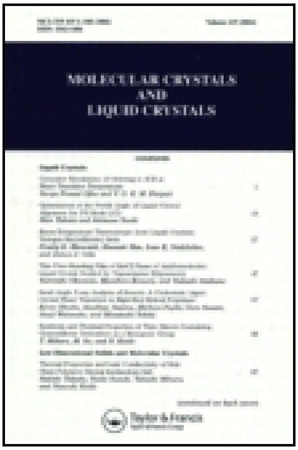

Molecular Crystals and Liquid Crystals Incorporating Nonlinear Optics

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl17

Curvature Elasticity Moduli of Bilayer Lipid Membranes

Isak Bivas [a]

[a] Institute of Solid State Physics, Bulgarian Academy of Sciences, Liquid Crystal Department, 72 Lenin Blvd., Sofia, 1784, BULGARIA

Version of record first published: 13 Dec 2006.

To cite this article: Isak Bivas (1987): Curvature Elasticity Moduli of Bilayer Lipid Membranes, Molecular Crystals and Liquid Crystals Incorporating Nonlinear Optics, 152:1, 311-326

To link to this article: http://dx.doi.org/10.1080/00268948708070961

Mol. Cryst. Liq. Cryst., 1987, Vol. 152 pp. 311-326
Photocopying permitted by license only

Printed in the United States of America

CURVATURE ELASTICITY MODULI OF BILAYER LIPID MEMBRANES

ISAK BIVAS
Institute of Solid State Physics, Bulgarian Academy of Sciences, Liquid Crystal Department, 72 Lenin Blvd., Sofia 1784, BULGARIA

Abstract It has been shown how the sum of curvature elasticity moduli $2k_c+\bar{k}_c$ of a bilayer lipid membrane (the symbols are the same as these used by Helfrich[1]) can be obtained, if the distribution of the lateral pressure along the thickness of the membrane is known, and the volume of the hydrophobic part of the membrane is kept constant. Cases of free and blocked flip-flop have been considered. A relation between the elasticity moduli of a bilayer and its constituent monolayers has been drawn for an arbitrary bilayer in which the chains of both monolayers do not interpenetrate each other. On the basis of a model previously worked out by us[2], numerical results of $(2k_c+\bar{k}_c)$ have been obtained. A comparison has been carried out with existing experimental results.

INTRODUCTION

According to Helfrich[1] the elastic free energy of curvature per unit area of curved bilayer lipid membrane w_c is:

$$w_c = \frac{1}{2}k_c(c_1 + c_2 - c_o)^2 + \bar{k}_c c_1 c_2 \qquad (1)$$

where c_1 and c_2 are the principal radii of curvature at the point where we determine w_c, k_c and $\bar{k}_c$ to be the curvature elasticity moduli conjugated to both scalars (c_1+c_2) and c_1c_2, which are connected with the deformation. The expression (1) includes all terms up to the second power of c_1 and c_2; c_o expresses the asymmetry of the bilayer, i.e. the difference in energy when the bilayer is curved to different sides. We consider only symmetric bilayers for which $c_o=0$, and will restrict our attention to the cases: $c_1=c_2=c$, for which

$$w_c = (2k_c+\bar{k}_c)c^2 + O(c^4) \tag{2}$$

There are several theoretical and experimental works[3-12] dealing with the problem of determining these phenomenological curvature elasticity coefficients. The case of membranes with free flip-flop is considered theoretically by Helfrich[3] and Israelachvili[4] the latter having neglected the interactions between the hydrophobic chains. Helfrich[3] has examined the general case, assuming the plane densities on both monolayers to be equal. From a thermodynamic point of view, however, the requirement that the total free energy should have a minimum is more appropriate. This requirement is being satisfied in this work.

