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A THEORY OF THE ELECTRIC FIELD-INDUCED PHASE TRANSITION OF PHOSPHOLIPID BILAYERS

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Summary

Improving the statistical mechanical model of Jacobs et al. (Jacobs, R.E., Hudson, B. and Andersen, H.C. (1975) Proc. Natl. Acad. Sci. U.S. 72, 3993—3997) we have constructed a model which describes not only the temperature but also the external field dependence of the membrane structure of phospholipid bilayers. In addition to the interactions between head groups, between hydrocarbon chains, and the internal conformational energy of the chains (which were considered in Jacobs' model), our model includes the energy of deformation and the field energy as well.

By the aid of this model we can explain the phenomenon of dielectric breakdown, the non-linearity of current-voltage characteristics, and the mechanism of membrane elasticity.

The free energy of the membrane, the average number of the *gauche* conformations in the hydrocarbon interior and at the membrane surface, *gauche* distribution along the chain, the membrane thickness, area and volume are calculated at different temperatures and voltages. The calculation also gives the temperature dependence of Young's modulus and that of the linear thermal expansion coefficient.

Introduction

Statistical thermodynamic models elaborated recently focused on the temperature-dependent order-disorder phase transition of lipid bilayers [1—7].

According to the experiments the order-disorder transition depends not only on temperature but it can be induced at constant temperature by variations in

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Abbreviation: DPPC, dipalmitoyl phosphatidylcholine.

pH and salt concentration [8] and by variations in pressure [9]. The phenomenon of the dielectric breakdown and the reflectivity measurements [10] clearly show the effect of an external electric field on the membrane structure. Our paper deals with this latter effect of an electric field normal to the bilayer membrane surface in detail.

By means of the present model we explain the non-linear character of current-voltage (*I-V*) curves, the phenomenon of the dielectric breakdown and the mechanism of the membrane elasticity. In this paper we describe the model, its statistical mechanical treatment and the numerical results. We calculate the *gauche* density, surface *gauche* density, the change of the probability of *gauche* formation along the chain length at different external voltages, and temperatures. We also calculate the temperature dependence of the linear thermal expansion coefficient and that of Young's modulus for dipalmitoyl phosphatidylcholine (DPPC).

Model

In the temperature-dependent membrane model of Jacobs et al. [1], the following interactions have been considered: chain-chain attractive and repulsive interactions, polar head-head interaction and conformational energy. The calculated transition temperatures and transition enthalpies for different acyl chain lengths agreed fairly well with the experimental data.

For describing the effect of external electric field another two energy terms have to be taken into consideration: the energy of flexibility and field energy terms.

The notations of Jacobs and coworkers are used unless otherwise noted.

The flexibility energy

We have to take into consideration the chain flexibility term also to describe the effect of the electric field on the membrane structure, because the hydrocarbon chains are subject not only to discrete changes of form (*trans-gauche* transition) but also to continuous deformation. Fig. 1 shows two possible conformations of a hydrocarbon chain in equilibrium and in deformed states.

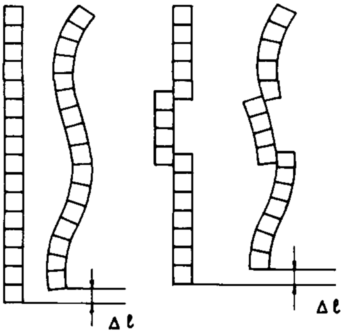


Fig. 1. Two possible conformations of a hydrocarbon chain in equilibrium and in deformed states. This simple representation of chains was applied by Scott [3].

The simplest form for the flexibility energy (H_{flex}) is:

$$H_{\mathrm{flex}} = \sum_{j=1}^{2N} \frac{1}{2} \frac{D}{l_j} (\Delta l_j)^2 \frac{A}{2N} \tag{1}$$

where l_j denotes the vertical equilibrium length of the jth chain at zero external voltage. According to Jacobs et al. [11] the effective vertical equilibrium length of a chain if i is the location of its first *gauche* bond is:

$$l_j(i) = \tfrac{1}{2}(m + i + 1)\, h_0 + f \tag{2}$$

where m is the number of carbon-carbon bonds which can exist in either a *gauche* or *trans* conformation, h_0 is the distance between bound carbon atoms ($h_0 = 1.27$ Å, [12]) f is the length of the head group ($f = 11$ Å, [13]). Δl_j is the actual change of the vertical length of the jth chain relative to the equilibrium chain length. D is the vertical Young's modulus of a single chain and it is assumed to be constant for different chain configurations and $A/2N$ is the cross-section area/chain.

