A SELF-CONSISTENT CHAIN MODEL FOR THE PHASE TRANSITIONS IN LIPID BILAYER MEMBRANES

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ABSTRACT We presented a mechanical model of a lipid bilayer menbrane. The internal conformations of a polar head group and double hydrocarbon chains in a lipid molecule were described on the basis of the isomeric bond-rotation scheme. The thermodynamic properties of the lipid membranes were represented by a density matrix that described the rotational isomeric states of the head groups and chains. The parameters that determined the density matrix were obtained in the presence of the intermolecular interactions, which depend on the conformation of the molecules. The interchain interaction was given by the Kihara potential, which depends on the shape of the chains. The Coulomb interaction between the polar head groups and the lateral pressure were considered. The calculation was made for the three lipid molecules corresponding to DMPC, DPPC, and DSPC. The model agreed well with the following experimental results: the temperature, the latent heat of the gel-to-liquid crystalline phase transition, the temperature dependencies of (*a*) the intermolecular distance, (*b*) the number of *gauche* bonds in a hydrocarbon chain, (*c*) the order parameter for the bond orientation, (*d*) the volume of the membrane, (*e*) the thermal expansion coefficients, and (*f*) the birefringence.

INTRODUCTION

We realize the comprehensive functions of biological membranes by combining various types of lipid and cholesterol molecules. To understand the relationship between the composition and the properties of the membranes, one should investigate the phase transitions that take place in the lipid membranes. The changes due to phase transitions in the physical and chemical properties of lipid bilayers have been actively studied (1). Various theoretical models have been proposed to study microscopically the mechanism of the phase transitions (2, 3). When one studies the relationship between the structure and the properties of membranes using a model, it is essential that the model shows how the properties of the membranes, such as the phase transition, change because of variation in the molecular structures of lipids, i.e., variation in the spatial structure of hydrocarbon chains and head groups, in the charge distribution of head groups, in the number of C—C bonds of hydrocarbon chains, and in the number and position of double C═C bonds in the chains.

We present a model for phospholipid bilayer membranes that attempts to illustrate the above-mentioned characteristics. The present model describes (*a*) the internal states of a lipid molecule in the membranes in terms of the isomeric bond conformations of the polar head group and hydrocarbon chains, which depend on the intermolecular interaction, (*b*) the interactions between the lipid molecules as represented by the potential functions, which depend on the conformations of the molecules, (*c*) the molecular structures of lipids, which are incorporated directly in the model by using a density matrix that describes the bond rotational isomeric states of the lipids, (*d*) the conformations of individual head groups and hydrocarbon chains and the packing states of the lipid molecules as determined self-consistently in the presence of the intermolecular interactions, which depend on the conformation of the lipid molecules, and (*e*) the various physical quantities of the membranes as represented in analytical forms based on the density matrix.

Marsh (4), Bothorel et al. (5), and McCammon and Deutsch (6) have also adopted the isomeric bond conformation scheme and considered the effect of the interchain interactions on the bond rotation energy, ϵ_c. They adjusted the value of the energy, ϵ_c, in the membrane so as to reproduce the phase transition temperature and the transition enthalpy. However, ϵ_c does not represent the real bond rotation energy, but is rather a parameter that determines the density matrix, which describes the thermodynamic states of the chains in the membrane, and is obtained by the variational principle.

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MODEL AND BASIC EQUATIONS

Description of the Model

Lipid bilayers in water undergo a gel-to-liquid crystalline phase transition, where the hydrocarbon chains change from an all-*trans*, rigid extended conformation in the gel phase to a highly degenerate rotational, isomeric, shortened kink-containing conformation in the liquid crystalline phase (1). We study theoretically the mechanism of the phase transition in bilayer membranes constructed with monomolecular phospholipids in water, and the variations in the properties of the membranes due to the phase transition. To solve the problem in such complex systems as lipid bilayer membranes, we introduce some simplifications. First, we do not consider explicitly the coupling between the two halves of a bilayer but do consider only a monolayer of lipid molecules. The effect of the coupling may be taken into account through a phenomenological potential acting on the monolayer. Second, we assume that the hydrocarbon chains of lipid molecules remain in a two-dimensional hexagonal lattice even above the gel-to-liquid crystalline transition (melting) temperature. Although this is not consistent with the observed loss of spatial order above the melting temperature, the effect of spatial disordering on the thermodynamic properties of the system in the melting process is very small: The change of entropy due to the spatial disordering is small (7) compared with the total entropy change on of the order of 10 k_B/molecule for typical bilayers (8). Therefore, the gel-to-liquid crystalline (melting) transition is considered to be caused by the intrachain entropy of isomerization. Third, we do not consider the interaction between the polar head groups and the hydrocarbon chains because it is not essential to the phase transition (2). This interaction has not been considered in any model. Fourth, we consider the spatial position of the polar head groups. However, the spatial order of the head groups in the membranes of double-chain lipids in water is not yet clear (9). We assume that the head groups of lipid molecules are set in a two-dimensional hexagonal lattice of which the lattice constant is the square root of two times that for the hydrocarbon chains. Any change in the relative position of the head groups to the chains does not affect the phase transition because of the third simplification.

Thus the Hamiltonian of the system, which is a monolayer of the lipid molecules with double saturated hydrocarbon chains, is represented as

$$H = H_{h0} + H_{c0} + V_h + V_c + V_r, \tag{1}$$

where H_{h0} and H_{c0} are the intrahead and intrachain Hamiltonians, respectively. V_h and V_c are the interhead and interchain interaction potentials, respectively, and V_r is the potential for the residual interactions. The internal state of a polar head group is denoted by the rotational isomeric conformation of the bonds, which are between anions and cations in the head group such as P^- and N^+ in a phospholipid. The internal state of a hydrocarbon chain is also represented by rotational isomeric conformation of the C—C bonds in the chain. We studied the case where the double hydrocarbon chains in the lipid molecule were equivalent to each other. The bonds in both the head groups and the chains took only three conformations, *trans*, *gauche*+, and *gauche*−, which are abbreviated as t, g^+, and g^-, respectively. The energy of an internal state of head and chain is given in terms of the rotation energy, ϵ_{h0} and ϵ_{c0}, of a bond and is the energy difference between a *trans* conformation and a *gauche* one, that is, given by the rotation energy times the number of the bonds with *gauche* conformation.

The interhead interaction, V_h, is denoted by Coulomb interactions between anions and cations in the different head groups and written as

$$V_h = \sum_{I>J} \frac{q_e^2}{\epsilon_{\text{eff}}} \left[\frac{1}{|X_I - X_J|} + \frac{1}{|X_I + \mathbf{x}_I - X_J - \mathbf{x}_J|} - \frac{1}{|X_I + \mathbf{x}_I - X_J|} - \frac{1}{|X_I - X_J - \mathbf{x}_J|} \right] \tag{2}$$

where $\pm q_e$ are the effective charges of the cation and anion, X_I is the position of the cation in the Ith molecule, which is a lattice point in the two-dimensional hexagonal lattice, $\mathbf{x}_I$ is the position vector from the cation to the anion in the Ith head group, and ϵ_{eff} is the dielectric constant of solvent. The distance betweeen the neighboring head groups is $\sqrt{2}D$. The interchain interaction, V_c, is represented by using the Kihara potential (10) that has been applied to the normal paraffins (11) and enabled us to reproduce the observed temperature dependences of the second virial coefficients with a great accuracy over a wide range of temperatures. We chose a cylinder as the core of a hydrocarbon chain for the Kihara potential and assumed that the axis of cylinder was perpendicular to the plane of membrane. Then V_c is written as

$$V_c = \sum_{I>J} U_0 \left[\left(\frac{p_c}{|R_I - R_J| - r_{cI} - r_{cJ}} \right)^{12} - 2\left(\frac{p_c}{|R_I - R_J| - r_{cI} - r_{cJ}} \right)^{6} \right], \tag{3}$$

where p_c and U_0 give the position and depth of the potential minimum, R_I is the position of the Ith chain and a lattice point in the two-dimensional hexagonal lattice where the distance between the neighboring points is D, and r_{cI} is the radius of the cylinder corresponding to the Ith hydrocarbon chain.

