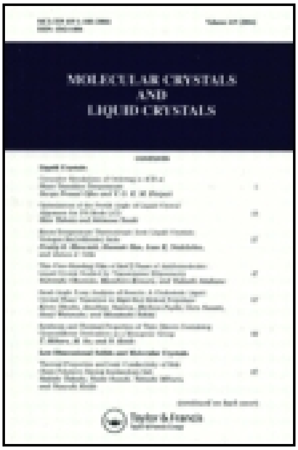

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# Statistical Mechanical Theory for Hydrophobic Core of Lipid Bilayer†

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A partition function is proposed for the molten hydrocarbon chains in the hydrophobic region of a lipid bilayer. In the construction, constancy of the volume of the bilayer is accepted as well as constancy of the density within the hydrophobic range when increasing the area of the bilayer. Marčelja's method[1] for determining the inter- and intramolecular interactions was used. The distribution of the lateral pressure along the thickness of the bilayer and the elasticity modulus of the bilayer (without taking into account the electrostatic interactions between the heads) were determined. Explicite calculations were made for lipids with one and two saturated alkyl chains with 12 carbon atoms per chain.

## INTRODUCTION

Some papers[1-19] propose statistical mechanical descriptions of monolayers and bilayers built up of amphiphilic molecules. The models used in these works make various simplifying assumptions stressing one or another important properties of the system. In Nagle's model[2] excluded volume interactions are the most important and the intermolecular attractions are taken in a simple mean field way. The rotational isomeric model of Flory[18] is applied.

In Marčelja's work[1] the most important is the orientational van der Vaals intermolecular interaction. One improved version of this model[39] takes into account the dependence of this interaction on the distance from the heads of the building molecules.

In his paper[3] Marsh has accepted, in essence, that in the molten state of the bilayer only conformations of the "kink" type are possible and uses Flory's rotational isomeric model to make statistical mechanical calculations to ob-

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tain some of the quantities connected with the main transition. Similar ideas have been used in an earlier work of Seelig and Niederberger.[30]

Scott in a series of papers[4–7] developed two different models. Assuming a restricted number of molecular conformations, he considers the effects of steric repulsion between molecules.

In the model of Dupin *et al.*[8] and Firpo *et al.*[9] the molecules are represented by a system of rectangles lying on one plane; it has been shown that this system undergoes phase transitions.

McCammon and Deutch[10] emphasize the cooperativity of conformational isomer generation. A maximum number of gauche$^\pm$ bonds between adjacent $CH_2$ groups is supposed per one hydrophobic chain.

Jackson[11] has introduced the interesting idea of a "forcing kink" and has accepted that the mean volume taken up by one molecule depends on its conformational state.

Bothorell *et al.*[12] have considered the effects of the excluded volume interactions in a monolayer of amphiphilic molecules with a comparatively short (6 carbon atoms) hydrophobic chain. They have used the rotational isomeric model of Flory for polymers too. As will be seen below, there are elements in their work common to the approach proposed by us.

In their model for phase transitions in mono- and bilayers Caille *et al.*[13] have considered two or more possible molecular conformations, every conformation having a fixed area, and on this basis have built the partition function.

Almost all of the models mentioned above try to give an explanation of the main transition—the melting of the hydrophobic chains. It is well known that this transition is accompanied by an increase in the volume of the hydrophobic region.

According to[21,22] the increase is 2.3–5%.

Even the highest values show comparatively little change of the volume. This suggests that if we stretch a bilayer with molten hydrophobic chains (Figure 1), its volume will change insignificantly. This means that a model neglecting this change will be highly realistic. In different forms this idea has been used by a number of authors.[23–26]

The fact that in the model with an unshrinkable hydrophobic core Young's modulus $E_Y$ (if we consider the bilayer as a solid body) is much lower than the bulk modulus of the liquid paraffin should be an indirect confirmation that this model is adequate to the real bilayer. We have tried to use this model applying many of the ideas described above.

## DESCRIPTION OF THE MODEL

In our model the molecules building up the bilayer consist of a hydrophilic head and one saturated unbranched hydrophobic alkyl chain having 12 car-

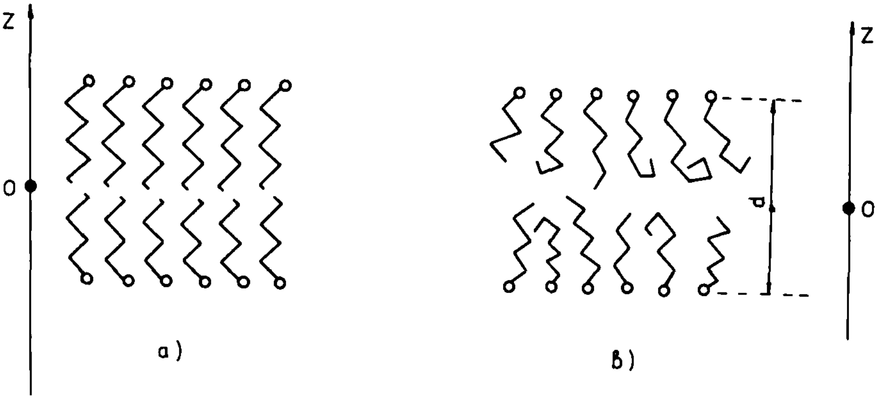

FIGURE 1 (a) Gel state of the membrane (below the phase transition); (b) Liquid crystalline state of the membrane (above the phase transition).

bon atoms. The lipids forming bilayers have usually two hydrophobic chains and more carbon atoms per chain. Because we were doing computer calculations, a higher number of carbon atoms could have increased very much the computational time (about three times for every additional carbon atom). We apply the results of our work to molecules with two hydrocarbon chains making the additional approximation that these two chains are entirely independent.