Here we have to mention Jacobs' result [11]: both the solid and fluid phases are characterized by a relatively flat interface between the two monolayers in a bilayer. This is caused by the relatively large loss of dispersion energy that would result from the formation of voids. Thus, the surface of the monolayers either in fluid or in gel phases are as close as is allowed by the short range repulsions, i.e. the interaction between the monolayers is constant at any bilayer conformation. Apart from a constant factor the product of the monolayer partition functions equals the partition function of the bilayer.

The field energy

In the case of non-zero external field, we have to consider the field energy (H_{field}) too, and the partition function of the monolayer (Q) will be [14]:

$$Q = \sum_{\substack{\text{all} \\ \text{configurations}}} \exp - (H_{\mathrm{monolayer}} - H_{\mathrm{field}})/kT \tag{3}$$

The external electric field perpendicular to the membrane surface compresses the membrane by the ponderomotive force. The ponderomotive force to the jth hydrocarbon chain is [15]:

$$F_j = \tfrac{1}{2}\, \epsilon_0 \epsilon_{\mathrm{m}} \frac{V^2}{L_j^2} \frac{A}{2N} \tag{4}$$

where ϵ_0 = the permittivity of the vacuum; ϵ_{m} = the relative permittivity of the membrane (it is about 2); V = the applied potential difference and $L_j = 2 \cdot l_j(i)$ the membrane thickness at the jth chain. When we defined L_j we took into consideration the membrane symmetry and the perfect fitting of the monolayer surface to each other [11]. However, the effect of the continuous deformation was neglected here in the calculation of L_j. Thus the work of the electric field on one monolayer of the membrane is:

$$H_{\mathrm{field}} = \tfrac{1}{2} \sum_{j=1}^{2N} F_j \Delta L_j = \sum_{j=1}^{2N} F_j \Delta l_j \tag{5}$$

Partition function

Applying several resonable approximations Jacobs et al. [1] constructed the following partition function of one layer of bilayer membrane:

$$Q(N, A, T) = Q_{\mathrm{HD}}(N, A, T) \times [Q_{\mathrm{CHAIN}}(T, P_{\mathrm{HD}})]^{2N} \times \exp - N(A_0/A)(\Delta H_{\mathrm{sub}} \cdot 2n + \delta)/kT \tag{6}$$

where

$$Q_{\mathrm{HD}}(N, A, T) = \left(\frac{\alpha^2 A_0}{N}\right)^N \exp N(0.06 - 0.12\alpha + 0.382\alpha^2 + 0.243\alpha^3 + \ldots) \tag{7}$$

is the configurational integral for hard disks in two dimensions [16—18],

$$Q_{\mathrm{CHAIN}}(T, P_{\mathrm{HD}}) = 1 + \sum_{i=1}^{m} (1 + 2\exp[-\epsilon/kT])^{m-i} \times \\ \times 2\exp - [\epsilon + P_{\mathrm{HD}} A_0 \gamma(m - i + 1)/N]/kT \tag{8}$$

where

$$P_{\mathrm{HD}} = (NkT/A_0)(2/\alpha + 1.9 + 0.67\alpha + 1.5\alpha^2 + \ldots)/(1 + \alpha) \tag{9}$$

is the hard disk pressure [16—18]. In these formulae A_0 is the close-packed area of the membrane and $\alpha = (A - A_0)/A_0$. Here T is the absolute temperature, k is the Boltzmann constant, $2N$ is the number of molecules in the bilayer membrane, $n(=m + 2)$ is the number of carbon atoms in the acyl chain. The parameters of the Jacobs model are: ϵ, the energy of a *gauche* bond relative to a *trans* bond, is known to be about 500 cal/mol for hydrocarbon chains [19], ΔH_{sub} is the heat of sublimation/CH_2 group of the long-chain hydrocarbon, its value is taken as —1840 cal/mol of CH_2 groups [20], δ is the strength of the interaction between the head groups, γ is a dimensionless adjustable parameter which is expected to be independent of chain length.

In the case of external electric field the flexibility and field energy terms have to be built in the partition function.