We believe that the residual interaction, V_r, which includes the interaction between the polar head groups and water, the coupling between the two halves of a bilayer, and the hydrophobic interaction between the hydrocarbon chains, is mainly responsible for keeping the bilayer in existence. The head groups are surrounded by a number of water molecules more or less permanently hydrogen bonded to the various oxygens in the head groups and this effect cannot be explained by the dielectric constant, ϵ_{eff}, in Eq. 2. The interchain interaction potential, V_c, given by Eq. 3 does not include the hydrophobic interaction by which the hydrocarbon chains are gathered to escape from water. We represent V_r phenomenologically as a function of the distance D between the nearest neighboring chains

$$V_r = \sqrt{3} N \gamma D^2, \tag{4}$$

where N is the number of lipid molecules in the monolayer and γ corresponds to the lateral pressure per hydrocarbon chain. This form of V_r seems reasonable because the interactions that keep the bilayer in existence are not changed drastically by the gel-to-liquid crystalline phase transition (2).

Basic Equations in Thermal Equilibrium States

The thermodynamic state of a phospholipid monolayer in water is represented by conformations of a polar head group and two hydrocarbon chains in each lipid molecule and by a spatial distribution of all the lipid molecules. The spatial distribution of the lipid molecules is fixed as a two-dimensional hexagonal lattice. The internal conformations of head groups and chains are described in terms of the isomeric rotations, that is, the *trans*- and *gauche*- bond conformations. Then, it is assumed that the thermodynamic properties of the monolayer are obtained by using the density matrix ρ,

$$\rho = \frac{\exp\left[-\beta(H_h + H_c)\right]}{Tr\left\{\exp\left[-\beta(H_h + H_c)\right]\right\}}, \tag{5}$$

where $\beta = 1/k_BT$, and H_h and H_c are the intrahead and intrachain model Hamiltonians, respectively. The model Hamiltonians, H_h and H_c, are obtained from the true intrahead and intrachain Hamiltonians, H_{h0} and H_{c0}, respectively, by replacing the bond rotation energies, ϵ_{h0} and ϵ_{c0}, with the variational parameters, ϵ_h and ϵ_c, respectively. Since the free energy, $F[\rho]$, based on the model or approximate density matrix, ρ, is always greater than the true free energy (12), the optimal density matrix ρ is obtained by minimizing $F[\rho]$ with respect to ρ. Therefore, the variational parameters, ϵ_h and ϵ_c, in the present density matrix (Eq. 5) are determined so as to minimize the $F[\rho]$ of the system. The density matrix (Eq. 5) in form is equivalent to that for the isomeric bond rotational model (13) of the free polymer chains, although the meaning of ϵ is essentially different in the two models: ϵ_h and ϵ_c in the present model are not the real bond rotation energies but are the parameters that describe the density matrix and are determined by the variational principle, which states that the many calculation techniques developed for the free polymer chains (13) can be used directly in the present form.

It has been suggested that by measuring the disordered bond conformation of a hydrocarbon chain in bilayer membranes (14, 15), the steric constraints due to the packing of neighboring head groups limit the accessible conformations of the bonds near the head groups. The disorder is important in the central region of the bilayer where the presence of chain-tail ends partially remove the steric constraints. The *gauche* bond is made more easily in the chain-tail region than in the bonds near the head group. Therefore, the conformation parameter, ϵ_c, which corresponds to the bond rotation energy, should change with the bond position along a chain. To illustrate the position dependence of ϵ_c simply, we divided a hydrocarbon chain into two parts such that the bonds in the top part remained in *trans* conformation at any temperature, that is, ϵ_c was fixed at infinity, and the bonds in the tail part formed rotational isomeric conformations as determined by the single conformation parameter, ϵ_c.

The free energy of the monolayer membrane is represented as

$$F = F_0 + Tr[\rho(H - H_h - H_c)], \tag{6}$$

$$F = k_B T \ln \{Tr[e^{-\beta(H_h + H_c)}]\}. \tag{7}$$

The calculation of F was carried out using the matrix methods developed for the free polymer chains (13). The statistical weight matrices, U_h and U_c, of which the elements are the statistical weights of a two-bond sequence in a head group and a hydrocarbon chain, respectively, are denoted as

$$U_x = \begin{array}{c|ccc} & (t) & (g^+) & (g^-) \\ \hline (t) & 1 & \sigma_x & \sigma_x \\ (g^+) & 1 & \sigma_x & 0 \\ (g^-) & 1 & 0 & \sigma_x \end{array} \tag{8}$$

where

$$\sigma_x = \exp(-\beta\epsilon_x), \tag{9}$$

and x represents head group (h) or chain (c). Then, F_0 is given by

$$F_0 = -Nk_B T(\ln Z_h + 2 \ln Z_c), \tag{10}$$

$$Z_h = J_1 U_h^{n_h} J, \tag{11}$$

$$Z_c = J_1 U_c^{n_c - n_0} J, \tag{12}$$

where

$$J_1 = [1\ 0\ 0], J^t = [1\ 1\ 1], \tag{13}$$

n_h and n_c are the numbers of the bonds in a head group and a chain, respectively, and n_0 is the number of bonds in a chain near the head that remain in trans conformation at any temperature.

The second term of Eq. 6 is rewritten as

$$\begin{aligned} Tr[\rho(H - H_h - H_c)] = {} & Tr[\rho(H_{h0} - H_h)] \\ & + Tr[\rho(H_{c0} - H_c)] + Tr[\rho V_h] \\ & + Tr[\rho V_c] + Tr[\rho V_r]. \end{aligned} \tag{14}$$

The first and second terms of Eq. 14 are represented by using Z_h and Z_c as

$$Tr[\rho(H_{x0} - H_x)] = qN(\epsilon_{x0} - \epsilon_x)\sigma_x \partial(\ln Z_x)/\partial\sigma_x, \tag{15}$$

where x denotes h or c, and q is 1 for x = h and 2 for x = c. The third term in Eq. 14 is represented as

$$Tr[\rho V_h] = \frac{q_c^2}{\epsilon_{eff}} \sum_{I>J} \cdot \left(\frac{2}{|X_I - X_J|} - \frac{1}{|X_I + \langle x_0 \rangle - X_J|} - \frac{1}{|X_I - X_J - \langle x_0 \rangle|} \right) \tag{16}$$

by using the approximation of $\langle V_h(x) \rangle = V_h(\langle x_0 \rangle)$, where $\langle x_0 \rangle$ means the thermal average $Tr[\rho x_I]$ of x_I and is independent of I. The spatial arrangement of a head group in an all-*trans* conformation is shown in Fig. 1. The value of $\langle x_0 \rangle$ is obtained by using the method developed for the free chain (16–18). The fourth term of Eq. 15 is given by

$$Tr[\rho V_c] = \sum_{I>J} U_0 \cdot \left[\left(\frac{p_c}{|R_I - R_J| - 2\langle r_c \rangle} \right)^{12} - 2 \left(\frac{p_c}{|R_I - R_J| - 2\langle r_c \rangle} \right)^{6} \right]. \tag{17}$$

The thermal average $\langle r_c \rangle$ of a core radius r_{cI} is

$$\langle r_c \rangle = r_{ct} + \eta \left\{ \left[\frac{1}{2n_c} \sum_{i=1}^{n_c} (\langle r_{i1}^2 \rangle + \langle r_{i2}^2 \rangle) \right]^{1/2} - r_{ct} \right\}, \tag{18}$$

where r_{ct} is the core radius in the all-*trans* conformation, $\langle r_{i1}^2 \rangle + \langle r_{i2}^2 \rangle$ is the thermally averaged value of square distance between the ith carbon atom and the cylinder axis normal to the membrane. The value of $\langle r_{i\lambda}^2 \rangle$ is obtained by using the method for the free chain (18). The reduction factor, η, in Eq. 18 takes into account the effect of mutual penetration of carbon atoms between the two hydrocarbon chains with gauche bonds. The value of η is determined so as to reproduce the observed shift of the interchain distance, D, due to the phase transition. The final term of Eq. 14 is the same as in Eq. 4.