For the lateral pressure the following definition is used:

$$P_{\mathrm{lat}} = \int_{-\infty}^{\infty} (\sigma_z - p)\,dz \tag{1}$$

where $\sigma_z$ is the tangential component of the pressure in a point with a coordinate $Z$ (see Figure 1) and $p$ is the common three-dimensional pressure, acting out of the membrane. Only the case of a flat bilayer has been considered in this work, so that curvature effects are absent.

The heads of the amphiphilic molecules are considered to be spherical in shape, so that they will not be put under any orientational Van der Vaals interaction. The heads lie in two planes (one per each monolayer of the bilayer). Because of their spherical shape and disposition they will interact like hard disks with a radius equal to that of the sphere (almost the same approach to the interaction between the heads is used by Jacobs *et al.*[18, 19]). We have used to a great extent the ideas of these works. The statistical mechanical model, applied by us is similar to that of Marčelja.[1] To determine the difference between the energies of the trans and gauche$^{\pm}$ states of the bonds between two adjacent $CH_2$ groups we use the rotational isomeric model of Flory.[20] Between two adjacent $CH_2$ groups the angle can be only 0° (trans) or $\pm 120°$ (gauche$^{\pm}$). In our opinion this approximation is proper at a temperature above the phase transition, while at lower temperatures (when the membrane is in gel-state) the properties of the membrane depend on the form of the potential wells of the energy around 0° and ±120°. Such a dependence of the energy of the bond on the angle between two adjacent $CH_2$ groups is proposed by Pechhold *et al.*[27] We use the values for the differences of the energies between trans and gauche$^{\pm}$ bonds as they are applied by Marĉelja,[1,28] namely, for the sequences $(t, g^{\pm})$ and $(g^{\pm}, g^{\pm})$ – 400 cal/mole and for the sequences $(g^{\pm}, g^{\mp})$ – 1800 cal/mole. Via the last higher value we take into account the fact that at the sequence $(g^{\pm}, g^{\mp})$ the energy increases because two $CH_2$ groups have to be very near in space.

For the disposition of the nearest to the head bonds we make the following assumptions. The bond between the head and the first C atom will be considered as a bond between two $CH_2$ groups. Because the head is a sphere in our model there is no need to specify if this bond is trans or gauche. The bond forms an angle of 35,3° with the normal to the bilayer. For the second carbon atom we accept two possibilities: it lies either on the normal to the bilayer passing through the head or in a plane parallel to the membrane and passing through the first carbon atom. The other carbon atoms are arranged according to the rotational isomeric model of Flory.[20] The only restriction on them is to be in the hydrophobic region. With positions of the first and the second carbon atoms chosen in this way all the other carbon atoms are located on equidistant planes, parallel to the membrane. We denote the distance between them with $\epsilon$.

Let us pass a normal to the plane determined by the carbon atom nearest to the head and the two hydrogen atoms belonging to it. The angle that this line forms with the normal to the bilayer will be used by us as a measure of the head tilt. In the real case the head can change its tilt (defined as above) in the continnum set between 0° and 90°. In our model this angle can take two values—0° and 60°. Unlike the model of Marĉelja[1] in our model we will not impose in advance any order parameter of the head—it will be obtained as a function of the applied lateral pressure (and it will be higher than that used by Marĉelja).

To determine the weights of both tilts permissible in our model, we make the next considerations. If the tilt of the head is between 0° and 30°, we accept it is 0°, and if the tilt is between 30° and 90°, we accept it is 60°. Consequently, the configurations with a tilt of 60° must be multiplied with a factor taking into account how much bigger the solid angle between 30° and 60° is than that between 0° and 30°. But this is not enough. When the head has a tilt of 0° every configuration can be rotated around the axis of the head at an angle of 0°–360°. At a tilted configuration such a rotation cannot always be realized because at some angles part of the hydrophobic chains could go out of the hydrophobic region. Moreover, we intuitively feel that there are some sterical restrictions on the tilted conformations. To take into account these restrictions, we diminish this factor three times. The value used in our calculations is 2.155.

Let the distance $d$ (Figure 1) between the planes, on which lie the heads of the amphiphilic molecules building up the bilayer is a whole number times $\epsilon$. All the quantities of the system are calculated for such thicknesses of the bilayer, and the results obtained are interpolated with arbitrary thicknesses.

If the lipid building bilayer has $n$ carbon atoms per chain, it is clear that the distance between the planes, on which lie the heads, is not larger than $2n + 1$ times $\epsilon$.

We replace every $CH_2$ group of the chain with a disk having an area of $S_{CH_2}$:

$$S_{CH_2} = \frac{V_{CH_2}}{\epsilon} \tag{2}$$

Here $V_{CH_2}$ is the volume of one $CH_2$ group.

By analogy the terminal $CH_3$ group is replaced by a disk with an area of $S_{CH_3}$:

$$S_{CH_3} = \frac{V_{CH_3}}{\epsilon} \tag{3}$$

where $V_{CH_3}$ is the volume of the $CH_3$ group.