These energies are functions of i and Δl, therefore the chain partition function is:

$$Q_{\mathrm{CHAIN}} = \{\sum_{i=1}^{m} [1 + 2\exp - \epsilon/kT]^{m-i} \times 2\exp - [\epsilon + P_{\mathrm{HD}}(A_0/N)\gamma(m - i + 1)]/kT \times \\ \times (-1) \cdot \int_0^{-l(i)} \exp - (H_{\mathrm{flex}} - H_{\mathrm{field}})/kT \cdot \mathrm{d}(\Delta l)\} + \\ + (-1) \cdot \int_0^{-l(i=m+1)} \exp - (H_{\mathrm{flex}} - H_{\mathrm{field}})/kT \cdot \mathrm{d}(\Delta l) \tag{10}$$

where $l(i = m + 1)$ is the length of an all-*trans* chain. For simplicity assume that

$$x = \frac{\Delta l}{l(i)}$$

$$\mathcal{A} = \tfrac{1}{2} D l(i) \frac{A}{2N} \tag{11}$$

$$\mathcal{B} = \tfrac{1}{8} \epsilon_0 \epsilon_{\mathrm{m}} \frac{1}{l(i)} \frac{A}{2N}$$

Thus the integral in Eqn. 10 will be:

$$\int_0^{-l(i)} \exp -(H_{\text{flex}} - H_{\text{field}})/kT \cdot \mathrm{d}(\Delta l) = l \int_0^{-1} \exp[-\mathcal{A}x^2 + \mathcal{B}xV^2]/kT\,\mathrm{d}x \approx$$

$$\approx l \int_0^{-\infty} \exp -\mathcal{A}\left(x - \frac{V^2\mathcal{B}}{2\mathcal{A}}\right)^2 \Big/ kT \times \exp\left(\frac{V^4\mathcal{B}^2}{4kT}\right) \times \mathrm{d}x = -\frac{l}{2}\sqrt{\frac{k\pi T}{\mathcal{A}}}\exp\left(\frac{\mathcal{B}^2}{4\mathcal{A}kT}V^4\right) \tag{12}$$

Finally, we have got the partition function of the bilayer membrane in a closed form. By means of this partition function one can calculate a number of thermodynamical properties of bilayer membrane. The determination of two model parameters D and γ will be discussed later.

Results and Discussion

Free energy (field-induced phase transition)

$[\ln Q]/N$ was calculated in the function of relative surface area at different external voltages. Calculations were carried out for DPPC, i.e. $n = 16$ at constant temperature. This calculated value is proportional to the free energy (F) of bilayer membrane (BLM), because:

$$F = -kT \ln Q_{\text{BLM}} = -2\,kT \ln Q = -2\,N\,kT\,[\ln Q]/N \tag{13}$$

where Q_{BLM} ($=Q^2$) denotes the partition function of bilayer membrane.

Equilibrium of the system is characterised by the free energy minimum, thus the maximum of $[\ln Q]/N$ determines the equilibrium relative surface area of bilayer membrane.

For better visualisation the maxima and minima of curves are represented with discrete black points and these points are connected with a dashed line (Fig. 2).

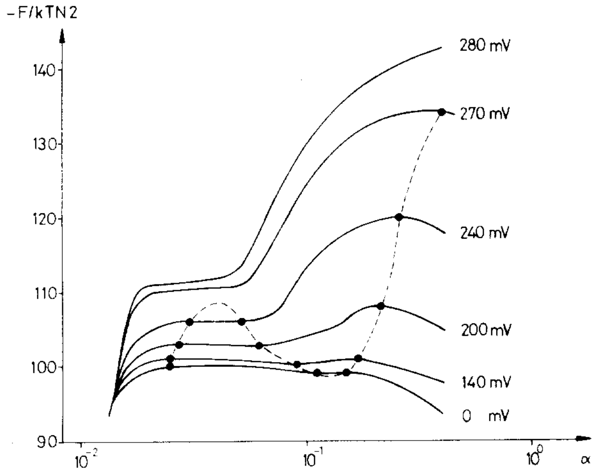


Fig. 2. Calculated relation between negative free energy (F) and relative area (α) at different external voltages (- - - - - -, local minimum and maximum points of the free energy curves: $T = 293$ K, $n = 16$).

Curves between 0 and 260 mV have two maxima, i.e. the system has two stable states, but the probability of the state belonging to the absolute maximum is much higher.

In the case of low voltages up to 140 mV the absolute maximum belongs to the smaller relative surface area. In this range of voltages α is about 0.024, i.e. we have a nearly close-packed system (gel phase of the membrane).

