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Electric Field-Induced Breakdown of Lipid Bilayers and Cell Membranes: A Thin Viscoelastic Film Model

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Summary. A simple viscoelastic film model is presented, which predicts a breakdown electric potential having a dependence on the electric pulse length which approximates the available experimental data for the electric breakdown of lipid bilayers and cell membranes (summarized in the reviews of U. Zimmermann and J. Vienken, 1982, *J. Membrane Biol.* **67**:165 and U. Zimmermann, 1982, *Biochim. Biophys. Acta* **694**:227). The basic result is a formula for the time τ of membrane breakdown (up to the formation of pores): $\tau=\alpha(\mu/G)/(\varepsilon_m^2\varepsilon_o^2 U^4/24\sigma Gh^3+T^2/\sigma Gh-1)$, where α is a proportionality coefficient approximately equal to $\ln(h/2\zeta_o)$, h being the membrane thickness and ζ_o the amplitude of the initial membrane surface shape fluctuation (α is usually of the order of unity), μ represents the membrane shear viscosity, G the membranes shear elasticity modules, ε_m the membrane relative permittivity, $\varepsilon_o=8.85\times10^{-12}\,F/m$, U the electric potential across the membrane, σ the membrane surface tension and T the membrane tension. This formula predicts a critical potential U_c; $U_c=(24\sigma Gh^3/\varepsilon_m^2\varepsilon_o^2)^{\frac{1}{4}}$ (for $\tau=\infty$ and $T=0$). It is proposed that the time course of the electric field-induced membrane breakdown can be divided into three stages: (i) growth of the membrane surface fluctuations, (ii) molecular rearrangements leading to membrane discontinuities, and (iii) expansion of the pores, resulting in the mechanical breakdown of the membrane.

Key Words membrane breakdown · viscoelastic films · membrane potential

Introduction

Electrical breakdown of membranes is termed the phenomena of sharply increased electrical conductivity of membranes (more than 8 orders of magnitude) under the application of electrical pulses of high intensity, which does not necessarily lead to an irreversible mechanical breakdown of the membrane (Zimmermann et al., 1981, 1982). The electrical breakdown of membranes occurs at different electrical potentials depending on the electrical pulse duration. The potential, above which the membrane undergoes an electrical breakdown, is called the critical potential (Zimmermann, Scheurich, Pilwat & Benz, 1981; Zimmermann & Vienken, 1982). The membranes usually break irreversibly at long pulse duration (Abidor et al., 1979; Zimmermann & Vienken, 1982). The electro-mechanical model of electric breakdown considers the membrane as an elastic body. Accordingly, the conditions for membrane rupture are derived from the balance of electrostatic and elastic forces (Crowley, 1973; Zimmermann, Pilwat & Riemann, 1974). This model does not predict the pulse length dependence of the breakdown potential. Zimmermann et al. (1981) and Zimmermann and Vienken (1982) have pointed out that two effects may contribute to this phenomenon: the viscoelastic properties of the membrane and the Born effect. While the latter effect is important at high potentials and very short times, here we confine our examination to the influence of membrane viscoelastic properties on the kinetics of electrical breakdown. In addition, we also take into consideration the influence of membrane surface tension.

As originally suggested by Jain, Maldarelli and Ruckenstein (1978), the stability of biological membranes can be examined by modelling them as thin liquid films. Recently the Jain treatment of the dynamics of biological membranes was extended to include their viscoelastic properties (Maldarelli & Jain, 1982; Steinchen, Gallez & Sanfeld, 1982). These authors used the "body force" approach to incorporate long-range intermolecular forces into the equations of motion. While interesting from a fundamental theoretical point of view, this ap-

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proach is difficult to apply to problems where the exact form of intermolecular potential is unknown. Here, we prefer the disjoining pressure approach, in which the effect of intermolecular interactions (and other constraints) can be included in the boundary conditions. Recently this approach has been successfully used to examine the stability of a simple membrane system—a liquid film between two membranes (Dimitrov, 1982). Applied rigorously, both approaches lead to the same results.

The basic goal of this work is to explain the dependence of breakdown potential on pulse duration and physicochemical properties of membranes by modelling them as thin viscoelastic films.