PHENOMENOLOGICAL RELATIONS CONNECTING THE ELASTICITY OF LIPID BILAYER WITH THE ELASTIC PROPERTIES OF ITS MONOLAYERS

We consider a symmetric bilayer lipid membrane consisting of molecules of one kind with a well defined boundary surface S between its two monolayers . For a spherically curved monolayer with an area "a" per molecule on the surface S, and a hydrostatic pressure in the volume phase to the side of the heads equal to the hydrostatic pressure in the volume phase when the bilayer is flat, the dependence of the free energy per molecule on the curvature c of the surface S can be written in a phenomenological form:

$$f^{mol}(a,c) = f^{mol}(a,0) + 2M(a)c + N(a)c^2 \tag{3}$$

Let the number of molecules per unit area of the flat symmetric bilayer with zero lateral pressure be $2K_o$. When it is not curved, every monolayer has K_o molecules. We denote one of the monolayers as first and the other as second. c is accepted to be positive if it tries to expand the first monolayer (i.e., if the center of curvature is to the side of the second monolayer). Let the number of molecules in the first monolayer be K_1 and in the second K_2, so that $K_1+K_2=2K_o$. We denote:

$$x = \frac{K_1-K_2}{2K_o} \; ; \; K_1+K_2 = 2K_o \tag{4}$$

Then $$K_1 = K_o(1+x); \quad K_2 = K_o(1-x) \tag{5}$$

Let us take a portion of the surface S with an area A=1 when the bilayer is flat and tension free. After curvature this area will be changed, and because of the symmetry of the membrane, the area will be an even function of c, i.e.:

$$A(c) = A(0)(1+\alpha c^2) + O(c^4) = 1 + \alpha c^2 + O(c^4) \tag{6}$$

The value of α can be calculated from the condition for the hydrostatic pressures on both sides of the membrane to be equal to the hydrostatic pressure in the volume phase when the bilayer is flat.

Let

$$a_o = \frac{1}{K_o} \tag{7}$$

a_o is the area per molecule on S in a flat bilayer with zero tension. Let a_1 and a_2 be the areas per molecule on S in the first and second monolayer. Then:

$$\begin{aligned} a_1 &= \frac{1+\alpha c^2}{K_1} = a_o(1+\alpha c^2)(1-x+x^2) \\ a_2 &= \frac{1+\alpha c^2}{K_2} = a_o(1+\alpha c^2)(1+x+x^2) \end{aligned} \tag{8}$$

The total free energy of curvature $w_c(c,x)$ of the bilayer per portion of S having area A=1 in the flat state is:

$$w_c(c,x) = K_1 f^{mol}(a_1,c) + K_2 f^{mol}(a_2,c) - 2K_o f^{mol}(a_o,0) \tag{9}$$

By substituting K_1 and K_2 from (5) and a_1 and a_2 from (8) into (9), expanding in Taylor's series up to x^2, xc and c^2, and using that $\left.\frac{\partial f^{mol}(a,0)}{\partial a}\right|_{a=a_o} = 0$, from (9) we get:

$$w_c(c,x) = \\ = \frac{2}{a_o}\left\{ \left(\frac{1}{2}a_o^2 \left.\frac{\partial^2 f^{mol}(a,0)}{\partial a^2}\right|_{a=a_o}\right)x^2 + \left(M(a_o) - a_o \left.\frac{\partial M}{\partial a}\right|_{a=a_o}\right)cx + N(a_o)c^2\right\} \tag{10}$$

Equation (10) is basic to our work. It allows us to connect

$(2k_c+\bar{k}_c)$ from (2) with M and N (cf eq.3) of the monolayer.

I. Blocked flip-flop. Then x=0 and:

$$w_c(c) = \frac{2}{a_o}N(a_o)c^2 \tag{11}$$

II. Free flip-flop. Then x is an internal parameter and:

$$\frac{\partial w_c(c,x)}{\partial x} = 0 \tag{12}$$

This is equivalent to the requirement that the chemical potentials of the molecules in the first and in the second monolayer be equal.

From (10) and (12):

$$x = -\frac{M(a_o)-a_o \left.\frac{\partial M}{\partial a}\right|_{a=a_o}}{a_o} c \tag{13}$$

and

$$w_c(c) = \frac{1}{a_o}\{2N(a_o) - \frac{\left(M(a_o)-a_o \left.\frac{\partial M}{\partial a}\right|_{a=a_o}\right)^2}{(a_o)^2 \left.\frac{\partial^2 f^{mol}(a,0)}{\partial a^2}\right|_{a=a_o}}\}c^2 \tag{14}$$

