle$ is given by

$$\langle n_g \rangle = \frac{\lambda_1 - f_t}{\lambda_2 - \lambda_1}. \quad (11)$$

Now the fraction of segments in gel phase Q , will be

$$\begin{aligned} Q &= 1 - \langle n_g \rangle, \\ &= \frac{1}{2} \left\{ 1 + (S - 1) / [(S - 1)^2 + 4 \sigma S]^{1/2} \right\}, \end{aligned} \quad (12)$$

where $S = f_t / f_g$ and $\sigma = f_{tg} / f_t$ are growth and nucleation parameters respectively.

$S = 1$ corresponds to the pressure at which $Q = 0.5$ and this gives the transition pressure $P = P_T$.

Now defining equilibrium constant (S) for liquid crystalline \leftrightarrow gel state for the 3/2 -order transition as:

$$\begin{aligned} S &= \exp \left\{ \frac{\Delta v P_T}{RT} \left[1 - \frac{P}{P_T} \right]^{3/2} \right\}, \\ &= \exp \left\{ \frac{\Delta v (P_T - P)^{3/2}}{RT P_T^{1/2}} \right\} \text{ for } P \leq P_T, \end{aligned}$$

$$\text{and } S = 1 \text{ for } P \geq P_T. \quad (13)$$

With this expression for S one obtains the Z as a function of the thermodynamic parameters pressure and temperature. It can then be shown easily that the third derivative of Gibb's free energy, $G = k T \ln Z + P v$ with respect to $(P_T - P)^{1/2}$

is the lowest derivative that is discontinuous and such a transition can be termed a fractional order (3/2) pressure phase transition.

In an earlier paper (Mehrotra *et al* 1979) an expression for transition pressure at different temperatures was obtained for a first order transition. If the temperature range is small the same expression provides a good approximation for the above specially in the linear transition region of 3/2 order transition.

$$P_T = P_{T_0} + \int_{T_0}^T \frac{\Delta s}{\Delta v} dT. \quad (14)$$

Since the molar change in entropy Δs during transition can be taken to be constant in the small temperature range of the order, say, of 1°C, the above expression reduces to:

$$P_T = P_{T_0} + \frac{\Delta H (T - T_0)}{T \Delta v}, \quad (15)$$

where use has been made of the relation $\Delta H = T \Delta s$, where ΔH is the molar change in enthalpy about the transition point. Thus transition pressure at different temperatures can be calculated and hence S as a function of pressure. Q is then obtained as a function of pressure. The experimental data available is in the form of ΔV vs P curves where ΔV is the change in volume per gram of the sample. We generate such curves through the following relation:

$$\Delta V = d_l (1 - Q) + d_g Q, \quad (16)$$

where d_l and d_g are the volume densities per gram of liquid crystalline and gel states respectively.

The input parameter (ΔH , T_0 , P_{T_0} , Δv) used here include overall effects (effect of unsaturation of hydrocarbon chain, headgroup effect) influencing the main transition; hence their explicit expressions are not required. Hysteresis effect is shown by drawing curves (ΔV vs P) for reverse transition as well.

3. Results and discussion

Two sets of experimental data named as series *A* and series *B* for transition pressures for two different samples of DPL are observed by Liu and Kay (1977). In series *A* transition pressures for transitions at six different temperatures whereas in series *B* transition pressures for transitions at three different temperatures are observed. Experimental transition pressures for series *A* along with calculated values are given in table 1. The values of input parameters are also shown. Transition enthalpy ΔH per mole is taken as 8.7 kcal/mole for both the series *A* and *B* for gel \leftrightarrow liquid crystalline transition.

Table 2 contains observed transition pressures for series *B* and corresponding calculated values alongwith other transition parameters σ and Δv . The volume den-

Table 1. Theoretical and experimental values of transition pressures (P_T) (series: A)

T (°C)	T (°K)	P_T (kg/cm ²)	
		Calculated	Experimental (Liu and Kay 1977)
41.35	314.35	1 (assumed)	1
42.51	315.51	51.66	50
43.52	316.52	95.56	92
44.53	317.53	139.00	137
45.51	318.51	181.00	184
46.49	319.49	222.70	218
47.50	320.50	265.40	264

$\Delta v = 0.036 \times 734.1$ ml/mole
 $P_{T_0} = 1$ kg/cm² $T_0 = 314.35^\circ\text{K}$, $\Delta H = 8.7$ kcal/mole

Table 2. Theoretical and experimental values of transition pressures (P_T) (series: B).