The Model

We consider the membrane as a thin viscoelastic film with fluctuating surfaces, bounded by two semi-infinite bulk phases (Fig. 1). The basic assumptions are:

1) The amplitudes of surface shape perturbations ζ_A and ζ_B (subscripts A and B refer to the upper and lower surfaces, respectively) are much smaller than the average membrane thickness h ($\zeta_{A,B} \ll h$), i.e., a linear stability analysis is used.

2) The surface shape perturbations can be represented as a superposition of surface waves with wave lengths λ_n much longer than the membrane thickness h. Further on, we will omit the index n, knowing that we examine an arbitrary surface wave with wave number k and length λ. Thus we use the Reynolds lubrication equations in the form (for details *see*, e.g., the recent review of Dimitrov, (1983))

$$\partial p/\partial r = \partial \tau_{rz}/\partial z \tag{1}$$

$$\partial p/\partial z = 0 \tag{2}$$

where p is the pressure in the membrane, r and z the radial and axial cylindrical coordinates, respectively (the assumption for axially symmetrical shape perturbations does not imply any limitations on the final results; here it is used mainly because of the natural axial symmetry of most of the biological and model membranes), and τ_{rz} the r, z component of the stress tensor σ_{ik} ($\sigma_{ik} = -p + \tau_{ik}$, i and k having the values 1, 2 or 3 when referring to Cartesian coordinates x_1, x_2 and x_3).

3) The membrane is an incompressible body, i.e.

$$\nabla_r u_r + \partial u_z/\partial z = 0, \qquad \nabla_r u_r = \partial u_r/\partial r + u_r/r \tag{3}$$

where u_r and u_z are the radial and axial components of the displacement vector u_i, respectively.

4) The membrane behaves as a viscoelastic, isotropic material, represented as a standard solid model, composed of a Kelvin body (with elastic modules G' and viscosity μ') in series with a linear spring (with elastic modulus G'_0) (*see* Fig. 2*a*). This model is equivalent to the three-element model shown in Fig. 2*b*: a Maxwell fluid (with viscosity μ and elasticity G_o) in parallel with a restoring spring (with elasticity G). As a matter of convenience, further on we use only the second modification.

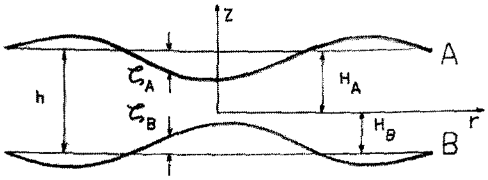

Fig. 1. Sketch of the model. The membrane is represented as a thin film, having two different surfaces A and B, fluctuating with amplitudes $\zeta_{A,B}$ around planes, placed at an average separation h (the average membrane thickness). The growth of the surface perturbations can result in a local membrane breakage (pore formation). H_A and H_B are the distances from an arbitrary plane $z=0$ to both surfaces (*also see* Appendix A)

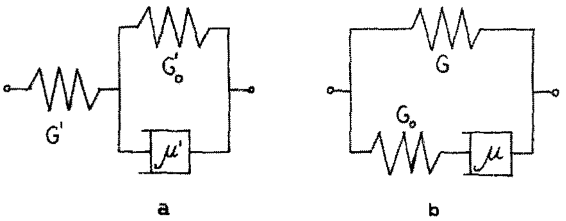

Fig. 2. Two viscoelastic models, equivalent to each other, used to represent the membrane dynamics: (*a*) a Kelvin body (G'_o, μ') in series with a spring (G') and (*b*) a Maxwell body (G_o, μ) in parallel with a spring (G)

It can be seen from Fig. 2*b* that when G_o is taken to be very large ($G_o = \infty$) a Kelvin body results (with G, μ); when $G=0$ the model reduces to the Maxwell one. For the three-element viscoelastic model, shown in Fig. 2*b*, the corresponding constitutive equation in cylindrical coordinates is (*see*, e.g., the works of Skalak, Schmid-Schonbein and Chien (1982) and Dimitrov (1983)):

$$\tau_{rz} + (\mu/G_o)\dot{\tau}_{rz} = G(\partial u_z/\partial z) + \mu(1 + G/G_o)(\partial v_r/\partial z) \tag{4}$$

where $\dot{\tau}_{rz}$ indicates the time derivative of τ_{rz} and v_r is the radial velocity ($v_r = \dot{u}_z$).