Comparing (11) and (14) with (2) we conclude that:

$$(2k_c+\bar{k}_c)^{blocked} = \frac{1}{a_o}2N(a_o) \tag{15}$$

$$(2k_c+\bar{k}_c)^{free} = \\ = \frac{1}{a_o}\{2N(a_o) - \frac{\left(M(a_o)-a_o \left.\frac{\partial M}{\partial a}\right|_{a=a_o}\right)^2}{(a_o)^2 \left.\frac{\partial^2 f^{mol}(a,0)}{\partial a^2}\right|_{a=a_o}}\} \tag{16}$$

Formulae (15) and (16) can be obtained if we superimpose the requirement that the area of the dividing surface between both monolayers comprising the bilayer does not change when the bilayer is curved. This additional requirement will change only the quantity α of (8). As can be seen from (10), in the second order of accuracy to c for a symmetric bilayer $w_c(c,x)$ and consequently $(2k_c+\bar{k}_c)$,do not depend on α. This is used later on in the paper, where the quantities M and N are calculated on the basis of a concrete model.

CALCULATION OF THE SUM OF THE ELASTICITY MODULI $(2k_c+\bar{k}_c)$ IF THE DISTRIBUTION OF THE LATERAL PRESSURE ALONG THE THICKNESS OF THE MEMBRANE IS KNOWN

The distribution of the density of the lateral pressure was calculated along the thickness of the bilayer consisting of molecules of two saturated alkyl chains, each chain having 12 carbon atoms[2]. This distribution was obtained after assuming that the volume of the hydrophobic part remains constant. The aim of this model[2] was to calculate the stretching elasticity modulus of the bilayer. We assumed that the heads of the molecules interact only sterically, like hard discs. When the bilayer is flat, the position of the plane in which the heads interact plays no role. But this is not so when the bilayer is curved. There are in principle two possibilities: the heads interact either in a plane coinciding with the boundary of the hydrocarbon region (Fig.1a), or in a plane at some distance s from this boundary (Fig.1b). In the present work we consider only the former. We disregard the latter because the interactions between the heads in our model are very simplified, and there is no use complicating them only in one point.

We assume once again that the volume of the hydrophobic region and the density of the material in it are kept constant when curving the bilayer.

In a flat membrane all the directions perpendicular to its normal are equivalent. The only curved state with the same property is the spherically deformed bilayer. This is why it is only the combination $(2k_c+\bar{k}_c)$ (cf eq.2) that can be obtained by using the earlier calculated results[2].

Because we consider only symmetric bilayers, we choose the surface dividing both monolayers of the bilayer as the keeping its area surface whose curvature is to be measured. The reason for this choice is given at the end of the previous section. Let us first assume that the chains of both monolayers do not interpenetrate one another. After this we will discuss the case when this is not true.

We divide the hydrophobic region of one of the monolayers of the bilayer into n layers with equal volumes via planes which are parallel to the bilayer when it is flat. The whole membrane is curved spherically so that the area A

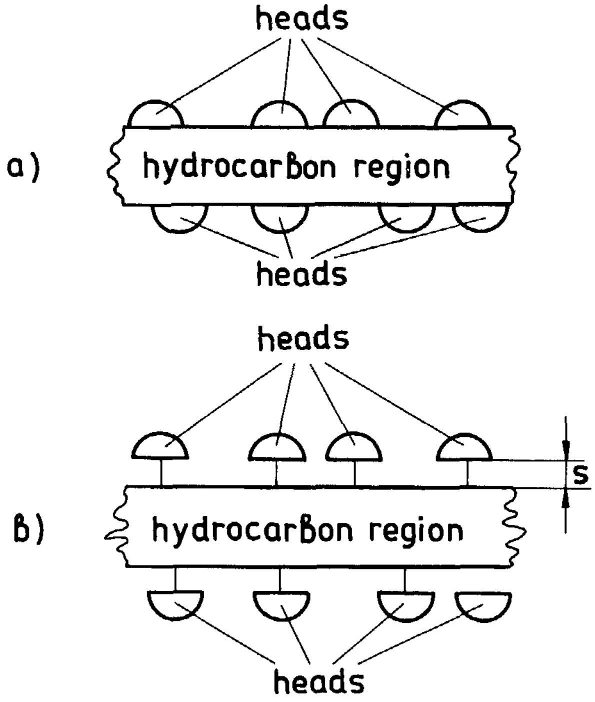

FIGURE 1. Different possibilities of disposition of the plane on which the heads lie of the molecules that heads are considered by us to interact only sterically, like hard discs.
a) the plane coincides with the border of the hydrocarbon region;
b) the plane is at a distance s from the boundary of the hydrocarbon region.