We accept that the density of the hydrophobic core is constant. It follows that each unit area of the planes on which lie the carbon atoms, contains such a mean number of disks whose area is independent of the position of the plane in the bilayer. Moreover, if the bilayer changes its thicknesses due to some applied force and does not change its density in the hydrophobic core, the mean area of the disks per unit area of the planes on which the carbon atoms lie must be independent of the bilayer thickness too.

Let the thickness of the bilayer be $d$ and the frame of reference be located so that the axis $Z$ is normal to the bilayer, and the center of the coordinate system be in the middle of the bilayer. Let the number of planes on which the carbon atoms are located be $\alpha$. Let for simplicity the three dimensional hydrostatic pressure be zero. Then the full lateral pressure in accordance with formula (1) can be presented as follows:

$$P_{\text{lat}} = \int_{-d/2}^{d/2} \sigma_z dz + \int_{-\infty}^{-d/2} \sigma_z dz + \int_{d/2}^{\infty} \sigma_z dz \tag{4}$$

where $\sigma_z$ is the density of the lateral pressure per unit length along $Z$.

Let

$$\gamma = \int_{-\infty}^{-d/2} \sigma_z dz = \int_{d/2}^{\infty} \sigma_z dz \tag{5}$$

We interpret $\gamma$ as the free energy per unit area of the oil-water interface. In our model

$$\int_{-d/2}^{d/2} \sigma_z dz = \sum_{\beta=1}^{\alpha} \pi_\beta + \Pi \tag{6}$$

where $\alpha$, as was mentioned above, is the number of planes, on which the carbon atoms lie, and $\pi_\beta$ is the lateral pressure on a plane with a number $\beta$. $\Pi$ is the lateral pressure due to the interactions between the heads.

Let $n$ be the number of the carbon atoms per chain of the hydrophobic tail. To make the statistical calculations we have to write the Hamiltonian of the system. Let our bilayer consist of $2N$ molecules, $N$ per every monolayer. Let $r^{2N}$ be the set of all $X$-$Y$ co-ordinates of the centers of the heads in the frame of reference as introduced above, $\Omega^{2N}$ be the conformations (the manifold of all trans and gauche$^\pm$ bonds between the adjacent $CH_2$ groups) of the molecules and $\theta^{2N}$ and $\varphi^{2N}$ be the tilts of the heads and the asimutal angles for every molecule. Then, the Hamiltonian of the system of molecules building up the bilayers following Jacobs *et al.*[18,19] can be written in the form:

$$H(r^{2N},\Omega^{2N},\theta^{2N},\varphi^{2N}) = H_{\text{head}}(r^{2N}) + H_{\text{disp}}(r^{2N},\theta^{2N},\varphi^{2N},\Omega^{2N}) + H_{\text{int}}(\Omega^{2N}) \tag{7}$$

The first term takes into account the fact that the heads interact like hard disks. If the area of the disk is less than the area of the minimal cross section of the hydrophobic chain we shall ascribe to it the area of this minimal cross section, otherwise it will have its own area. Let us denote the so defined area of the disk with $A_0$. If the mean area per disk is $A$, the molecular dynamics calculations give the high density expansion for the partition function $q_{HD}$ and for the hard disk pressure $P_{HD}$. The expressions for these quantities are:[29,18]

$$q_{HD} = (l^2/\rho_0)^N \exp[N(0{,}06 + 0.1l + 0.385l^2 + \cdots)] \tag{8}$$

$$P_{HD}A/k_BT = 2/l + 1.90 + 0.67l + 1.5l^2 + \cdots \tag{8a}$$

where $l = (A - A_0)/A_0$. The expansion in $l$ is truncated to the second order for $P_{HD}A/k_BT$ as given in (8a).

So, considering the first right-hand side term of Eq. (7) we accept it as independent of the other, and via Eq. (8a) we take into account its contribution. We point out, that $\Pi$ from (6) is equal to $P_{HD}$ in our model.

Our aim is to investigate mainly the behavior of the alkyl chains. That is why we consider the interactions between the heads in a comparatively simple form—as a repulsion between hard disks.

Certainly there are other interactions with a more complicated origin which we have disregarded. They are reviewed briefly in Gruen's paper[39] and include electrical interactions, hydrogen bonds between the heads and interactions due to the specific chemical structure. The heads are neither rigid, nor with a circular cross section (we expect they are eliptical in shape). Nevertheless we think this way of consideration gives a true order of magnitude of the interaction between the heads. The minimal cross section of the heads $A_0$ can be considered to be an adjustable parameter, with which we can fit the experimental value of the mean area per molecule in the bilayer.

The other terms in the Hamiltonian concern only the interactions between the hydrophobic chains: $H_{\text{int}}$ is the internal energy depending on the number and the location of the trans and gauche$^{\pm}$ bonds in the chains; $H_{\text{disp}}$ is the orientational van der Vaals intermolecular interaction. They are considered in a mean field approximation. For this purpose we consider one molecule located in the mean field formed by the adjacent molecules. Following Marĉelja[1] the energy of interaction $E^i$ of one hydrophobic chain (in its $i$-th conformation) with this field and the interaction between the adjacent $CH_2$ groups are:

$$E^i = E^i_{\text{int}} + E^i_{\text{disp}} + E^i_p \tag{9}$$

$E^i_{\text{int}}$ is the internal energy depending on the number and the location of the trans and gauche$^{\pm}$ bonds in the chain. Again following Marĉelja[1]

$$E^i_{\text{disp}} = -\phi \sum_{j=1}^{n-1} \left(\tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2}\right) \tag{10}$$

$\theta_j$ is the angle between the normals to the plane of the bilayer and to the plane determined by the $j$-th (counted from the head) carbon atom and the hydrogen atoms belonging to it.