According to Fig. 2 at about 140 mV a field-induced first-order phase transition takes place in the DPPC bilayer at 20°C, because the maxima of the curve are of equal height. The external electric field shifts the phase transition temperature of bilayer membrane towards the lower temperatures! The physical reason of this tendency is the structure-loosening effect of the electric field on the membrane. In the following this effect will be treated in details.

Above 140 mV the absolute maximum belongs to the higher α value ($\alpha > 0.17$), i.e. the probability of a more fluid, liquid-crystalline phase is higher compared to the gel phase. This calculated 17% abrupt area increase is of the same order of magnitude, though somewhat smaller, as the experimentally measured 20—40% temperature-induced area change during the phase transition for DPPC bilayer lamellae [12]. In this voltage range the membrane structure becomes continuously more and more fluid. With increasing voltages α increases from 0.17 to 0.25.

At 260 mV the local maximum belonging to the smaller α value disappears, the only stable state of the membrane is at $\alpha \approx 0.3$. Further slow (quasi-static) voltage increase results in a catastrophic loosening of the structure. At 280 mV the membrane does not have a stable equilibrium state, the curve increases monotonously, i.e. the membrane ruptures. Thus our model accounts for the phenomenon of the dielectric breakdown. Consequently, the dielectric breakdown is a phase transition of the system when α jumps from a finite value to an infinite one.

Thermodynamic averages in two-state systems

Let

$$F(\alpha_1) \quad \text{and} \quad F(\alpha_2) \left(= -\frac{kT \ln Q(\alpha_2)}{N} \right) \tag{14}$$

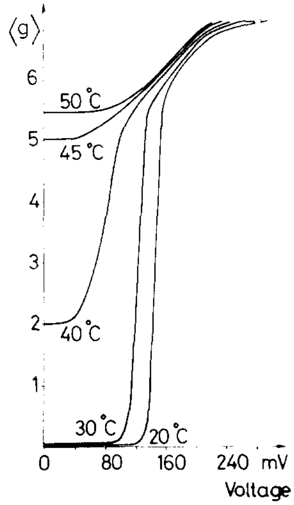
be the free energy/molecule of the stable states. The thermodynamic average of any characteristic value $h(\alpha)$ of the system can be calculated in the following way:

$$\langle h \rangle = \frac{h(\alpha_1) \exp - F(\alpha_1)\mathcal{N}/kT + h(\alpha_2) \exp - F(\alpha_2)\mathcal{N}/kT}{\exp - F(\alpha_1)\mathcal{N}/kT + \exp - F(\alpha_2)\mathcal{N}/kT} \tag{15}$$

where $\mathcal{N}$ is the cooperative unit size of the system. Yellin and Levin [21] have estimated the cooperative unit size of DPPC to be from 11 to 49 molecules.

Linear gauche density

Let us examine the process of field-induced membrane structure loosening in details. For this purpose we calculate the number of structural defects, i.e. the number of *gauche* states in the membrane at different external conditions. For



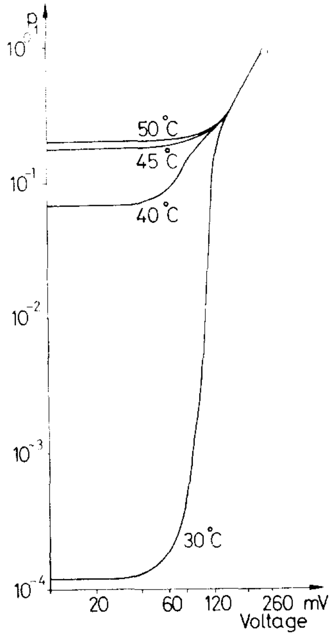


Fig. 3. Voltage dependence of the average *gauche* number/hydrocarbon chain ($\langle g \rangle$), at different temperatures. ○, instability point of the system ($n = 16$).

Fig. 4. The double logarithmic plot of the probability of *gauche* formation near the surface (p_1) against the external voltage, at different temperatures ($n = 16$). ○, instability point of the system.

a given α the average *gauche* number/chain is [14]:

$$\langle g(\alpha) \rangle = -\frac{kT}{2N} \frac{\partial \ln Q(\alpha)}{\partial \epsilon} \tag{16}$$

After calculating $\langle g(\alpha_1) \rangle$ and $\langle g(\alpha_2) \rangle$ by means of Eqn. 15 we get $\langle g \rangle$. In Fig. 3 $\langle g \rangle$ is plotted against the external voltage at different temperatures for DPPC ($n = 16$). Fig. 3 shows a sudden increase of *gauche* number at about 100—140 mV, below the phase transition temperature of DPPC membranes. In these cases the order-disorder phase transition takes place under the effect of the external field. Above the phase transition temperature the characteristic features of the curves change. Instead of the jump of the *gauche* number a monotone increase of the curves can be seen from about 50 to 80 mV. In agreement with measurements [22] the calculated breakdown potential decreases slightly with increasing temperature.