The values of the conformation parameters ϵ_h and ϵ_c in the head group and the chain, respectively, the values of the interchain distance D, and the values of the angles χ_h and φ_h, which determine the spatial arrangement of the head group, are obtained so as to minimize the free energy (Eq. 6).

Equations for the Physical Quantities of the System

We were able to illustrate various physical properties of lipid bilayers by using the present model in which the physical properties are represented

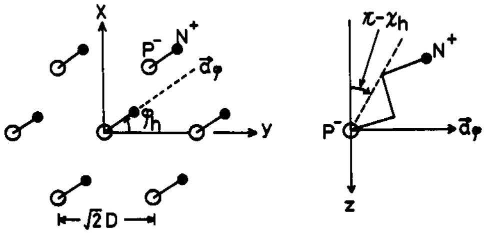

FIGURE 1 The spatial arrangement of a polar head group of an all-*trans* conformation. The x and y axes are in the plane of membrane, and the z axis is perpendicular to the plane and points from the head group to the hydrocarbon chain. $\sqrt{2}D$ is the distance between the neighboring lipid molecules.

in analytical form by using the statistical mechanics of the free polymer chains.

Order Parameter. The order parameter for the gel-to-liquid crystalline transition of the membranes in the present model is the fraction ρ_{ct} of the C—C bond with *trans* conformation in a hydrocarbon chain, since the various studies of the membranes have confirmed that the disordering of the chain conformation in the interior of the bilayer can lead to the main phase transition. The fraction ρ_{ct} is almost equal to 1 in the gel phase, whereas ρ_{ct} becomes noticeably <1 in the liquid crystalline phase. ρ_{ct} is obtained from the equation

$$\rho_{ct} = \frac{n_0}{n_c} + \frac{1}{n_c Z_c}\left\{\frac{\partial}{\partial\tau}\left[J_1(U_c E_\tau)^{n_c - n_0} J\right]\right\}_{\tau=1}, \tag{19}$$

where

$$E_\tau = \begin{bmatrix} \tau & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}. \tag{20}$$

Latent Heat and Transition Entropy. The latent heat, ΔH, accompanied by the gel-to-liquid crystalline phase transition is given by

$$\Delta H = W(T_m + 0) - W(T_m - 0), \tag{21}$$

$$W(T) = N\left(\epsilon_{h0}\sigma_h \frac{1}{Z_h}\frac{\partial Z_h}{\partial \sigma_h} + 2\epsilon_{c0}\sigma_c \frac{1}{Z_c}\frac{\partial Z_c}{\partial \sigma_c}\right) + Tr[\rho(V_h + V_c + V_r)], \tag{22}$$

where T_m is the transition temperature. The change of the entropy ΔS in the phase transition is obtained by

$$\Delta S = S(T_m + 0) - S(T_m - 0), \tag{23}$$

$$S(T) = Nk_B\left(\ln Z_h + \frac{\epsilon_h\sigma_h}{k_B T Z_h}\frac{\partial Z_h}{\partial \sigma_h} + 2\ln Z_c + \frac{2\epsilon_c\sigma_c}{k_B T Z_c}\frac{\partial Z_c}{\partial \sigma_c}\right). \tag{24}$$

Cross Section and Root Mean Square (rms) Length of a Hydrocarbon Chain. The thermally averaged mean cross section of a chain is obtained by

$$\langle A_c \rangle = \frac{\pi}{n_c}\sum_{i=1}^{n_c}\left[\langle r_{i1}^2 \rangle + \langle r_{i2}^2 \rangle\right], \tag{25}$$

where $\langle r_{i\lambda}^2 \rangle$ is the thermal average $Tr[\rho r_{i\lambda}^2]$ of $r_{i\lambda}^2$ and $r_{i\lambda}$ is the λ component of the position of the ith carbon atom in the chain. The value of $\langle r_{i\lambda}^2 \rangle$ is obtained by using the method of Flory and Jernigan (18). The rms length, L_c, of a chain is obtained by $\langle r_{i\lambda}^2 \rangle$ for $i = n_c$ and $\lambda = 3$ as

$$L_c = [\langle r_{n_c 3}^2 \rangle]^{1/2}. \tag{26}$$

Fraction of the Bonds with Trans Conformation in a Head Group. The fraction ρ_{ht} is given by

$$\rho_{ht} = \frac{1}{n_h Z_h}\left\{\frac{\partial}{\partial\tau}\left[J_1(U_h E_\tau)^{n_h} J\right]\right\}_{\tau=1}. \tag{27}$$

Thermal Expansion Coefficient. The coefficients $\zeta_\parallel$ and $\zeta_\perp$, which are parallel and perpendicular to the plane of the membrane, are

$$\zeta_\parallel = \frac{1}{D}\frac{\partial D}{\partial T}, \zeta_\perp = \frac{1}{L_c}\frac{\partial L_c}{\partial T}, \tag{28}$$

respectively, where D is the distance between the nearest neighboring chains.

Concentration of the 2gl Kinks. Conformation sequences (the 2gl kinks) such as g^+tg^- and g^-tg^+ are more favorable than another sequences including *gauche* conformations because the increase of chain radius due to *gauche*-bond formation in the form of a 2gl kink is very small compared with that in other forms. The concentration, ρ_{gtg}, of the 2gl kinks is obtained by

$$\rho_{gtg} = \left(1 - \frac{n_0}{n_c}\right)\frac{2}{Z_c}\sum_{l=1}^{n_c - n_0 - 3}\{J_1 U_c^l B_2 U_c B_1 U_c B_3 U_c^{n_c - n_0 - l - 3} J\}, \tag{29}$$

where $B_i (i = 1 \sim 3)$ is the 3×3 matrix whose elements are zero except for $(B_1)_{ii} = 1$.