The sum is obtained from the methylene groups only. The $CH_3$ group is accepted as entirely spherical and not giving any contribution in the orientational interaction:

$$\eta = \frac{1}{n-1}\left\langle \sum_{j=1}^{n-1} \left(\tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2}\right)\right\rangle \; ; \; \phi = V_0\eta \tag{11}$$

$n$ is the number of carbon atoms per chain. In formula (10) we do not include the factor $n_{tr}/n$ used by Marĉelja.[1] The explicit calculations are made with a value of the coupling constant $V_0 = 680$ cal/mole—used by Marĉelja. The most important part of our model is the determination of $E_p$. According to Marĉelja $E_p = P.A$, where $P$ is the lateral pressure and $A$ is the area ascribed to every conformation in a special way. In our model we start from the requirement that on each of the planes on which the carbon atoms lie, the density of the disks should be constant. Let the lateral pressure on a plane with a number $\beta$ be $\pi_\beta$ and let the area of the disks on this plane in the $i$-th conformation of the molecule be $S_{\beta i}$. Then for the energy $E^i_p$ we use the expression:

$$E^i_p = \sum_{\beta} \pi_\beta S_{\beta i} \tag{12}$$

The pressures $\pi_\beta$ must be chosen so as to ensure the above requirement. We note that there are planes on which lie carbon atoms from molecules belonging to both monolayers of the bilayer.

The partition function for the chain (not including the interaction between the heads) is:

$$q_{\text{chain}} = \sum_{\text{all conf.}} \exp(-E_i/k_B T) \tag{13}$$

The self-consistent equation for the molecular field $\phi$ is:

$$\phi = \frac{V_0}{n-1} \sum_{\text{all conf.}} \left[ \sum_{j=1}^{n-1} \left(\tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2}\right) \right] \exp[-E_i(\phi, \pi_\alpha)/k_B T]/q_{\text{chain}} \tag{14}$$

The solution of this equation depends on the choice of the parameter $V_0$. The fact that we do not introduce the factor $n_{tr}/n$, used by Marĉelja, does not eliminate the dependence of $\eta$ on $V_0$. The general partition function of the system of $2N$ molecules building up the bilayer at constant lateral pressure and thickness is (assuming the interactions between the heads to be independent):

$$Q = [q_{\text{chain}}(\delta, \bar{A})]^{2N} \tag{15}$$

$\bar{A}$ is the mean area per molecule in the bilayer, $\delta$ is the effective lateral pressure, acting on the hydrophobic core: $\delta = P_{\text{lat}} - 2P_{HD}$ and $P_{\text{lat}} = 2\gamma$ for the "natural" state of the membrane when outer forces are not applied to it (see (5)).

The Gibbs potential per chain $G$ is:

$$G(\delta, \bar{A}) = \frac{1}{2N}[-k_B T \ln \{Q(\delta, \bar{A})\}] + \tfrac{1}{2}\phi \sum_{j=1}^{n-1} \left< \tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2} \right>$$

$$= -k_B T \ln (q_{\text{chain}}) + \tfrac{1}{2}\phi \sum_{j=1}^{n-1} \left< \tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2} \right> \tag{16}$$

The term $\frac{1}{2}\phi \sum_{j=1}^{n-1} \left< \frac{3}{2}\cos^2\theta_j - \frac{1}{2} \right>$ has to take into account that interchain interaction is not counted twice in the internal energy. And because $\bar{A}$ is an internal parameter, $G$ must have a minimum in the dependence on this parameter. Consequently:

$$\frac{\partial G}{\partial \bar{A}} = 0 \tag{17}$$

$G(\bar{A})$ depends on $\bar{A}$ via the number $\alpha$ of planes on which lie the carbon atoms. For $\bar{A} = 2V/\alpha\epsilon$, where $V$ is the volume of the hydrophobic chain, $G$ can be represented in the form:

$$G(\delta,\bar{A}) = -k_BT \ln\left\{\sum_{\text{all conf.}} \exp\left[-\left(E^i_{\text{int}} + E^i_{\text{disp}} + \sum_{\beta=1}^{\alpha} \pi^0_\beta S_{\beta i} + \sum_{\beta=1}^{\alpha}\frac{\delta}{\alpha}S_{\beta i}\right)\Big/k_BT\right]\right\} - \tfrac{1}{2}\phi\sum_{j=1}^{n-1}\left<\tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2}\right> \tag{18}$$

where

$$\pi^0_\beta = \pi_\beta - \frac{\delta}{\alpha} \tag{19}$$

and

$$\delta = \sum_{\beta=1}^{\alpha}\pi_\beta \tag{20}$$

$$\sum_{\beta=1}^{\alpha}\frac{\delta}{\alpha}S_{\beta i} = \frac{\delta}{\alpha}\sum_{\beta=1}^{\alpha}S_{\beta i} = \frac{\delta}{\alpha}\frac{V}{\epsilon} = \frac{\delta\bar{A}}{2} \tag{21}$$