Gauche formation near the surface

The probability of gauche formation near the membrane surface is:

$$p_1(\alpha) = Q_{\mathrm{CHAIN}}(i = 1)/Q_{\mathrm{CHAIN}} \tag{17}$$

where $Q_{\mathrm{CHAIN}}(i = 1)$ means one term of the chain partition function with $i = 1$. p_1, the average of $p_1(\alpha_1)$ and $p_1(\alpha_2)$, could be calculated from Eqn. 15. In Fig. 4. $\log p_1$ is plotted against the logarithm of the external voltage, at different temperatures for DPPC. These curves are similar to the $\langle g \rangle$-V curves. The voltage dependence of p_1 is very important in the conductivity properties of bilayer membranes. In the case of inorganic ions, the rate-limiting step of the ionic conduction of unmodified bilayer membranes is the jump of ions into the membrane [23,24]. The entrance probability of the ion is proportional to the ion concentration of the solution in the immediate vicinity of the membrane surface on one hand and to the number of vacant transport sites near the surface, i.e. to p_1 on the other hand [22,25]. If we compare the conductivity-voltage curve for egg phosphatidylcholine measured by Miyamoto and Thompson [26] (see their Fig. 8) above the phase transition temperature at 36°C with the calculated p_1-V curve for DPPC above the phase transition temperature at 50°C, good agreement can be observed. Thus, the non-linear character of I-V curves of bilayer membranes could be interpreted only by the voltage dependence of the *gauche* number near the membrane surface, without assuming any other mechanisms as charge injection, Wien effect etc. [27].

Gauche distribution along the chain

The probability of *gauche* formation on the jth bond from the head group is:

$$P_j = p_j + p \sum_{i=1}^{j-1} p_i \tag{18}$$

where $p_i = \langle Q_{\mathrm{CHAIN}(i)} / Q_{\mathrm{CHAIN}} \rangle$ is the probability of the first *gauche* on the ith bond, and

$$pp_i = \frac{2 \exp - \epsilon/kT}{1 + 2 \exp - \epsilon/kT} \cdot p_i \tag{19}$$

is the probability that the first *gauche* is on the ith bond and another one is on the jth bond. Fig. 5a and b show the probability of *gauche* formation as a function of a position along the chain at different temperatures and voltages for DPPC. At low voltages (0—140 mV) the probability of *gauche* formation increases towards the terminal ends of the hydrocarbon chains. Below the phase transition temperatures the shapes of these curves can be compared with the results of NMR order parameter measurements [28].

Below the phase transition temperature this similarity suggests a linear relationship between the segmental molecular order parameter $S_{\mathrm{mol}(j)}$ and P_j. According to Seelig and Seelig [29] the linearity is valid but only if kink conformations are in the chains, namely

$$S_{\mathrm{mol}(j)} = S_{0°} (1 - P_j) + S_{60°} P_j \tag{20}$$

where $S_\beta = (3 \cos^2\beta - 1)/2$

Above the phase transition temperature this linear relationship between $S_{\mathrm{mol}(j)}$ and P_j doesn't exist (see Fig. 5), i.e. new types of chain conformations develop beside the kinks. Nagle and Wilkinson [30] and Scott [31] obtained a similar conclusion on the types of chain conformations.

Characteristic dimensions of the bilayer

In Figs. 6—8 temperature and voltage dependence of several characteristic values are shown.