5) The pressure p of an interfacially deformed membrane can be calculated as (for details *see*, e.g., Dimitrov, 1983)

$$p + \Pi'(\zeta_A + \zeta_B) = -\sigma_A \Delta_r \zeta_A = -\sigma_B \Delta_r \zeta_B; \;\; \Delta_R = \partial \nabla_r/\partial r \tag{5}$$

where Π' denotes the derivative ($d\Pi/dh$) of the disjoining pressure Π with respect to membrane thickness h and $\sigma_{A,B}$ the tensions of the membrane surfaces. The disjoining pressure term takes into account the surface interaction forces due to the membrane properties themselves, as well as those arising when external constraints are applied. For example, if an external electrical field induces a membrane potential U, the additional disjoining pressure Π_{el} will be

$$\Pi_{el} = -\varepsilon_m \varepsilon_0 U^2/2h^2 \tag{6}$$

where ε_m is the relative dielectric constant of the membrane material and ε_o the permittivity of free space.

6) Due to surface tension gradients (particularly, arising from surface activity species), the tangential components of the surface displacements and their respective

velocities are very small and are assumed to be zero (Dimitrov, 1983). Thus

$$u_r = 0 \tag{7}$$

at both surfaces.

The results were calculated based upon these assumptions (*see* Appendix A) and are shown in the next section.

Results

The final result is the relationship between the angular velocity ω (in our case ω has only a real part β) and the wave number k

$$\omega = \beta = -[12G + h^3k^2(\bar{\sigma}k^2 - \Pi')]/[12\mu(1 + G/G_o) + \mu h^3 k^2(\bar{\sigma}k^2 - \Pi')/G_o] \tag{8}$$

where $\bar{\sigma} = \sigma_A \sigma_B(\sigma_A + \sigma_B)^{-1}$. Recall, ω is a measure of the velocity of growth of the surface shape perturbations: $\partial\zeta_{A,B}/\partial t = \omega\zeta_{A,B}$, respectively, $\zeta_{A,B}$ is proportional to $\exp(\omega t)$, t being the time. Hence, when the real part of ω, the growth coefficient β, is greater than unity, $\beta > 0$, the system is unstable and the membrane will break; in the opposite case, $\beta < 0$, the membrane is stable and at $\beta = 0$ a marginally stable state occurs. The condition $\beta > 0$ may be satisfied for many waves, among them being one or several waves with largest growth coefficients β_d. This wave will break the membrane, hence it is called the dominant wave. The reciprocal value of the growth coefficient β_d for the dominant wave β_d^{-1} is a measure of the breaking time τ ($\tau \approx \beta_d^{-1}$) for local regions of the membrane. It is that time which is necessary for the surface shape perturbation to travel from an initial, equilibrium amplitude ζ_o to the position of zero local membrane thickness, thus forming pores in the membrane.

We now follow this idea to present a theory as simple as possible for the kinetics of electrical field-induced membrane breakdown. Because of the lack of appropriate experimental data (at our present knowledge) for more complicated viscoelastic models, we will only consider here in detail the simple case of a Kelvin body ($G_o = \infty$). It is a reasonable representation of cell membranes (Evans & Skalak, 1980). We consider a symmetrical membrane ($\sigma_A = \sigma_B = \sigma$). In addition, we will assume that the disjoining pressure Π is entirely determined by the electric field-induced membrane potential ($\Pi = \Pi_{el}$), i.e., we will use Eq. (6) to express Π'; thus $\Pi' = \varepsilon_m \varepsilon_o U^2/h^3$.

Following the above assumptions, Eq. (8) reduces to

$$\omega = \beta = -\frac{G}{\mu} - \frac{\sigma h^3 k^4}{24\mu} + \frac{\varepsilon_m \varepsilon_o U^2 k^2}{12\mu}. \tag{9}$$

The dominant wave number k_d will be found by the condition $\partial\beta/\partial k = 0$ at $k = k_d$. Substituting the dominant wave number thus obtained in Eq. (9) and equating the breaking time τ to β_d^{-1} (with a constant of proportionality α), we obtain (*see* Appendix B)

$$\tau = \alpha\left(\frac{\mu}{G}\right) \bigg/ \left(\frac{\varepsilon_m^2 \varepsilon_o^2 U^4}{24\sigma G h^3} - 1\right) \tag{10}$$

where the proportionality factor α is of the order of unity and is calculated to be approximately equal to $\ln(h/2\zeta_o)$, ζ_o being the initial shape perturbation amplitude, due to thermal fluctuations or other effects (ζ_o is usually of the order of angstroms) (*see* Appendix B).