We use the expression (21) for all the values of $\bar{A}$. Then

$$G(\delta,\bar{A}) = -k_BT \ln\left\{\sum_{\text{all conf.}} \exp\left[-\left(E^i_{\text{int}} + E^i_{\text{disp}} + \sum_{\beta=1}^{\alpha} \pi^0_\beta S_{\beta i}\right)/k_BT\right]\right\} - \tfrac{1}{2}\phi\sum_{j=1}^{n-1}\left<\tfrac{3}{2}\cos^2\theta_j - \tfrac{1}{2}\right> + \frac{\delta\bar{A}}{2} = F_0(\bar{A}) + \frac{\delta\bar{A}}{2}$$

If we know the values of $F_0(\bar{A})$ for all the values of $\bar{A}$, the condition (17) will take the form:

$$\frac{\partial F_0(\bar{A})}{\partial\bar{A}} + \frac{\delta}{2} = 0 \tag{21a}$$

Substituting $\delta$ we get the equality $[\delta = P_{\text{lat}} - 2P_{HD} = 2(\gamma - P_{HD})]$:

$$\frac{\partial F_0(\bar{A})}{\partial\bar{A}} = P_{HD}(\bar{A}) - \gamma \tag{22}$$

Let a lateral pressure $P^0_{\text{lat}}$ be applied. We can suppose that $\gamma$ will not change. Then if the system is in equilibrium equation (22) will take the form $[P_{\text{lat}} = 2\gamma + P^0_{\text{lat}}$ and $\delta = 2(\gamma - P_{HD} + P^0_{\text{lat}}/2)]$:

$$\frac{\partial F_0(\bar{A})}{\partial\bar{A}} = P_{HD}(\bar{A}) - \gamma - \frac{P^0_{\text{lat}}}{2} \tag{23}$$

$$P^0_{\text{lat}}(\bar{A}) = 2\left[-\frac{\partial F_0}{\partial\bar{A}} + P_{HD}(\bar{A}) - \gamma\right] \tag{23a}$$

$P^0_{\text{lat}}$ will change the area $\bar{A}$. Consequently, the steric interaction $P_{HD}(\bar{A})$ will be changed too.

The main problem is the determination of the dependence $F_0(\bar{A})$. We calculated $F_0(\bar{A})$ for 10 values of $\bar{A}$ when $V_0 = 680$ cal/mole when $\alpha$ is a whole number. The values for an arbitrary $\bar{A}$ are obtained via the interpolation with a function of the kind:

$$F_0(\bar{A}) = \sum_{i=1}^{m} \frac{a_i}{\bar{A}^{i-1}} \quad m = 10$$

The parameters $a_i$ are chosen so that for the ten special values of $\bar{A}$ mentioned above the values of $F_0(\bar{A})$ are equal to those calculated below.

We made a computer program calculating the values of $F_0(\bar{A})$, $\pi^0_\beta$ and the order parameter for every $CH_2$ group. First we assigned values $\pi^0_\beta = 0$ for all $\beta$ and $\alpha$, and arbitrary values to the molecular field $\phi$. Having calculated $\pi^0_\beta$ we do not know yet $\delta (\delta = \sum_\beta \pi_\beta)$. By definition $\sum_\beta \pi^0_\beta = 0$. $\delta$ can be determined only through the derivative $\partial F_0(\bar{A})/\partial \bar{A}$ [formula (21a)]. An iterative procedure was done to determine such values of $\pi^0_\beta$ and $\phi$ that the uniform population of the planes and the self-consistent Eq. (14) were reached with accuracies 3% and 0,5% respectively. This was done with 25 iterations, each one being 1h 30 minutes long. The calculations were done with an EC 10-22 computer (with a performance similar to that of IBM 360).

## RESULTS AND DISCUSSION

The temperature used is $T = 303°\text{K} = 30°\text{C}$. The $CH_2$ and $CH_3$ groups have volumes (Luzzati *et al.*[31]) of: $V_{CH_2} = 27\text{Å}^3$, $V_{CH_3} = 54\text{Å}^3$. The value of $A_{\min} = 20{,}4\text{Å}^2$ found by the same authors is used for the area of the minimal cross-section of one saturated hydrocarbon chain. Then the distance $\epsilon$ between two adjacent planes, on which lie the carbon atoms, is:

$$\epsilon = \frac{V_{CH_2}}{A_0} = \frac{27}{20.4} = 1{,}32\,\text{Å}$$

The value for $\epsilon$ used by D. Gruen[39] is slightly different—$\epsilon = 1{,}25$ Å. Having in mind that he uses for the volumes of one $CH_2$ group and one $CH_3$ group the same values as ours, it can be concluded that the areas of the disks in our model have to be increased by about 5,6%. This should decrease the values of $\pi^0_\beta$, calculated by us by the same percent and should stretch the axis corresponding to the area/molecule in the diagram $P_{\text{lat}}$ vs. area/molecule by 5,6%. We do not know the origin of the value of $\epsilon$, chosen by D. Gruen. Maybe it is connected with the fact that the cross section of the all-trans chain is 20,4 Å$^2$ in the frozen state of the chains, while Gruen's model (ours too) is for the molten states of the chain. Our calculations were made with the value $\epsilon = 1{,}32$ Å.