T (°C)	T (°K)	P_T (kg/cm ²)		σ	ΔV
		Calculated	Experimental (Liu and Kay 1977)		
43.19	316.19 (314.69)	85 (84.597)	82 ± 3	1×10^{-4}	$0.041 - 0.080 Q$
44.15	317.15 (315.65)	130 (129.4)	126 ± 3	3.0×10^{-4}	$0.0425 - 0.081 Q$
45.13	318.13 (316.63)	176 (175.2)	167 ± 3	6.0×10^{-4}	$0.045 - 0.084 Q$

$\Delta v = 0.033 \times 734.1$ ml/mole $\Delta H = 8.7$ k cal/mole.

sity of gel and liquid crystalline phase can be found by matching the calculated and experimental values for the completely ordered and disordered phase. The relation between ΔV and Q at any temperature is also indicated in table 2. Then ΔV vs P transition curves can be generated. Hysteresis effect (Lee 1977) is shown by drawing curves (ΔV vs P) for reverse transition. The hysteresis in transition is about 1.5°C . Using relation $P_1/T_1 = P_2/T_2$ the transition pressure for reverse transition (P_2) can be calculated. The bracketed quantities in table 2 show the pressure and temperature for the reverse transition thus showing the hysteresis effect. Figure 1 shows the theoretical and experimental transition curves (ΔV vs P) for gel to liquid crystalline transition and the theoretical curve for the reverse liquid crystalline to gel transition.

Transition pressure (P_T) increased with temperature. Due to rise in temperature gauche rotations about C-C bonds occur, resulting in a disordered system. Hence further pressure is needed to bring chains to their van der Waals radii in order to have ordered system. Increase of P_T with T is almost linear which suggest gel \leftrightarrow liquid crystalline transition is analogous to the melting of paraffins and polyethylene. Nu-

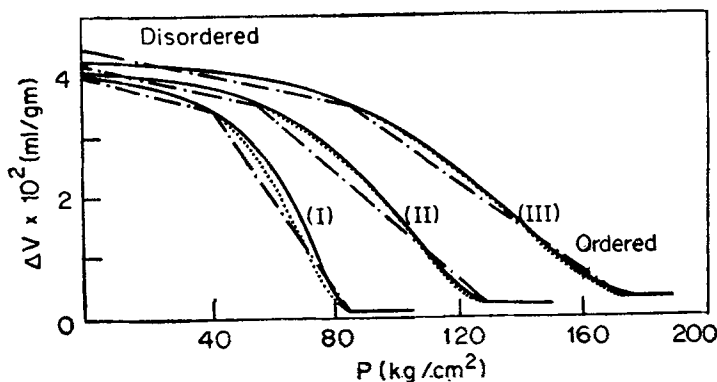


Figure 1. Theoretical and experimental transition curves and hysteresis effect at different temperatures.

cleation parameter increases almost linearly with temperature; it is so because nucleation is easier at higher temperatures. Hysteresis effect is found to be more pronounced in case of transition at lower temperatures. Thus as transition pressure increases there is a gradual decrease in hysteresis effect.

The transition curves are asymmetric and are different from the curves for a first order or a second order phase transition. The theoretical transition curves for a $\frac{3}{2}$ -order transition show remarkable agreement with the experimental one.

In the above analysis no distinction is made in two gauche states (g_1 and g_2). Inclusion of this with possible changes in the transition matrix will be the subject of a future communication.

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References

- Agnihotri R C, Mehrotra C, Gupta V D and Srivastava Vandana 1981 *Pramana* **17** 361
 Chapman D, Williams R W and Ladbroke B D 1967 *Chem. Phys. Lipids* **1** 445
 Cronan J E and Gelmann E P 1975 *Bacteriol. Rev.* **39** 232
 Fox C F 1972 *Sci. Am.* **226** 30
 Kasteleyn P W 1963 *J. Math. Phys.* **4** 287
 Lee A G 1975 *Prog. Biophys. Mol. Biol.* **29** 3
 Lee A G 1976 *Nature (London)* **262** 545
 Lee A G 1977 *Biochem. Biophys. Acta* **472** 237
 Liu L and Kay R L 1977 *Biochemistry* **16** 3484
 Mehrotra C, Agnihotri R C and Gupta V D 1979 *Natl. Acad. Sci. Lett.* **2** 75
 Nagle J F 1973 *Proc. Natl. Acad. Sci. (USA)* **70** 3443
 Singer S J 1972 *Structure and function in biological membranes* (ed) L I Rothfield (New York: Academic Press)
 Singer S J and Nicolson G L 1972 *Science* **175** 720
 Stier A and Sackmann E 1973 *Biochem. Biophys. Acta* **311** 400
 Zimm B H and Bragg J K 1959 *J. Chem. Phys.* **31** 526