Order Parameter in the Bond Orientation. The degree of order, S_3, for a spatial orientation for each C—C bond in a hydrocarbon chain is known by measuring deutrium nuclear magnetic resonance (NMR) spectra or electron spin resonance (ESR) spectra of a free radical bound to the C—C bond. The degree of order S_{3i} for the ith bond is defined (19) as

$$S_{3i} = 3/2\,\langle \cos^2\theta_{3i} \rangle - 1/2, \tag{30}$$

where θ_{3i} is the angle between the Z axis, which is perpendicular to the membrane layer, and the ζ axis, which is one of the NMR and/or ESR principal axes of the deutrium substituted in (a free radical bounded to) the ith bond. $\langle \cos^2\theta_{3i} \rangle$ is obtained by

$$\begin{aligned}\langle \cos^2\theta_{3i} \rangle = \frac{1}{Z_c}&(e_z^t \otimes e_z^t)(T_0 \otimes T_0) \\ &\cdot [T(0) \otimes T(0)]^{n_0 - 1}(J_1 \otimes E_9) \\ &\times (U_c \otimes E_9)\,\|T \otimes T\|]^{i - n_0} \\ &\cdot (E_3 \otimes e_\zeta \otimes e_\zeta)U_c^{n_c - i} J,\end{aligned} \tag{31}$$

$$e_\zeta = \sum_{j=1}^{3} \mathbf{e}_j(i) A_{j3}(i), \tag{32}$$

where $\mathbf{e}_j(i)$ is the jth unit vector in the coordinate system fixed to the ith C—C bond (13), $\otimes$ means the direct product

$$T_0 = \begin{bmatrix} -1 & 0 & 0 \\ 0 & -\cos(\theta_0/2) & \sin(\theta_0/2) \\ 0 & \sin(\theta_0/2) & \cos(\theta_0/2) \end{bmatrix}, \tag{33}$$

$$T(\phi) = \begin{bmatrix} -\cos\phi & -\cos\theta_0\sin\phi & \sin\theta_0\sin\phi \\ \sin\phi & -\cos\theta_0\cos\phi & \sin\theta_0\cos\phi \\ 0 & \sin\theta_0 & \cos\theta_0 \end{bmatrix}, \tag{34}$$

$(\Pi - \theta_0)$ is the C—C—C bond angle, E_n is the n-dimensional unit matrix

$$\| T \otimes T \| = \begin{bmatrix} T(0) \otimes T(0) & 0 & 0 \\ 0 & T(2\pi/3) \otimes T(2\pi/3) & 0 \\ 0 & 0 & T(-2\pi/3) \otimes T(-2\pi/3) \end{bmatrix}, \quad (35)$$

and $A_{jk}(i)$ is the transformation matrix element between the NMR and/or ESR principal axes and the bond fixed axes.

Polarization and Birefringence. The refractive index of the membrane in the direction perpendicular to the membrane plane $n_\perp$ differs from that in the plane $n_\|$. Birefringence $\Delta n = n_\| - n_\perp$ is calculated by using the polarization constants of hydrocarbon chains (5) as

$$n_\lambda^2 = \left(1 + \frac{8\pi}{3} N_0 \alpha_{\lambda\lambda}\right) \bigg/ \left(1 - \frac{4\pi}{3} N_0 \alpha_{\lambda\lambda}\right), \quad (36)$$

where λ is x, y, z, and N_0 is the number of pairs of chains per unit volume. The polarization constants $\alpha_{\lambda\mu}$ are obtained from the polarization constants $\alpha^0_{\lambda\mu}$ of a C—C bond as

$$\begin{aligned} \overline{\alpha} &\equiv [\alpha_{xx}, \alpha_{xy}, \alpha_{xz}, \alpha_{yx}, \alpha_{yy}, \alpha_{yz}, \alpha_{zx}, \alpha_{zy}, \alpha_{zz}] \\ &= \left\{ \frac{n_0 + 1}{2} (T_0 \otimes T_0) + \frac{n_0 - 1}{2} \right. \\ &\quad \left. \cdot (T_0 \otimes T_0)[T(0) \otimes T(0)] \right\} \overline{\alpha}_0 \\ &\quad + \sum_{i=n_0+1}^{n_c} \frac{1}{Z_c} (T_0 \otimes T_0)(J_1 \otimes E_9) \\ &\quad [(U_c \otimes E_9) \| T \otimes T \|]^{i-n_0} \\ &\quad \times (E_3 \otimes \overline{\alpha}_0) U_c^{n_c - i} J \end{aligned} \quad (37)$$

for odd n_0 and

$$\begin{aligned} \overline{\alpha} &= \frac{n_0}{2} \{ (T_0 \otimes T_0) \\ &\quad + (T_0 \otimes T_0)[T(0) \otimes T(0)] \} \overline{\alpha}_0 \\ &\quad + \sum_{i=n_0+1}^{n_c} \frac{1}{Z_c} (T_0 \otimes T_0) \\ &\quad \cdot [T(0) \otimes T(0)](J_1 \otimes E_9) \\ &\quad \times [(U_c \otimes E_9) \| T \otimes T \|]^{i-n_0} (E_3 \otimes \overline{\alpha}_0) U_c^{n_c - i} J, \end{aligned} \quad (38)$$

for even n_0, where

$$\overline{\alpha}_0^t = [\alpha^0_{xx}, 0, 0, 0, \alpha^0_{yy}, 0, 0, 0, \alpha^0_{zz}]. \quad (39)$$

The volume for the pair of chains is estimated by

$$v_{pc} = \sqrt{3} D^2 \times L_c, \quad (40)$$

and N_0 is $1/v_{pc}$. We obtain $n_\perp$ and $n_\|$ by substituting α_{zz} and $1/2(\alpha_{xx} + \alpha_{yy})$, respectively, into $\alpha_{\lambda\lambda}$ in Eq. 36.

CALCULATED RESULTS AND COMPARISON WITH EXPERIMENTS

Numerical Calculation

It is necessary to estimate the possible values of the parameters included in the present model to calculate the physical quantities described in the previous section. The bond rotation energy, which is the energy difference between the *gauche* and the *trans* conformations in a free hydrocarbon chain, has been observed and calculated (20) and is ~500 cal/mol. For the bond rotation energies ϵ_{h0} and ϵ_{c0} in the head group and the chain, respectively, we measured a value of 500 cal/mol^{-1}. The bond length, b_0, and the bond angle $(180° - \theta_0)$ are 1.3 Å and 112°, respectively. The number of the C—C bonds, n_c, in a hydrocarbon chain equals 14, 16, and 18, whereas the number n_h in the head group is fixed at 2. We estimate 6, 7, 8 for the number of the bonds, n_0, that remain in *trans* conformation at any temperature. Rothman (21) obtained reasonable results when $n_0 = 5$ and when $n_0 = 6$, and Marsh (4) also obtained reasonable results with the experiments using $n_0 = 4$. The charge of an electron is chosen as the effective charge q_e of a head group, and the dielectric constant of water is adopted as the constant ϵ_{eff} in the interhead interaction V_h. The values of the parameters U_0 and p_c in the interchain interaction potential V_c are determined as follows. It is assumed that the core of the Kihara potential for normal paraffins is a cylinder. The radius and length of the cylinder for normal paraffins in the all-*trans* conformation are $(b_0/2) \sin(\theta_0/2)$ and $n_c b_0 \cos(\theta_0/2)$, respectively. The values of U_0 and p_c for $n_c = 2\sim7$ were determined to reproduce the observed values of the second virial coefficients (11). Because we have no datum of the virial coefficients for normal paraffins when $n_c = 14$, 16, 18, we estimated the values of U_0 and p_c by extrapolating the values for $n_c = 2 \sim 7$ to the cases in which $n_c = 14$, 16, 18. Then U_0 values were 1,739, 1,834, and 1,900 k_B for $n_c = 14$, 16, and 18, respectively, and $p_c = 3.9$ A for all n_c. The value of γ in the residual interaction, V_r, was determined in order to reproduce the observed temperature, T_m, of the phase transition in the case of $n_c = 16$. We obtained $\gamma = 239$, 210, 181 dyn/cm when $n_0 = 6$, 7, 8, respectively, where we used the value (22) of T_m for diacylglycerophosphocholine. Finally the reduction factor for a thermal averaged core radius (Eq. 18) was determined in order to reproduce the observed difference (23) between the interchain distance, D, before and after the phase transition in case of $n_c = 16$. We obtained $\eta = 0.256$, 0.296, 0.377 for $n_0 = 6$, 7, 8, respectively.