According to our model the hydrophobic core is homogenous and with flat boundaries. If the molecule has $n$ carbon atoms in the chain, the hydrophobic core can consist of not more than $2n$ planes. The minimal area per molecule will then be:

$$S_{\min} = \frac{(n-1)A_{\min} + 2A_{\min}}{n} = \frac{n+1}{n} A_{\min} \tag{24}$$

We have done our calculations for a hydrocarbon chain with 12 carbon atoms. Then

$$S_{\min} = \frac{13}{12} \times 20.4 = 22.1\ \text{Å}^2 \tag{24a}$$

For the values of $F_0(\bar{A})$ and $\pi^0_\beta(\bar{A})$ the results are in Tables I and II.

We note that $\pi^0_\beta = \pi^0_{(\alpha-\beta)}$ for $\beta > \alpha$.

It can be seen that the lateral pressure behaves irregularly as a function of the layer index $\beta$. But this is a complicated system, whose density must be kept constant and we think there are no evidences that regular behavior is to be expected. The distribution of the lateral pressure along the thickness of the membrane can be eventually proved via adsorption of small hydrophobic molecules into the bilayer.

The results predicted by our model for the order parameter of the different $CH_2$ groups for some values of the mean area per molecule are presented in Figure 2. The order parameters depend in our model only on the mean area per chain. This dependence is expressed via $\alpha$—the quantity that determines the thickness of the bilayer, and at the same time the area per alkyl chain because of the constancy of the volume of the chain.

The $P'_{\text{lat}} - \bar{A}$ diagrams for one and two chains per molecule, and for a different value of the areas of the heads are plotted in Figure 3.

$$P'_{\text{lat}} = -\partial F_0(\bar{A})/\partial \bar{A} + P_{HD}(\bar{A})$$

The obtained results give the possibility to calculate an interesting parameter of the membrane—its elastic modulus of compressibility:

$$E = \bar{A}\,\frac{\partial P^0_{\text{lat}}}{\partial \bar{A}} = -2\bar{A}\,\frac{\partial^2 F_0}{\partial \bar{A}^2} + 2\bar{A}\,\frac{\partial P_{HD}(\bar{A})}{\partial \bar{A}}$$

TABLE I

Dependence of $F_0$ on the mean area per molecule $\bar{A}$. For the meaning of $F_0(\bar{A})$ see the text.

| $\bar{A}$(Å$^2$) | 23.06 | 24.11 | 25.26 | 26.52 | 27.92 | 29.47 | 31.2 | 33.15 | 35.36 | 37.89 |
|---|---|---|---|---|---|---|---|---|---|---|
| $\dfrac{F_0(\bar{A})}{k_BT}$ | 7.1927 | 7.1750 | 7.1253 | 7.0739 | 7.0289 | 6.9913 | 6.9579 | 6.9289 | 6.9037 | 6.8770 |

## TABLE II

Dependence of the lateral pressure $\pi_\beta^0$ on the thickness of the bilayer and the position of the plane in it. $\alpha$ is the total number of planes (within the bilayer), on which are situated the carbon atoms. $\beta$ is the number of these planes, counted from one of the planes, on which are situated the heads of the molecules.

| $\beta$ \ $\alpha$ | 23 | 22 | 21 | 20 | 19 | 18 | 17 | 16 | 15 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2.85 | 2.69 | 2.12 | 1.35 | 0.552 | −0.171 | −0.803 | −1.34 | −1.77 | −2.14 |
| 2 | −1.46 | −1.41 | −1.14 | −0.866 | −0.640 | −0.448 | −0.285 | −0.165 | −0.038 | −0.106 |
| 3 | −1.73 | −1.61 | −1.27 | −0.932 | −0.672 | −0.503 | −0.420 | −0.346 | −0.526 | −0.561 |
| 4 | −1.01 | −0.681 | −0.34 | −0.114 | −0.005 | 0.013 | −0.041 | −0.322 | −0.345 | 0.005 |
| 5 | −0.648 | −0.390 | −0.250 | −0.252 | −0.373 | −0.436 | −0.986 | −0.908 | −0.353 | 0.240 |
| 6 | −0.597 | −0.495 | −0.516 | −0.640 | −0.692 | −1.38 | −1.04 | −0.202 | 0.536 | 1.00 |
| 7 | −0.189 | −0.269 | −0.482 | −0.67 | −1.64 | −0.916 | 0.235 | 1.09 | 1.51 | 1.56 |
| 8 | 0.475 | 0.080 | −0.369 | −1.58 | −0.270 | 1.12 | 1.93 | 2.19 | 1.99 | |
| 9 | 1.77 | 0.711 | −0.910 | 0.777 | 2.16 | 2.72 | 2.66 | | | |
| 10 | 1.99 | −0.317 | 1.66 | 2.93 | 3.16 | | | | | |
| 11 | −1.15 | 1.69 | 3.00 | | | | | | | |
| 12 | −0.59 | | | | | | | | | |