of the dividing surface and the number of molecules in the monolayer rest unchanged (see Fig.2, where R is the radius of the dividing surface and $c=1/R$). In this section we do not impose any requirement on the value of A. The m-th layer is at a distance z from the dividing surface, when the membrane is flat, and at a distance z' when the dividing surface is spherically curved with curvature c. We denote the area of the m-th layer with A' after curving it (in the flat state $A'=A$). Then if the volume of each of the layers does not depend on the curvature, it

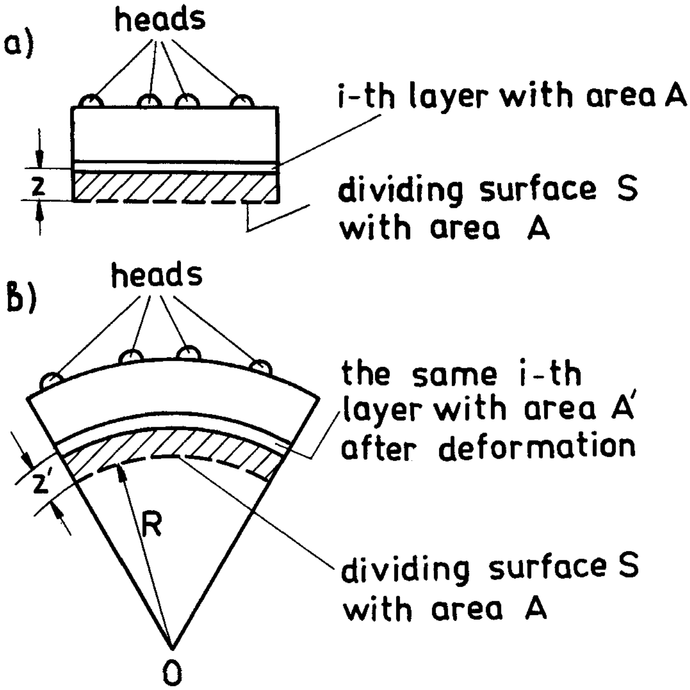

FIGURE 2. Disposition of some layer of the monolayer in a flat (a) and in a curved (b) state. In this work, the volume between this layer and the dividing surface between the two monolayers S (this volume is denoted by the hatched region in this figure) does not change through the deformation. z and z' denote the distances of the layer from the dividing surface S before and after the deformation. A'(z,R) depends on the radius of curvature R and the distance z of the layer from the surface S in the flat state. The area of the surface S does not change when we curve the monolayer.

is easy to prove that

$$\begin{aligned} z'(c) &= z(1-zc) \\ A'(z,c) &= A(1 + 2zc - z^2c^2) \end{aligned} \tag{19}$$

For the monolayer at Fig.2, R is positive.

If A_i is the area of the i-th layer, counted from the dividing surface, A_i can be obtained using formula(19),in which $z=\frac{i}{n}d$ where i is the number of the layer and d is the thickness of the hydrophobic core of the flat monolayer.

According to our assumption the free energy of a curved monolayer F^m consists of two parts: the free energy F^{1m} of the plane on which the heads of the molecules are situated and on which the contact between the water and the hydrophobic core takes place and the free energy F^{2m} of the hydrophobic core.

Our considerations begin with F^{2m}. F^{2m} can be considered to depend entirely on the area of each of the layers into which we have divided the monolayer, i.e. $F^{2m}=F^{2m}(A_1,A_2,...,A_n)$. Expanding within the Taylor's series we obtain:

$$F^{2m} = F^{2m}(A_1,A_2,...,A_n) =$$

$$= F^{2m}(A,A,...,A) + \sum_{i=1}^{n} \left(\frac{\partial F^{2m}}{\partial A_i}\right)\Bigg|_{\substack{A_k=A\\k=1,n}} (A_i - A) +$$

$$+ \frac{1}{2}\sum_{i,j=1}^{n} (A_i - A)(A_j - A)\frac{\partial^2 F^{2m}}{\partial A_i \partial A_j}\Bigg|_{\substack{A_k=A\\k=1,n}} + \ldots \tag{20}$$

Here $F^{2m}(A,A,...,A)$ is the free energy of the hydrophobic core for the noncurved state, A is the area of the dividing surface and A_i, the area of the i-th layer after the deformation.