The numerical calculations were made as follows. The free energy (Eq. 6) was minimized with respect to the conformation parameters, ϵ_h and ϵ_c, of the head group and chain and the interchain distance, D, at each temperature in a wide temperature range by using the SIMPLEX method (24). Then the optimal values of ϵ_h, ϵ_c, and D were obtained as functions of temperature. The various physical quantities of the membranes were obtained as functions of temperature by substituting the values of ϵ_h, ϵ_c, and D into the equations in the previous section.

Transition Temperature, Latent Heat, and Transition Entropy

The calculated values of the transition temperature, T_m, the latent heat, ΔH, and the transition entropy, ΔS, in the gel-to-liquid crystalline phase transition are listed in Table I for the membranes of lipid molecules with $n_c = 14$, 16, and 18 in the cases of $n_0 = 6$, 7, and 8, where the experimental values for glycerophosphocholines (22) are also cited for comparison. Table I shows that the calculated values for $n_0 = 7$ agree consistently well with the observed data.

The dependence of T_m on the number, n_c, of the C—C bonds becomes weaker with decreasing n_0. When $n_0 = 5$, values of T_m when $n_c = 14$, 16, and 18 become nearly equal to each other. This is consistent with the estimate (25) that the rate of variation of T_m decreases with increasing n_c, and T_m becomes nearly independent of n_c when $n_c > 22$. The dependence of T_m on n_c becomes less sensitive with decreasing γ, and T_m decreases with increasing n_c for small values of γ. There are many phospholipids (1) that have transition temperatures independent of the chain length. It is possible for the present model to reproduce the thermodynamic properties of such phospholipids.

Chapman et al. (26) have shown that a decrease in hydration of polar head groups increases the T_m. We consider the effect of the hydration in the present model through the variation of the dielectric constant, ϵ_{eff}, of the solvent in Eq. 2 and of the residual interaction, V_r, in Eq. 4. The dependences of T_m and ΔH on the value of ϵ_{eff} are shown in Fig. 2 in the case where $n_c = 16$ and $n_0 = 7$. The rather strong effect of the head group interaction, V_h, or T_m and ΔH arises from the fact that the contribution of V_h to the free energy is rather large and becomes comparable with that of the interchain interaction V_c when ϵ_{eff} decreases to 10. Then, the tendency of the head group interaction to suppress an increase of the intermolecular distance becomes appreciable. The calculated dependence of T_m on ϵ_{eff} is consistent with the observation (26). It is difficult at present to estimate the change in the value of γ due to the change in the condition of the membrane (2). Therefore we show only the calculated results for the variations of T_m and ΔH due to the change of γ. In the case where $n_c = 16$, $\gamma = 210$ dyn/cm, and $n_0 = 7$, T_m and ΔH increase by 16 K and 0.5 kcal/mol, respectively, due to the increase in γ by 20 dyn/cm.

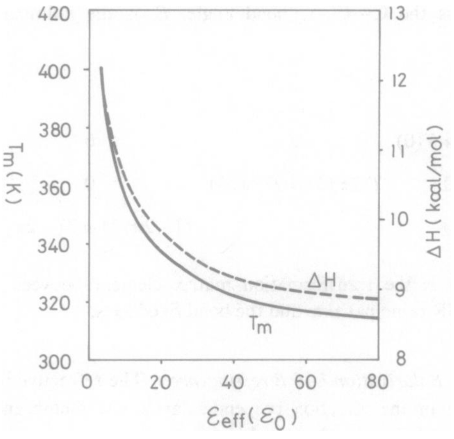

FIGURE 2 Dependence of the transition temperature, T_m, and the latent head, ΔH, on the dielectric constant, ϵ_{eff}, of the solvent in the case where $n_c = 16$ and $n_0 = 7$. ϵ_0 is the dielectric constant of the vacuum.

TABLE I
CALCULATED VALUES OF T_m(K), ΔH(kcal/mol), AND ΔS (cal/mol, deg)

	n_c								
	14			16			18		
	T_m	ΔH	ΔS	T_m	ΔH	ΔS	T_m	ΔH	ΔS
n_0									
6	298.5	7.20	24.1	314.6	10.2	32.5	323.1	13.0	40.2
7	293.5	5.58	19.0	314.6	8.88	28.2	325.8	11.8	36.2
8	279.3	3.74	13.4	314.6	7.70	24.5	333.4	11.0	33.0
Observed*	297.1	5.4	18.2	314.6	8.70	27.6	328.1	10.6	32.4

*Mabrey and Sturtevant (22).

Conformation Parameters, Intermolecular Distance, and Head Group Arrangement

The internal conformations of a head group and a hydrocarbon chain are determined by the conformation parameters, ϵ_h and ϵ_c, respectively. The dependences of ϵ_h and ϵ_c on temperature are shown in Fig. 3 for the lipids with $n_c = 14$,

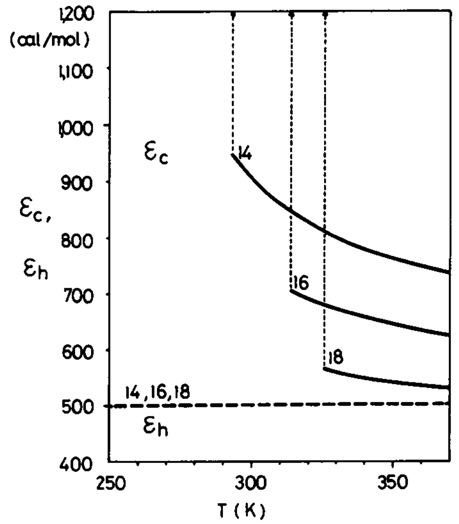

FIGURE 3 The temperature dependences of the conformation parameters ϵ_c and ϵ_h in the case of $n_0 = 7$. The solid (——) and dashed (– – –) curves are for ϵ_c and ϵ_h, respectively, and the smaller dashed lines (---) show the phase transition. The numbers above the curves denote the number of bonds n_c in a hydrocarbon chain.

16, 18 in case of $n_0 = 7$. The value of ϵ_h is always 500 cal/mol in the range of 200 ~ 400 K. This means that the probability of *gauche* conformation is the same as that for a free head group. The values of ϵ_c for $T < T_m$ are infinite and therefore the *gauche* conformations are absolutely prohibited in the gel phase. In the liquid crystalline phase, ϵ_c takes finite values and decreases with increasing temperature, that is, the C—C bonds rotate more easily at higher temperature. The value of ϵ_c at $T > T_m$ decreases with increasing n_c, that is, the longer the chain length is, the more easily the bonds rotate. However, the *gauche* conformations are less likely in the liquid crystalline phase of the lipid molecules than in a free hydrocarbon chain because the values of ϵ_c are higher than 500 cal/mol in all chains.

The temperature dependences of ϵ_h and ϵ_c in the cases of $n_0 = 6$ and 8 are qualitatively equivalent to those in Fig. 3. When the value of n_0 becomes large enough, the curve of the free energy, F vs. ϵ_c, has a single minimum value at any temperature and ϵ_c varies almost continuously with temperature. The physical meaning of this result will be discussed in the last section.