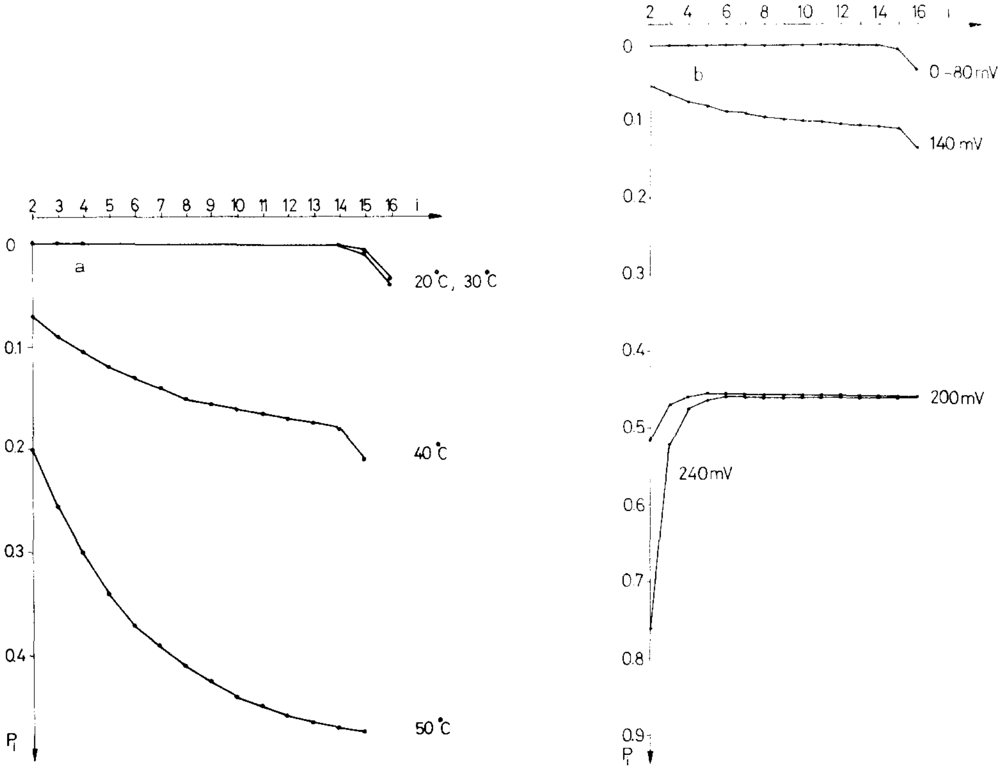


Fig. 5. The probability of *gauche* formation (P_i) as a function of a position along the chain (i) at different temperatures (a) and voltages at 30° C (b) (n = 16).

Relation between external voltage and relative area

By means of Eqn. 15 the average value of the relative area $\langle \alpha \rangle$ could be calculated. Voltage dependence of the relative area (see Fig. 6) is similar qualitatively to the relation between lateral pressure and area/polar head for DPPC monolayers [32]. However, as a consequence of this comparison one can state that the lateral pressure and external voltage act on the membrane conformation in opposite direction.

Average length of a lipid molecule

The average length $\langle l \rangle$ could be given by:

$$\langle l \rangle = \left\langle \sum_{i=1}^{m+1} l(i) \frac{Q_{\mathrm{CHAIN}}(i)}{Q_{\mathrm{CHAIN}}} \right\rangle \tag{21}$$

The relative change of the length is:

$$\frac{\Delta l}{l_0} = \frac{\langle l \rangle}{l_0} - 1 \tag{22}$$

where $l_0 = l(i = m + 1)$ is the length of the molecule in all-*trans* state. From NMR order parameter measurements Seelig and Seelig [29] have estimated the effective length of the palmitic acyl chain to be 13.7 Å in DPPC at 42°C.

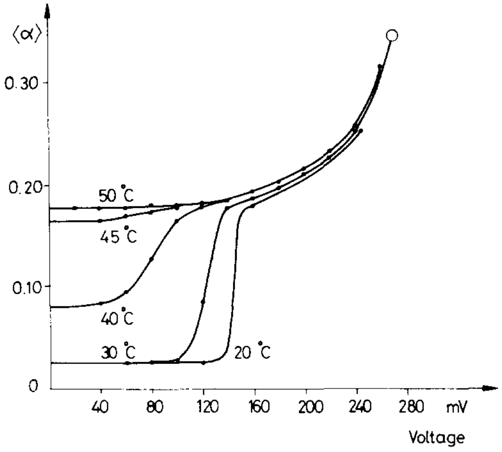


Fig. 6. Calculated relation between the relative area ⟨α⟩ and external voltage at different temperatures (n = 16).

According to our calculations the effective length is 13.3 Å at the same temperature.