Later on we use that

$$\frac{\partial F^{2m}}{\partial A_i}\Bigg|_{\substack{A_k=A\\k=1,n}} = -p_i \tag{21}$$

where p_i is the lateral pressure acting on the i-th layer in the flat state and is equal to the density of the lateral pressure at the point where the layer is found, multiplied by the thickness of this layer. Then for the free energy of the hydrophobic core F^{2m} we get:

$$F^{2m}(A_1,A_2,...,A_n) = F^{2m}(A,A,...,A) -$$

$$- \sum_{i=1}^{n} p_i(A_i - A) - \frac{1}{2}\sum_{i,j=1}^{n} (A_i - A)(A_j - A)\frac{\partial p_i}{\partial A_j}\Bigg|_{\substack{A_k=A\\k=1,n}} \tag{22}$$

The second term of the right hand side of (22) can be easily calculated. It is more complicated to evaluate the third term. To do this evaluation we make the following considerations and approximations. Let $(p_1,p_2,...,p_n)$ be a set of pressures applied to each of the layers of the monolayer. Let the areas of these layers at the pressures thus applied be $(A_1,A_2,...,A_n)$. Let us now change the area A_i of the i-th layer by the quantity δA_i), keeping the areas of the other layers unchanged. This will cause changes in the pressures p_j. Strictly speaking, δp_j is different from zero for every j, but it can be expected that δp_j is considerably different from zero only if the i-th and the j-th layers are near enough to one another. It can be expected that the change in A_i will cause changes in p_j if the length of one CH_2 group is not less than the distance between the i-th and the j-th layers.

Let us denote

$$m_n = \frac{\varepsilon}{d}n \tag{23}$$

where ε is of the order of one half of the distance between the n-1 carbon atom and the n+1 carbon atom in an all-trans saturated alkyl chain (i.e. $\varepsilon \simeq 1.3$ Å). Quantitatively, we assume that δp_j is considerably different from zero if $|i-j|<m_n$. It can be expected that p_j has a maximum at j=i. Then for low enough s the following is fulfilled:

$$\delta p_{j+s} = \delta p_{j-s} \tag{24}$$

The second assumption made by us is that the equality (24) is fulfilled for every $s<m_n$. These two assumptions can be summarized in this way:

$$\left.\frac{\partial p_i}{\partial A_k}\right|_{\substack{A_k=a \\ k=1,n}} \approx 0 \text{ if } |k-i|>m_n \tag{25}$$

$$\left.\frac{\partial p_{i+s}}{\partial A_i}\right|_{\substack{A_k=A \\ k=1,n}} = \left.\frac{\partial p_{i-s}}{\partial A_i}\right|_{\substack{A_k=A \\ k=1,n}} \text{ if } |s|<m_n \tag{26}$$

Using equations (25) and (26), the third term of the right hand side of (22) acquires the form:

$$-\frac{1}{2}\sum_{i,j=1}^{n}(A_i - A)(A_j - A)\frac{\partial p_i}{\partial A_j}\Bigg|_{\substack{A_k=A\\ k=1,n}} \approx$$

$$\approx -2c^2\left(\frac{Ad}{n}\right)^2\sum_{i=1}^{n} i^2\frac{\partial p_i}{\partial A} \qquad (27)$$

where $\partial p_i/\partial A$ is the derivative connected with the change of p_i when the areas of all the layers of which the monolayer consists are changed by the same quantity. This derivative can be calculated from our former results[2] for the distribution of the lateral pressure along the thickness of the membrane for different values of area per molecule.