The very interesting consequences of Eq. (10) are:

1) It predicts a critical potential

$$U = U_c = \left(\frac{24\sigma G h^3}{\varepsilon_m^2 \varepsilon_o^2}\right)^{\frac{1}{4}} \quad \text{at } \tau = \infty. \tag{11}$$

At smaller potentials ($U < U_c$) the breaking time is negative, i.e., the membrane is stable, and its lifetime is infinity.

2) With increasing potential (above the critical value U_c) the breaking time τ decreases, just as observed by experiment. We can present this dependence in the following simple, dimensionless form

$$\bar{\tau}^{-1} = \bar{U}^{-4} - 1 \tag{12}$$

where $\bar{\tau} = \tau/\tau_r = (G/\alpha\mu)\tau$ and $\bar{U}^4 = U^4/U_c^4 = \varepsilon_m^2 \varepsilon_o^2 U^4/24\sigma G h^3$.

At first, we compare the expression for the critical potential U_c with the predictions of previous theories (Crowley, 1973; Zimmermann et al., 1974). For this purpose it is convenient to rewrite Eq. (11) in another form

$$U_c^2 = \left(\frac{8\sigma}{hE}\right)^{\frac{1}{2}} \frac{Eh^2}{\varepsilon_m \varepsilon_o} \tag{13}$$

where we have introduced the Young modulus E, equal to $3G$ for incompressible bodies. The expression (Eq. (13)) differs from the prediction of the electro-mechanical model (Zimmermann et al., 1974), where the contribution of the σ

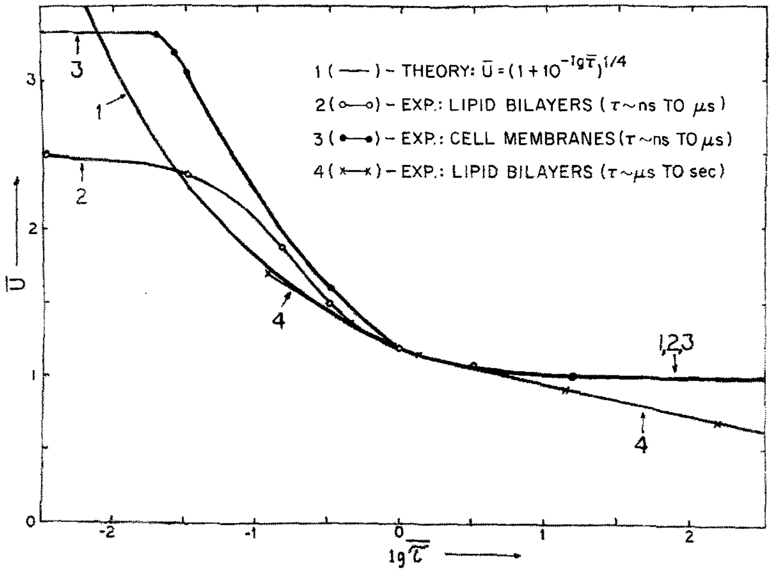

Fig. 3. Comparison of the theoretical prediction for the dependence of the dimensionless time of membrane breakdown $\bar{\tau}$ on the dimensionless electric potential $\bar{U}$ (Eq. (14)) (curve 1) with the experimental data of Benz and Zimmermann (1980) (curve 2, o—o, is for cholesterol bilayers at 40° C and curve 3, ●—●, for cell membranes of *V. utricularis* at 18° C) and those of Abidor et al. (1979) for bilayers from general phospholipids at 27° C (curve 4, ×—×)