Fluctuation of the chain length

The fluctuation of the chain length is:

$$\sigma = \sqrt{\langle l^2\rangle - \langle l\rangle^2}$$

where

$$\langle l^2\rangle = \left\langle \sum_{i=1}^{m+1} l^2(i) \frac{Q_{\text{CHAIN}(i)}}{Q_{\text{CHAIN}}} \right\rangle \tag{23}$$

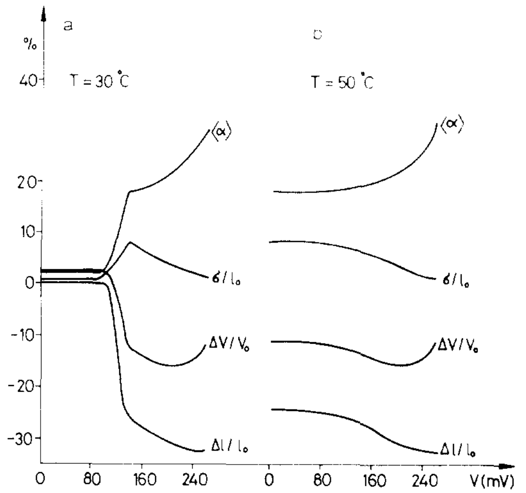
According to the results of Jacobs et al. [11] this fluctuation causes a roughness of the bilayer water interfaces and not of the interface between the two monolayers in the bilayer. Meanwhile in the case of monolayer experiments one can expect a more expressed roughness at the terminal end of the molecules. At this point we do not agree with Marcelja [4] in the interpretation of σ although our calculated temperature dependence of σ is similar to Marčelja's one.

Young's modulus

The voltage and temperature dependence of membrane thickness (Figs. 7 and 8) are available for the calculation of Young's modulus and the thermal expansion coefficient, respectively. Taking into consideration that average pressure $\langle p\rangle$ on the membrane is:

$$\langle p\rangle = \frac{1}{2}\,\epsilon_o\epsilon_m \frac{V^2}{\tau^2} \tag{24}$$

where $\tau = 2\ \langle l\rangle$, therefore Young's modulus could be calculated in the fol-



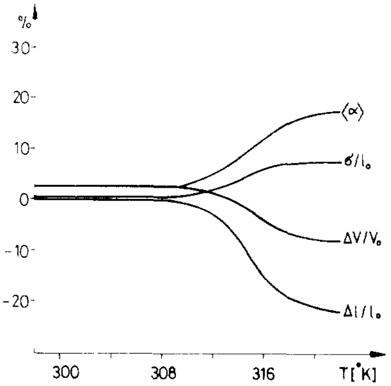


Fig. 7. Voltage dependence of relative values of area ($\langle\alpha\rangle$), fluctuation of the chain length (σ/l_0), volume change ($\Delta V/V_0$), hydrocarbon chain length change ($\Delta l/l_0$) at 30° C (a) and 50° C (b) ($n = 16$).

Fig. 8. Temperature dependence of relative values of area ($\langle\alpha\rangle$), fluctuation of the chain length (σ/l_0), volume change ($\Delta V/V_0$), hydrocarbon chain length change ($\Delta l/l_0$) for DPPC.

lowing way:

$$Y^{-1} = \frac{1}{\tau}\frac{\partial \tau}{\partial \langle p\rangle}\bigg|_{\langle p\rangle=0} = \frac{1}{\left\{\epsilon_0\epsilon_{\mathrm{m}} \cdot \frac{V}{\tau}\left[\frac{1}{(\partial\tau/\partial V)} - \frac{V}{\tau}\right]_{V=0}\right\}} \tag{25}$$

Table I shows the calculated values of Young's modulus Y at different temperatures for DPPC. The calculated values of Young's modulus depend very strongly on the membrane conformation. The more ordered is the membrane structure the higher is the value of the Young's modulus. Our calculations are supported by experimental results. Requena et al. [33] measured $Y \approx 10^5$–$10^7\ \mathrm{N \cdot m^{-2}}$ for egg phosphatidylcholine bilayer membrane above the phase transition temperature and similar values were found also by Passechnik and Hianik [34]. But in the presence of cholesterol in bilayer membrane, the value of Y was raised to $3 \cdot 10^8\ \mathrm{N \cdot m^{-2}}$ [34]. Taking into consideration the freezing effect of cholesterol on the membrane structure we can assume that Y value for pure egg phosphatidylcholine bilayer membrane will also rise considerably

TABLE I

CALCULATED VALUES OF YOUNG's MODULUS FOR DPPC BILAYER AT DIFFERENT TEMPERATURES

	Temperature (°C)			
	20	30	40	50
Young's modulus ($\mathrm{N \cdot m^{-2}}$)	$9 \cdot 10^9$	$2 \cdot 10^8$	$5 \cdot 10^5$	$6 \cdot 10^6$