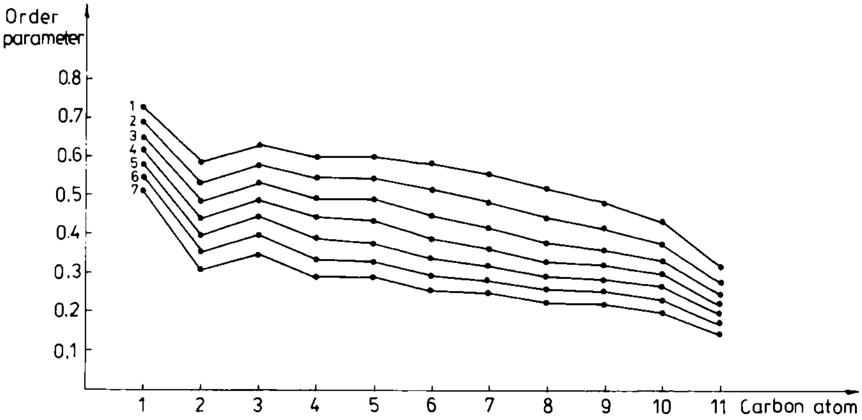

FIGURE 2 Order parameter at different mean area $\bar{A}$ per chain as a function of a position along the chain: 1. $\bar{A} = 26.52\,\text{Å}^2$; 2. $\bar{A} = 27.92\,\text{Å}^2$; 3. $\bar{A} = 29.47\,\text{Å}^2$; 4. $\bar{A} = 31.2\,\text{Å}^2$; 5. $\bar{A} = 33.15\,\text{Å}^2$; 6. $\bar{A} = 35.36\,\text{Å}^2$; 7. $\bar{A} = 37.89\,\text{Å}^2$.

For different areas of the heads of molecules with two hydrophobic chains the values of the elasticity modulus are shown in Figure 4.

Let use compare the theoretical results with the experimental data.

It is known from the NMR data[32] that the $CH_2$ group nearest to the head has a higher order parameter—after that follows "saturation"—some $CH_2$ groups have almost the same order parameter and after that it sharply decreases. Such behavior is achieved in the Marčelja model.[1] Our model, having many common features with that of Marčelja, shows the same behavior of the order parameter as Marčelja. In accordance with the experiment the order parameter of the first carbon atom is higher than the plateau. The calculated order parameters depend highly on the thickness of the bilayer. To compare them wth the experimentally measured order parameters, we should have additional information for the thickness, for example, from X-ray scattering. If we accept the area per molecule to be $70\text{Å}^2$ ($35\text{Å}^2$ per chain),[40,41] $\alpha$ will be 15.

It is interesting to compare the elasticity modulus of the bilayer, predicted by our model, with the available experimental results. The elasticity modulus of a bilayer has not very often been measured. Usually, conclusions are made for the elasticity of the bilayer from the elasticity modulus of compressibility of monolayers at the oil-water or air-water interface. No doubt some relation between monolayers and bilayers exists, but we stress the great difference between them. In the monolayer at the oil-water interface, for example, the molecules of the oil can freely penetrate into the regions, where the density of the lateral pressure is negative. And they will penetrate until this density becomes positive (because of the reservoir of hydrophobic molecules without attached ends). That is why we think that the elasticity of the bilayer must be considerably higher than that of the monolayer at the oil-water interface.