As was mentioned above, in the flat monolayer the distance of the i-th layer from the dividing surface is $z_i = \frac{i}{n}d$ where d is the thickness of the flat monolayer. From equation (19), equation (22) acquires the following form (we denote $F^{2m}(A,c)=F^{2m}(A_1,A_2,\dots,A_n)$, where A_i is the area of the i-th layer at spherical deformation with curvature c of the dividing surface having area A, and $F^{2m}(A,0)= F^{2m}(A,A,\dots,A)$:

$$F^{2m}(A,c) = F^{2m}(A,0) + c\sum_{i=1}^{n}\left[(-p_i)2dA\frac{i}{n}\right] +$$

$$+ c^2\sum_{i=1}^{n}\left[p_i d^2 A - 2\frac{\partial p_i}{\partial A}A^2 d^2\right]\frac{i^2}{n^2} \qquad (28)$$

In our considerations, the free energy F^{1m} consists of the free energy of interaction of the hard discs with which we replace the polar heads, and the free energy due to the contact between the water and the hydrophobic core. For the interaction between the hard discs, we assume that it depends on the number of discs per unit area and on the area of each disc. For the contact between the water and the hydrophobic core, we accept that it is exhibited at the points not occupied by the hard discs, and that it has a free energy per unit area equal to the surface tension γ of the oil-water interface. γ depends on the radius r of curvature of the interface this dependence having the form[13]

$$\gamma_r = \gamma_\infty\left(1 - \frac{2\delta}{r} + \frac{3\delta^2}{r^2}\right) + O\left(\frac{1}{r}\right)^3 \qquad (29)$$

In (29) γ_∞ and γ_r are the surface tensions of the flat and of the spherically curved (with a radius of curvature r) oil-water interfaces. As it was shown earlier[14], the change of γ when the oil-water interface is curved has a non-negligible effect on the values of the curvature elasticity moduli. This is why we include this effect in our calculations as well. For the value of δ we use the assessment[14] $\delta=5.47$ Å. Note that in (29) R is positive if the center of curvature is to the oil side. Finally:

$$F^{lm} = F_{HD}(A') + \gamma_{R'}(A'-A_{min}) \tag{30}$$

R' and A' are the radius and the area, respectively, of the surface where the heads interact. A_{min} is the minimal area of the flat membrane; this area can be obtained if the disks, representing the heads, are densely packed on the surface where these are situated. F_{HD} is the free energy of interaction of the hard discs representing the heads, and has the form[15]:

$$F_{HD}(A') =$$

$$= -LkT(2\ln\beta + 0.06 + 0.12\beta + 0.385\beta^2 + 0.243\beta^3 + \ldots) \tag{31}$$

where

$$\beta = \frac{a'-a_{min}}{a_{min}} = \frac{A'-A_{min}}{A_{min}}, \quad a' = \frac{A'}{L}, \quad a_{min} = \frac{A_{min}}{L},$$

k is the Boltzmann constant, T is the absolute temperature, a' is the mean area per head, a_{min} is the minimal area per head when the heads are densely packed and L is the number of heads on the plane where they interact. A' can be obtained from (19) for z=d. If R is the radius of curvature of the dividing surface, the radius of curvature of the surface on which the heads lie is:

$$R' = R + d' \tag{32}$$

d' can be expressed by (19), where z=d. From (29), (30) and (31):

$$F^{lm}(A,c) = F^{lm}(A,0) + \left(2dA\frac{\partial F_{HD}}{\partial A'}\bigg|_{A'=A}\right)c +$$

$$+ \left(\frac{1}{2}\frac{\partial^2 F_{HD}}{\partial A^2}4d^2A^2 - Ad^2\frac{\partial F_{HD}}{\partial A}\right)c^2 + \gamma_\infty\left[2dA - 2\,(A - A_{min})\right]c -$$

$$- \gamma_\infty\left[Ad^2 + 2\delta d(A + A_{min}) - 3\delta^2(A - A_o)\right]c^2 \tag{33}$$

The total free energy F^m of the monolayer is:

$$F^m(A,c) = F^{1m}(A,c) + F^{2m}(A,c) = F^m(A,0) +$$

$$+ \left(2dA\frac{\partial F_{HD}}{\partial A} + 2\gamma_\infty dA - 2\gamma_\infty \delta(A-A_{min}) - \sum_{i=1}^{n} 2\frac{i}{n}dAp_i\right)c +$$

$$+ \left(2d^2A^2\frac{\partial^2 F_{HD}}{\partial A^2} - Ad^2\frac{\partial F_{HD}}{\partial A} - \gamma_\infty Ad^2 - 2\gamma_\infty \delta d(A + A_{min}) +\right.$$

$$\left.+ 3\gamma_\infty \delta^2(A - A_{min}) + \sum_{i=1}^{n} (p_i Ad^2 - 2\frac{\partial p_i}{\partial A}A^2d^2)\frac{i^2}{n^2}\right)c^2 \qquad (34)$$