The spatial distribution of the hydrocarbon chains is determined solely by the intermolecular distance, $\sqrt{2}D$, because it is assumed that both the head groups and the chains construct a two-dimensional hexagonal lattice in both the gel and liquid crystalline phases, and that the chain axis is perpendicular to the plane of the membrane. The calculated thermal variations of D are shown in Fig. 4 in the cases where $n_c = 14$, 16, 18 and $n_0 = 7$. It has been observed (23, 27, 28) that the interchain distance, D, changes discontinuously by 0.4–1.5 A due to the gel-to-liquid crystalline phase transition. Therefore, we adjusted the value of η in Eq. 18 such that the discontinuous change of D due to the transition becomes 1.0 A for the lipid molecules of $n_c = 16$. Then, the shifts of D for $n_c = 14$ and 18 are 0.66 and 1.29 A, respectively. The magnitude of the shift increases with increasing numbers of C—C bonds, n_c. The thermal variation of D is quite small in the gel phase, whereas the interchain distance increases gradually with temperature in the liquid crystalline phase.

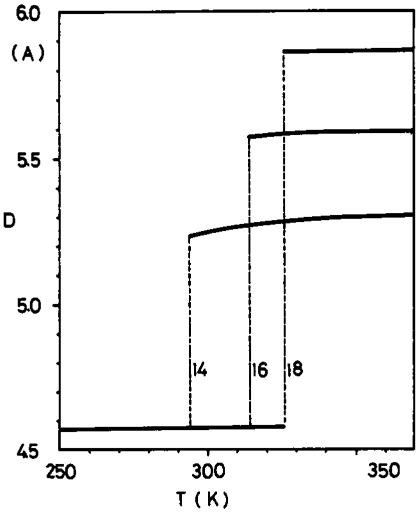

FIGURE 4 The thermal variations of the interchain distance D in the case of $n_0 = 7$. The numbers attached denote the bond number, n_c, of the chain.

The internal conformation of hydrocarbon chains depends on the packing state of the chains. As the packing is loosened, that is, the steric constriant is weakened, it becomes easier to form the *gauche* bonds. This is realized in the present model by the following mechanism. The conformation parameter ϵ_c of the hydrocarbon chain depends on the interchain distance D through the interchain interaction, Eq. 3. The relation, $D - 2\langle r_c \rangle = p_c$, between D and the core radius $\langle r_c \rangle$ of the chain is derived from the condition that the interaction energy, Eq. 17, is minimized with respect to D. Because the contribution of the interchain interaction energy to the free energy of the system is exceedingly large, the relation is always approximately realized in the membrane. The core radius $\langle r_c \rangle$ increases with D. As Eq. 18 shows the value of $\langle r_c \rangle$ increases with decreasing ϵ_c. Thus ϵ_c decreases with increasing D, that is, the number of *gauche* bonds in the chain increases with the interchain distance. The reduction factor η for the core radius (Eq. 18) also depends generally on the interchain distance with η remaining constant. This point will be discussed in the last section.

The spatial arrangement of the head group is given by the two angles, χ_h and ϕ_h, shown in Fig. 1. The values of χ_h and ϕ_h, which minimize the free energy, are $\pi/2$ and 0, respectively. The head chain of P^-—N^+ is parallel to the membrane surface and faces the nearest neighbor molecule. Experimental results (9, 29, 30) showed that the overall orientation of the head group in many phospholipids is parallel to the membrane surface both above and below the phase transition.

Order Parameter of the Phase Transition, Fraction of the *Trans* Bonds in a Head Group, Concentration of 2gl Kinks, and Order Parameter for the Bond Orientation

The fraction ρ_{ct} of the C—C bond with *trans* conformation in a hydrocarbon chain is one of the measures for the gel-to-liquid crystalline phase transitions, that is, an order parameter. The temperature dependences of ρ_{ct} for the lipid molecules with $n_c = 14$, 16, 18 are shown in Fig. 5 in the case where $n_0 = 7$. The values of ρ_{ct} are always 1.0 in the gel phase ($T < T_m$) and become abruptly 0.88, 0.82, and 0.78 at $T = T_m$ for $n_c = 14$, 16, and 18, respectively. In the liquid crystalline phase ($T > T_m$), ρ_{ct} decreases gradually with increasing temperature and also decreases with an increasing number of C—C bonds, n_c. It has been estimated from ESR (31) and NMR (14, 32) measurements that the value of ρ_{ct} is in the range of 0.70–0.85. Nagle and Wilkinson (33) have shown from density measurements that the discontinuous changes, $\Delta\rho_{ct}$, at the main transition temperature T_m are 0.22, 0.23, and 0.20,

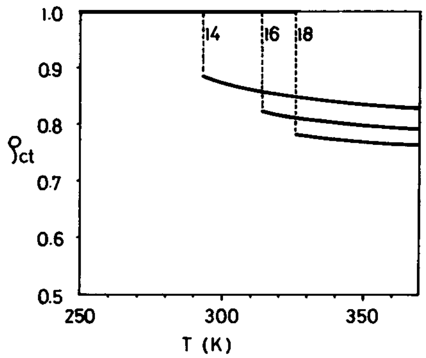

FIGURE 5 The temperature dependences of the fraction ρ_{ct} of the *trans* bonds in a hydrocarbon chain for $n_c = 14, 16, 18$ in the case of $n_0 = 7$. The numbers above the curves denote the value of n_c.

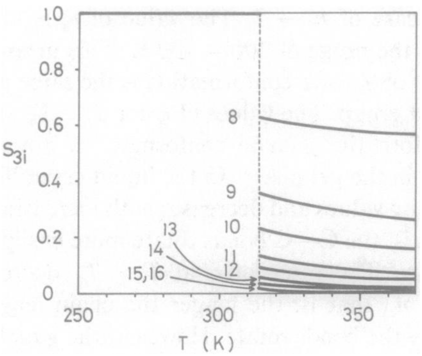

FIGURE 6 The temperature dependences of the order parameters S_{3i} for the bond orientation in a hydrocarbon chain with $n_c = 16$ as a function of the bond position i in the case of $n_0 = 7$. The numbers given denote the value of i.

when $n_c = 14$, 16, and 18, respectively. The calculated results agree well with the observed results. The calculated temperature dependence of ρ_{ct} below T_m is consistent with the observed result (14) that the conformation of the chains is almost independent of temperature. However, it has been estimated (33, 34) that the chain has one or two *gauche* bonds at T near and below T_m, whereas there exists no *gauche* bond below T_m in the calculation as seen in Fig. 5. The reason for the disagreement will be considered in the last section.

The calculated temperature dependence of the fraction ρ_{ht} of the *trans* bond in a head group does not depend on the bond number, n_c, of the hydrocarbon chains. The values of ρ_{ht} decrease almost exponentially with increasing temperature. The values in the temperature region near the phase transition are ~0.6 and decrease gradually. This is consistent with the findings of Vaz et al. (35) who concluded based on NMR data that head groups do not change their conformation as the temperature is varied, even when the phase transition is traversed. Akutsu (36) has shown based on the analysis of the infrared and Raman spectra that the O—C—C—N$^+$ chains of phospholipids are in the *gauche* conformation in both the gel and liquid crystalline phases. This calculated result is also consistent with our conclusion.

We calculated the temperature dependence of the concentration of the 2g1 kinks, ρ_{gtg}, in the hydrocarbon chains when $n_c = 14$, 16, 18, and $n_0 = 7$ by using Eq. 29. There is no kink below T_m. The value of ρ_{gtg} changes discontinuously at $T = T_m$ by 0.04, 0.09, and 0.16 when $n_c = 14$, 16, and 18, respectively, and increases gradually with temperature. Seelig and Niederberger (14) have shown from analysis of deutron labeling NMR spectra that $\rho_{gtg} = 0.08$. Schindler and Seelig (32) estimated ρ_{gtg} for DPPC ($n_c = 16$) as 0.04 based on the model of Marcelja (37). Therefore, our calculated result is reasonable.