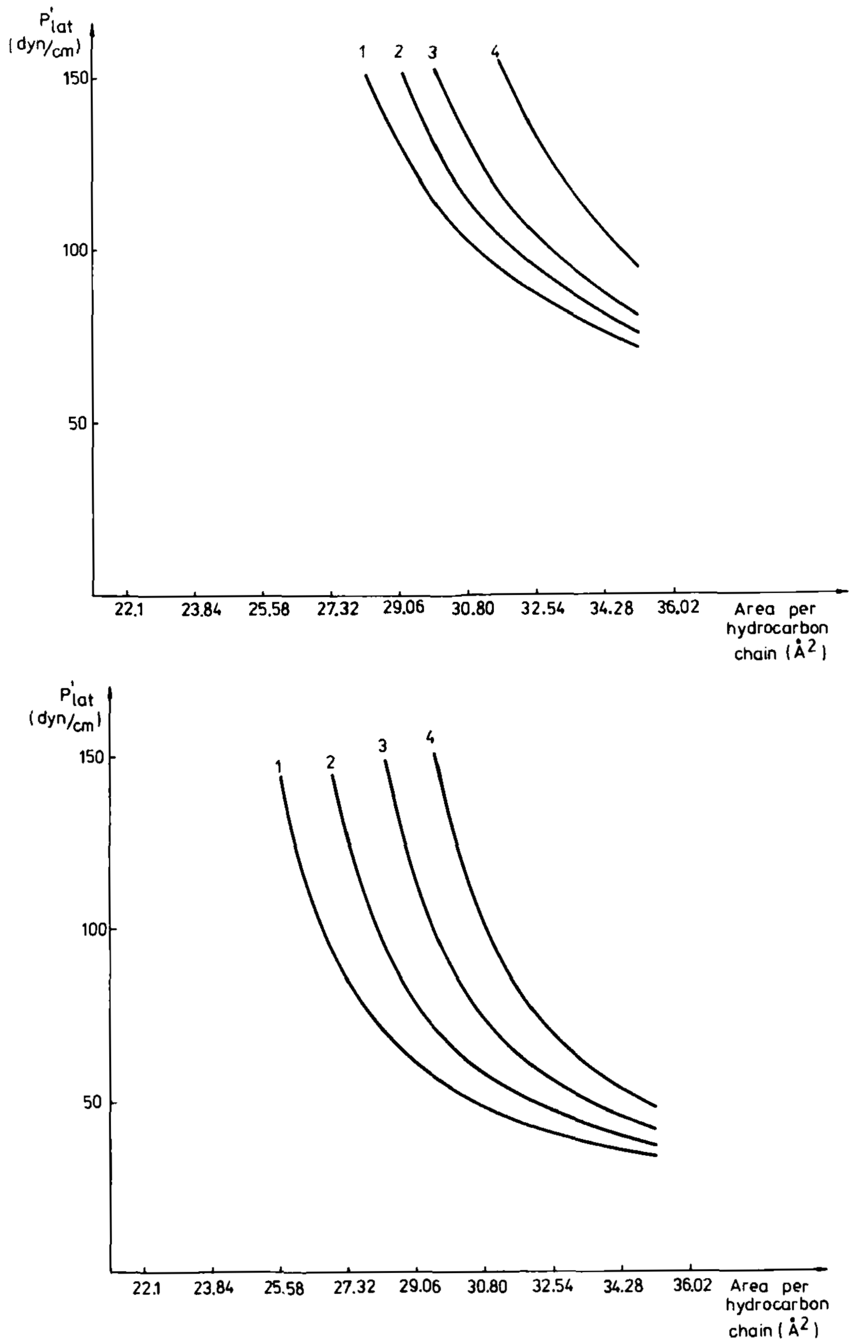

FIGURE 3 $P'_{lat} - \bar{A}$ diagrams, calculated according to our model. $P'_{lat} = -\partial F_0(\bar{A})/\partial\bar{A} + P_{HD}(\bar{A})$ (a) one hydrophobic chain: 1. $A_0 = 22.97$ Å$^2$; 2. $A_0 = 23.84$ Å$^2$; 3. $A_0 = 24.71$ Å$^2$; 4. $A_0 = 26.45$ Å$^2$; (b) two hydrophobic chains: 1. $A_0 = 45.94$ Å$^2$; 2. $A_0 = 48.55$ Å$^2$; 3. $A_0 = 51.16$ Å$^2$; 4. $A_0 = 53.77$ Å$^2$; With $A_0$ we denote the area of the head (for the definition of this area see the text).

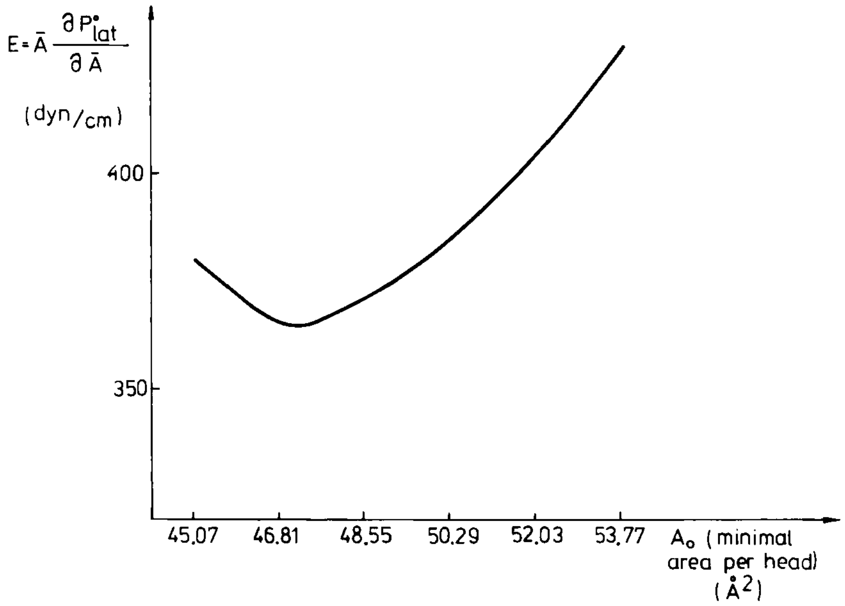

FIGURE 4 Elasticity modulus $E = \bar{A}\partial P^0_{lat}/\partial\bar{A}$ as a function of the minimal area $A_0$ per head in the "natural" state of the membrane (i.e. when $P^0_{lat} = 0$).

For a bilayer consisting of lipid molecules with two alkyl chains having 12 carbon atoms per chain as can be seen from Figure 4, the elasticity modulus varies from 365 dyn/cm to 440 dyn/cm. Its dependence on the minimal area per head has a minimum at 47.2 Å$^2$. The mean area per head corresponding to this minimal area is 62.4 Å$^2$. In their recent work[42] Kwok *et al.* have measured the elasticity modulus of lecithin bilayers. They have found the value of 99 ± 22 dyn/cm. We have no information on what kind of lecithin was used in their experiment. Probably this was egg-yolk lecithin. The middle number of carbon atoms per chain in the egg-yolk lecithin is more than 12, and above all there are double bonds. That is why we expect the results for the dilauril lecithin elasticity modulus to be higher. Our elasticity modulus is about 400 dyn/cm. This value is of the same order as that of Kwok *et al.*,[42] and the measured elasticity of the erythrocyte membrane.[33,34] Above all, we expect that the including of electrical interactions will decrease the elasticity modulus.

Some conclusions can be made for membranes built from lipid molecules with one hydrophobic chain. Figure 3a shows that these membranes are absolutely unstable at lateral pressures on the bilayer of less than 60 dyn/cm. Consequently, they cannot exist if $\gamma = 50$ dyn/cm. The experiment shows that till now bilayer membranes from amphiphilic molecules with one hydrophobic chain are produced only as vesicles.[37] These vesicles are stable only when a large enough part of the molecules have uncharged hydrophilic heads (the charges of the heads reduce $\gamma$).

The behavior of the membrane when the electrical effects are included is still being studied.

We also intend to apply our approach to cylindrical and spherical micelles.

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