If in (34) A=a, where "a" is the area per molecule on the surface S, which divides the two monolayers constituting the bilayer (in this case in F_{HD}, given by formula (31), L=1) the equation (34) will have the form given by formula (3) from the previous section.This means that we can express the coefficients M(a) and N(a) from (3) - these are simply the expressions in the square brackets when A=a and N=1, which expressions are multiplied by c and c^2. Knowing M(a) and N(a),we can determine the quantity $(2k_c+\bar{k}_c)$ for blocked and free flip-flop with (15) and (16) from the previous section.

RESULTS AND DISCUSSION

Earlier we calculated the distribution of the lateral pressure along the thickness of membrane consisting of amphiphilic molecules with two hydrophobic chains with 12 carbon atoms per chain for ten values of the thickness at discrete points for each thickness.[2] In the present work, the values of the density of the lateral pressure are obtained through interpolation for an arbitrary thickness, and for an arbitrary point in the bilayer. In doing this, one additional requirement is imposed: this density in the hydrophobic core tends to zero as the heads are approached. So we tried to take into account the fact that very near the heads water molecules can penetrate into the hydrophobic region; thus, the distribution of the hydrocarbon material along the normal to the membrane does not change with a jump when we leave the hydrophobic region, but decreases smoothly to zero.

The results[2] obtained earlier predict some interpenetration of the hydrocarbon chains of both monolayers in the bilayer. The percentage of this interpenetration depends on the area per chain (the molecule has two chains); the values calculated are given in Table I. In our opinion, it is this interpenetration that makes one of the differences between the behavior of half the bilayer and that of the monolayer at the air-water interface, in which monolayer one molecule occupies the same mean area as in the bilayer. Although the air-hydrocarbon boundary is almost flat (at small enough areas per molecule) in the monolayer at the air-water interface, there is no need for such a restriction in the bilayer.

TABLE I. Percentage of penetration of the chains of the molecules of one monolayer into the other monolayer of the bilayer for different mean areas per chain. The calculations are done on the basis of the results of our earlier work.[2]

Area per chain (Å^2)	Percentage of interpenetration
23.0609	2.17
24.1091	2.71
25.2571	4.31
26.5200	5.26
27.9158	6.95
29.4667	8.25
31.2000	10.16
33.1500	11.79
35.3600	13.90
37.8857	15.75

The percentage of interpenetration predicted by us is comparatively small, but it must be taken into account. We do this by considering as a dividing surface the surface which divides the hydrocarbon core of the bilayer into two parts, the volumes of which are proportional to the number of the heads in each of these parts.

In our previous considerations[2] there exists the parameter of minimal area per head that is equal to the area of the disc representing the head. The values calculated for $(2k_c+\bar{k}_c)$ for blocked and free flip-flop, depending on the value of this parameter, are given in Table II. Table III gives the same quantities, without taking into account the

TABLE II. Values calculated for the sum $(2k_c+\bar{k}_c)$ for the cases of blocked and free flip-flop (denoted by $(2k_c+\bar{k}_c)^{bl}$ and $(2k_c+\bar{k}_c)^{free}$, respectively) for different values of the minimal area per head for a lipid bilayer composed of lipid molecules with two hydrophobic saturated alkyl chains, each chain having 12 carbon atoms. Remember that we consider the hydrophilic heads of the molecule to be hard discs with definite area.

Minimal area per head (Å^2)	$10^{12}\times(2k_c+\bar{k}_c)^{bl}$ (erg)	$10^{12}\times(2k_c+\bar{k}_c)^{free}$ (erg)
less than 44.20	0.92	0.81
44.20	9.76	-0.637
45.07	9.50	-0.563
45.94	9.28	-0.526
46.81	8.98	-0.549
47.68	8.58	-0.638
48.55	8.29	-0.518
49.42	8.09	-0.420
50.29	7.82	-0.369
51.16	7.66	-0.248
52.03	7.43	-0.227

change in the tension at the curved oil-water interface.