The order of parameter S_{3i} for bond orientation in the hydrocarbon chains when $n_c = 14$, 16, and 18 is calculated as a function of the bond position i and temperature by using Eq. 30. The result for the temperature dependence of S_{3i} is shown for lipid when $n_c = 16$ as a function of i in Fig. 6, where $n_0 = 7$, and we chose $A_{j3}(\mathrm{i})$ such that the value of S_{3i} becomes 1.0 in the *trans* conformation. Mely et al. (15) found that the temperature dependence of S_{3i} is quite weak below T_m. The calculated result is consistent with our observation. The calculated values of S_{3i} for $\mathrm{i} \geq 8$ change discontinuously at $T = T_m$ and decrease gradually with increasing temperature. Hubbel and McConnell (31) observed the discontinuous decrease of S_{3i} at the transition temperature. The calculated dependence of S_{3i} on the bond position i is shown for the lipids with $n_c = 14$, 16, and 18 at a temperature just above T_m in Fig. 7. The value of S_{3i} is constantly 1.0 in the region of $i = 1{\sim}7$ and decreases sharply with increasing i. The value of S_{3i} for $\mathrm{i} \geq 8$ decreases at $T > T_m$ with increasing chain length (n_c). The observed order parameters $S_{3,ob}$ for the bond orientation

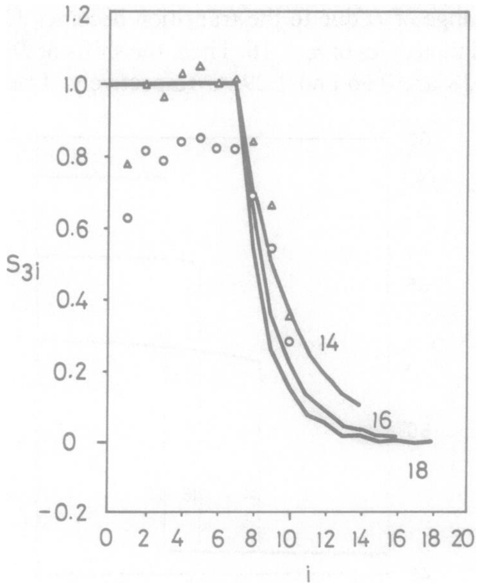

FIGURE 7 The dependence of S_{3i} on the bond position i at T just above the transition temperature in the case of $n_0 = 7$. The numbers given above the curves denote the value of n_c. The open circles and triangles (0, Δ) represent the observed data scaled by $S_0 = 0.7$ and 0.57, by Seelig and Niederberger (14).

consists of two such multiplicative components (14, 38, 39) where one, S_{3i}, is due to the *trans-gauche* isomerization and the other, S_0, is due to the reorientation of entire chain with respect to the bilayer normal, that is, $S_{3,ob} = S_{3i} \times S_0$. Because we only consider the isomeric disorder of S_{3i} in the nontilted chains, the deuterium-label order parameter, $S_{3,ob}$, observed by Seelig and Niederberger (14) is scaled by a factor S_0 for comparison of the calculated S_{3i} with the observed data. The observed values of S_{3i} scaled by $S_0 = 0.7$ (14) and $S_0 = 0.57$ (38, 39) are also shown in Fig. 7 by open circles and triangles, respectively. The reasonable agreement between the calculated and observed S_{3i} is obtained for $S_0 = 0.57$.

Cross Section and Length of a Hydrocarbon Chain and Thermal Expansion Coefficients

The thermally averaged mean cross section $\langle A_c \rangle$ of hydrocarbon chains with $n_c = 14, 16, 18$ are calculated by using Eq. 25 in case of $n_0 = 7$ as a function of temperature. The values of $\langle A_c \rangle$ are held constant at 0.8 A^2 below T_m and increase discontinuously by 13, 26, and 40 A^2 when n_c = 14, 16, and 18, respectively, at T_m, and gradually increase with increasing temperature above T_m. Note that the observed cross section of a hydrocarbon chain does not correspond to $\langle A_c \rangle$ but rather to $\sqrt{3}D^2/2$, which is the area of the membrane surface per chain. The values of $\sqrt{3}D^2/2$ at temperature just above T_m are 23.7, 26.9, and 29.7 A^2 for n_c = 14, 16, and 18, respectively. Therefore, the chains with $n_c = 18$ in the membrane penetrate each other at $T > T_m$ and the chains with $n_c = 16$ just touch each other.

The chain length, L_c, is calculated for n_c = 14, 16, 18 by using Eq.26 in the case where $n_0 = 7$ as a function of temperature, T. The value of L_c is independent of T in the gel phase and equals 15.2, 17.3, 19.4 A when n_c = 14, 16, 18, respectively. The length L_c changes discontinuously at T_m and decreases gradually with increasing temperature. The value of the change in L_c at T_m is 2.9, 4.7, and 6.9 A for n_c = 14, 16, and 18, respectively. The observed changes in membrane thickness (26, 32, 40, 41) are in the range of 7–12 A, that is, the changes in the thickness of a monolayer are 3.5–6 A. Because the contribution of the head group to the change seems small, the calculated values are in a good agreement with the experiments.

The volume of a membrane is calculated by $V = 2\sqrt{3}ND^2L_c$. The volume increases $\Delta V/V$ because the gel-to-liquid crystalline phase transition is 6.6, 6.1, and 5.5% for n_c = 14, 16, and 18, respectively. The observed value (32) is 2.9, 3.8, and 4.3%. The calculated values of $\Delta V/V$ are rather sensitive to the value of n_0. They are 10, 14, and 16% when $n_0 = 8$ and 0, −2, and −4% when $n_0 = 6$. The result for $n_0 = 7$ is the most probable with respect to the volume change.

The temperature dependence of the thermal expansion coefficients $\zeta_\parallel$ and $\zeta_\perp$, which are situated parallel and perpendicular to the membrane plane, is calculated for n_c = 14, 16, and 18 by using Eq. 28 in the case of $n_0 = 7$. The result is shown in Fig. 8. The values of $\zeta_\perp$ and $\zeta_\parallel$ just above T_m are -1.9×10^{-3} and 4.9×10^{-4}/°C, respectively, for $n_c = 14$, -1.0×10^{-3} and 1.3×10^{-4}/°C for n_c = 16, and -5.1×10^{-4} and 2.6×10^{-5}/°C for $n_c = 18$. The values of both $|\zeta_\perp|$ and $\zeta_\parallel$ decrease with increasing n_c and T. The value of $\zeta_\perp$ is 0 below T_m. The experimentally determined linear thermal expansion coefficients for several lipid membranes in the liquid crystalline phase are -2×10^{-3}/°C (43) and 1.0×10^{-3}ml/g°C (33). The calculated value corresponding to them is $(\zeta_\perp + 2\zeta_\parallel)$ and the values obtained become negative for the three chains. Marcelja (37) calculated $\zeta_\perp$ based on his model and obtained $\zeta_\perp$ between -2×10^{-3}/°C and -3×10^{-3}/°C for $n_c = 10$. The values of $\zeta_\perp$ in the present calculation seem reasonable above T_m, but not so below T_m. The values of $\zeta_\parallel$ are reasonable if the true value of $(\zeta_\perp + 2\zeta_\parallel)$ is on the order of -1×10^{-3}/°C, but they are too small if the true value is on the order of 1×10^{-3}/°C.