TABLE II

CALCULATED TEMPERATURE DEPENDENCE OF THE LINEAR THERMAL EXPANSION COEFFICIENT (β) AT $V = 0$ FOR DPPC

	Temperature (°C)		
	27	42	48
$-\beta$ (°C^{-1})	$4 \cdot 10^{-5}$	$4 \cdot 10^{-2}$	$3 \cdot 10^{-3}$

below the phase transition temperature. These facts support our calculations and show the shortcomings of Crowley's model [15] where a voltage-independent elastic modulus was used.

Linear thermal expansion coefficient

By means of the relation between the membrane thickness and temperature (see Fig. 8) one can calculate the linear thermal expansion coefficient β of the membrane as a function of temperature (see Table II). For egg phosphatidylcholine multibilayers [35] in the fluid state the experimentally determined linear thermal expansion coefficient is $-2 \cdot 10^{-3}$/°C, which is in excellent agreement with the calculated values for the fluid phase of DPPC. Similar to Young's modulus, the thermal expansion coefficient depends also very strongly on the order of the membrane structure.

Volume increase

Figs. 7 and 8 show the temperature and voltage dependence of the membrane volume. The relative volume change is:

$$\frac{\Delta V}{V_0} = \frac{\tau(1 + \langle\alpha\rangle)}{2\,l_0} - 1 \qquad (26)$$

Here, in contrast with the experimental findings [30], our calculations resulted in a volume decrease at the transition temperature. Furthermore, the negative values of the relative volume change would mean an unlikely collapse of the membrane material.

As we shall treat in a subsequent paper in detail, this problem could be eliminated by taking into consideration the dependence of A_0 on the actual conformations of the molecules. Namely, the molecules, though considered to be hard disks, have internal degrees of freedom and the close-packed area (A_0) of the membrane increases when these states are excited thermally, electrically or mechanically.

Determination of model parameters

We determined γ in the same way as Jacobs et al. [1]. For suitable γ, at the transition temperature of DPPC the two minima of free energy-area curve have to be equally low, when the external pressure, i.e. external voltage is zero. Thus γ is 0.3999 if the interaction energy of the head groups (δ) is taken to be -650 cal/mol. Nagle [36] has estimated δ to be about -500 cal/mol. D is fitted so that the membrane ruptures between 200 and 300 mV. Thus for a free hydrocarbon chain D is $7\ \mathrm{N} \cdot \mathrm{m}^{-2}$, which is much less than the Young's modulus of a close-packed system of the hydrocarbon chains of a bilayer. In our calculations the cooperative unit size ($\mathfrak{N}$) was taken to be 11 [21].

Conclusions

In this paper we demonstrate that first-order phase transition of phospholipid bilayers could be induced not only by changes in temperature [30,32] but also by an external electric field normal to the membrane surface. Further increasing of the external electric field leads to another sudden loosening of the membrane structure, when the membrane ruptures. In contrast to Crowley's [15] phenomenological model this model is a microscopical treatment of the dielectric breakdown.

By means of our model we found a strong correlation between the field-dependent membrane structure and its charge transfer properties, i.e. the increasing number of the structural defects at higher voltages causes the non-linear current-voltage characteristics of bilayer membrane. This assumption refers not only to the ionic but also the electronic charge transport. As is generally accepted [37,38], the electron wave functions near the band edges are strongly perturbed by structural disorders and become localized. They give rise to tailing of density of states well into the gap, and overlapping of valence and conduction band may or may not occur. Thus the electronic conductivity of the membrane increases with increasing number of structural defects.

As our model is based on the Jacobs' model [1] we obtained similar values to those of Jacobs and coworkers for the transition temperatures and transition enthalpies of different phospholipid membranes, but our model inherited the shortcomings too (volume decrease at the phase transition).

In the simple case when we neglect the deformation energy term, the effect of the field on the membrane structure is insignificant even at 1 V external field though according to the experiments phospholipid bilayer membranes rupture at about 240 mV [26]. Thus one cannot explain the membrane elasticity either only by entropy or energy change. Finally we conclude that at suitably high field strengths the membrane behaves as a non-ideal elastic material in which an elastic-after effect takes place. The role of this field-induced defect formation could be very important in the transport processes of biological membranes as was pointed out recently by Cope [39] and Schwarz [40].

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