The calculated values for blocked flip-flop are of expected order of magnitude. For free flip-flop more special is the case when the area of the hard disk, representing the head, is less than the minimal area a^{o}_{min} of the hydrophobic part (the two hydrophobic chains) of the molecule. For the molecules under consideration this quantity was calculated elsewhere[2]: $a^{o}_{min} = 44.2$ Å^2. In this case the actual area of the head has no importance because the discs cannot touch one another and consequently cannot interact. We make the natural assumption that now the pressure due to steric interactions is not concentrated on the plane where the heads lie, but is distributed uniformly along the thickness of the membrane, and that the role of the quantity a_{min} in (31) is played by a^{o}_{min}. The area a' in (31) is measured on the plane halving the thickness of the monolayer. Obviously, if we change the

TABLE III. *The same quantities as in TABLE II, in the* case when the tension at the curved oil-water interface is not taken into account.

Minimal area per head ($\mathring{A}^2$)	$10^{12}\times(2k_c+\bar{k}_c)^{bl}$ (erg)	$10^{12}\times(2k_c+\bar{k}_c)^{free}$ (erg)
less than 44.20	2.50	1.24
44.20	11.80	-0.649
45.07	11.52	-0.554
45.94	11.27	-0.506
46.81	10.94	-0.540
47.68	10.51	-0.665
48.55	10.19	-0.532
49.42	9.96	-0.408
50.29	9.67	-0.347
51.16	9.47	-0.197
52.03	9.23	-0.184

area of the disk, the values of the sums $2k_c+\bar{k}_c$ will not change with a jump (as our results show), but smoothly in any region around a^o_{min}.

One necessary condition for the existence of thermodynamically stable vesicles is that the sum $2k_c^{free}+\bar{k}_c$ be positive. Consequently in the frames of the model used by us such vesicles can exist only when the area of the hydrophilic head is less than the area of the hydrophobic part of the amphiphilic molecule. Otherwise, when the heads are larger than the chains, our model predicts negative values of $2k_c^{free}+\bar{k}_c$, i.e. impossibility for thermodynamically stable vesicles to exist. Similar result has been obtained by the Petrov-Derzhanski-Mitov model[12] too.

ACKNOWLEDGEMENTS

I wish to thank Prof. A. Derzhanski and Dr. A. G. Petrov for fruitful discussion and their valuable advices in preparing this work.

REFERENCES

1. W. Helfrich, Z. Naturforsch., 28c, 693 (1973).
2. I. Bivas and A. Derzhanski, Mol.Cryst. Liquid Cryst., 64, 1771 (1981).
3. W. Helfrich, Z. Naturforsch., 29c, 510 (1974).
4. J. N. Israelachvili, D. J. Mitchell and P. W. Ninham, J. Chem. Soc. Faraday Trans. II, 72, 1525 (1976).
5. W. Helfrich and H. J. Deuling, J. Physique, 36-C1, 327 (1975).
6. F. Brochard and J. F. Lennon, J. Physique, 36, 1035 (1975).
7. R. M. Servuss, W. Harbich and W. Helfrich, Biochim.Biophys.Acta, 436,900 (1976).
8. M.B. Schneider, J.T. Jenkins and W.W.Webb, J. Physique, 45, 1457 (1985).
9. H. Engelhard, H. P. Duwe and E. Sackmann, J. Physique Lett., 46, L395 (1985).
10. I. Bivas, P. Hanusse, P. Bothorel, J. Lalanne and O. Aguerre-Chariol, J. Physique, 48, 855 (1987).
11. W.Harbich, R.M.Servuss and W.Helfrich, Z.Naturforsch., 33, 1013 (1978).
12. The Petrov-Derzhanski-Mitov model: A. G. Petrov and A. Derzhanski, J. Physique Coll., 37, C3-155 (1976); A. G. Petrov, M.D.Mitov and A. Derzhanski, Phys. Lett. A, 65A, 374 (1978); M. D. Mitov, Ph. D. Thesis, Sofia University, Sofia (1981); A. G. Petrov and I.Bivas, Progress in Surface Sci., 16(4), 389 (1984).
13. S.Ono and S. Kondo, in Handbuch der Physik, edited by S. Fluegge (Springer, Berlin, 1960), Vol. 10, p. 134.
14. I. Bivas, Phys. Lett., 94A, 114 (1983).
15. R. E. Jacobs, B. Hudson and H. C. Andersen, Proc. Natl. Acad. Sci. USA, 72, 3993 (1975).