Polarization Constants and Birefringence

The temperature dependence of the polarization constants of hydrocarbon chains is calculated by using Eq. 37 where the values of $\alpha^{O}_{\lambda\lambda}$ (λ = x, y, z) are obtained by using (5, 44) $\alpha^{O}_{\lambda\lambda} = \alpha^{CC}_{\lambda\lambda} + 2\alpha^{CH}_{\lambda\lambda}$, where $\alpha^{CC}_{\lambda\lambda}$ = 0.07, 0.07, 1.38 A^3 and $\alpha^{CH}_{\lambda\lambda}$ = 0.60, 0.60, 0.82 A^3 for λ = x, y, z, respectively. The result is shown in Fig. 9 for n_c = 14, 16, and 18 in case of n_0 = 7. The polarization constants $\alpha_\parallel = (\alpha_{XX} + \alpha_{yy})/2$ parallel to the membrane plane increase discontinuously due to the phase transition, whereas those $\alpha_\perp = \alpha_{zz}$ perpendicular to the plane decrease. The temperature dependence of the birefringence Δn is calculated by using $\alpha_\parallel$ and $\alpha_\perp$ and is shown in Fig. 10. It is reasonable to assume that the value of Δn is larger in the gel phase than in the liquid crystalline

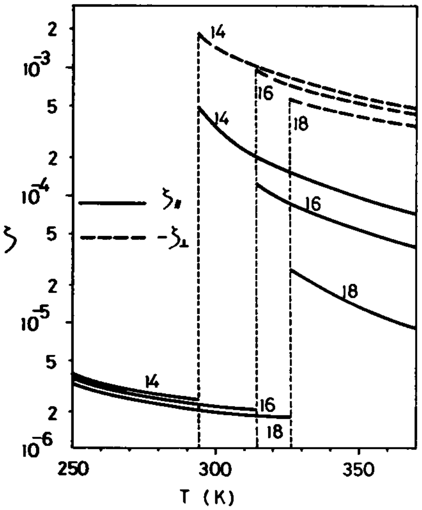

FIGURE 8 The temperature dependences of the thermal expansion coefficients $\zeta_\parallel$ and $\zeta_\perp$ situated parallel and perpendicular to the membrane plane for n_c = 14, 16, and 18 in case of n_0 = 7. The values of $\zeta_\perp$ below T_m are 0.

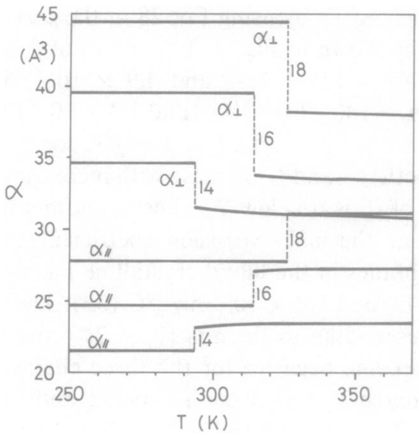

FIGURE 9 The temperature dependences of the polarization constants $\alpha_\parallel$ and $\alpha_\perp$ situated parallel and perpendicular to the membrane plane for n_c = 14, 16, 18 in the case of n_0 = 7.

phase because the structural anisotrophy of the membrane becomes much smaller due to the phase transition. The observed value (45) is 0.022 at room temperature. The calculated values are larger than the observed values by several factors.

DISCUSSION

The self-consistent chain model illustrates well and consistently most of the observed properties of the lipid bilayer membranes. However, the model is far from perfect for several reasons:

(*a*) It is assumed that the statistical probability for the internal conformations of a hydrocarbon chain is determined only by the conformation parameter ϵ_c,

(*b*) It is assumed that the first n_0 bonds in the hydrocarbon chain are fixed in the *trans* conformation,

(*c*) The assumption that the lipid molecules are distributed in a two-dimensional hexagonal lattice even in the liquid crystalline phase is made for simplicity,

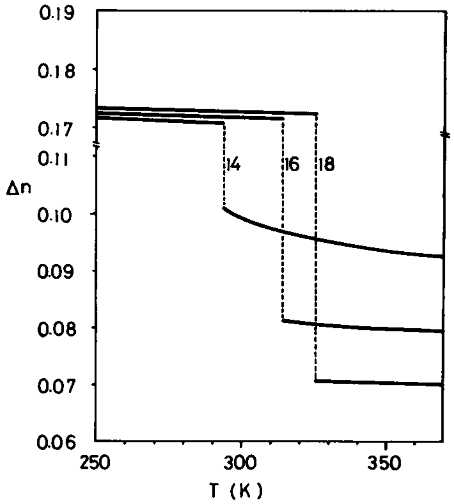

FIGURE 10 The temperature dependences of the birefringence Δn for n_c = 14, 16, and 18 in the case n_0 = 7.

(*d*) The model fails to give a proper account of the temperature dependences of the fraction of the *trans* bonds, ρ_{ct}, below T_m and of the thermal expansion coefficients, $\zeta_\perp$ and $\zeta_\parallel$, below T_m.

Even if the conformation parameter ϵ_c is determined self-consistently by taking the interchain interaction into account, it is unavoidable for a hydrocarbon chain in the membrane to adopt a large-area conformation of relatively low internal energy with the same statistical probability as in a free hydrocarbon chain with the bond rotation energy of ϵ_c. The neighboring chains of such large-area conformations should avoid each other due to the steric repulsion in the membranes. Some bonds of one chain penetrate into vacant spaces due to kink formations of the other chains. In the present model the effect of such a mutual penetration due to the cooperative steric repulsion of the gel-to-liquid crystalline phase transitions has been partially taken into account by introducing the core reduction factor η in Eq. 18. The factor η may be interpreted as a measure of the cooperativity in the conformational change of the hydrocarbon chains. The cooperativity becomes stronger as η decreases. Another attempt to consider the effect of the cooperative steric repulsion is to change the position of ϵ_c as a function of the bond position i along a chain. The value of ϵ_c may become larger in the region near the head group and smaller in the tail region. The position dependence of ϵ_c in the single chain was approximated in the present model by a single step function in order to reproduce the essential features of the membranes using a simple function and to save time computationally.

As the chains spread out, it became easier to bend them. We considered the chain-spreading effect in the present model through the interchain interaction (Eq. 17) and the definition of the core radius (Eq. 18) as mentioned in the previous section. For the chain-spreading effect it seems useful to consider the dependence of the core reduction factor, η, on the interchain distance, D. The mutual penetration decreased with increasing D. We examined several such functional forms of D for η as η_0, η_0/D; η_0/D^2, $1 - \exp(-D\eta_0)$ and $D\eta_0$, , where η_0 is an adjustable parameter. It was found that by comparing the calculated values of T_m, ΔH, and ΔS with the observed results, the simplest form $\eta = \eta_0$ gave the most reasonable results for all three lipids with n_c = 14, 16, and 18.

The failures described in the model, more specifically those mentioned in *d*, arose mainly from the assumption given in *b*. When the free energy F is minimized by changing the number n_0 of the fixed bonds, F decreases for $n_0 = 12$ in the temperature region of 250–300 K in the case of n_c = 16. Then the value of ϵ_c is between 900 and 800 cal/mol and ρ_{ct} is between 0.94 and 0.92. When the temperature changes from 250 to 300 K, the value of the interchain distance increases from 4.75 to 4.79 A. Then the thermal expansion coefficient $\zeta_\parallel$ becomes 0.2×10^{-3}/°C. Therefore a more reasonable description of the membranes in the gel phase may be obtained if the free energy is decreased with respect to n_O adding to ϵ_c and D. However, the minimization has been made with respect to only ϵ_c and D, because computations are time consuming.

It is not clear how much assumption *c* concerning the molecular distribution in the liquid-crystal phase affects the results. However, this effect is not essential because the short-range arrangement of the lipid molecules in the liquid crystalline phase seems to be the same as in the gel phase (9).

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