surface tension was not taken into account, by a factor of $e(8\sigma/hE)^{\frac{1}{2}}$, e being the basis of the natural logarithm. It has been noted by Benz and Zimmermann (1980) that membranes, according to the electro-mechanical model, have to be compressed by about 40% to induce breakdown. It seems unlikely, especially in the case of some lipid bilayers, where a value for E as high as 1.4×10^8 N/m^2 has been reported (Alvarez & Latorre, 1978). It is seen from Eq. (13) that low critical potentials U_c can occur due to low surface tension σ, even in the case of large Young modulus E. Hence, the average membrane thickness may not be changed significantly, but only the local shape perturbations can increase their amplitudes ζ, leading to local breaking of the membrane and pore formation. White (1974) presented a value of 3.72×10^5 N/m^2 ($\varepsilon_m = 2.24$ and $h = 3.5 \times 10^{-9}$ m) for bilayers made from oxidized cholesterol in n-decane. Membrane surface tension σ is usually not measured in breakdown experiments. (It is known that it is very sensitive to different surface active contaminants.) Assuming E of the order of 10^5 to 10^8 N/m^2 and σ in the range from 10^{-2} to 1 mN/m, we obtain that the factor $e(8\sigma/hE)^{\frac{1}{2}}$ varies (at $h \sim 5$ nm) from 10^{-2} to 10. For example, for bilayers from oxidized cholesterol in n-decane (with the data of White (1974) cited above) $e(2\sigma/hE)^{\frac{1}{2}} = 2.14 \times 10^2 \sigma^{\frac{1}{2}}$. For this system the electro-mechanical model predicts $U_c = 0.29$ V, but the experimentally measured value is 0.40 V (Benz & Zimmermann, 1980). Our results coincide with the experimentally measured value at $\sigma = 0.1$ mN/m, which is a quite expected and reasonable value. It follows from Eq. (13) that with decreasing surface tension σ the critical potential decreases. As is now well known, surface-active substances strongly destabilize membranes. In the limiting case of zero surface tension, we arrive at a zero critical potential, where the membrane is unstable.

In order to compare the theory with the experimental data for dependence of potential U on time of breaking τ, let's rewrite Eq. (12) in another form

$$\bar{U} = [1 + 10^{-(\lg\bar{\tau})}]^{\frac{1}{4}}. \tag{14}$$

Figure 3 shows this universal curve (curve 1), compared with experimental data of Benz and Zimmermann (1980) (curve 2, o—o: bilayers made from oxidized cholesterol in n-decane, at 40° C in 1 M KCl; and curve 3, ●—●: membranes of cells of the giant alga *Valonia utricularis* at 18° C) and of Abidor et al. (1979) (curve 4, ×—× : bilayers from general phospholipids at 27° C). Their data were processed in a manner similar to the theoretical curve: the potential, corresponding to a given experimental point (or the average of several points, if there is more than one point corresponding to the same time), is made dimensionless by using the measured critical potential U_c (the potential at the longest time). The respective time is also made dimensionless with the aid of the characteristic time τ_f (*see* Eq. (12)). We choose τ_f in order to fit the experimental data. For the data of Abidor et al. (1979) we used two experimental points at short times in order to determine the critical potential U_c and the characteristic time τ_f. It is seen from Fig. 3 that, while the theoretical curve fits the experimental data of Benz and Zimmermann (1980) well (excluding the divergence at very short times — less than 1 μsec for the lipid bilayers), it coincides with the data of Abidor et al. (1979) only for short times (short, compared to the other part of the curve; the shortest time is 100 μsec). The characteristic times τ_f, used to fit the experimental data, are equal to 3, 31, and 720 μsec for the curves 2, 3 and 4, respectively. According to Eq. (12) $\tau_f = \alpha\mu/G$. Here the proportionality factor $\alpha = \ln(h/2\zeta_o)$ is estimated at $h = 3.5$ nm and $2\zeta_o = 0.5$ nm to give $\alpha = 2$. Taking G equal to 4×10^5 N/m^2 (this is a value presented by White (1974), but at 20° C) we obtain for the viscosity μ of bilayers from cholesterol ($\tau_f = 3$ μsec) a quite reasonable value of 0.6 N sec/m^2. This is the order of magnitude of the microviscosity of many lipid bilayers (*see*, e.g., Houslay & Stanley, 1982). If we suppose that the elasticity modulus of the cell membrane of *V. utricularis* is of the same order of magnitude ($G = 4 \times 10^5$ N/m^2), then its viscosity will be ten times greater ($\mu = 6$ N sec/m^2) than the viscosity of the lipid bilayer, which also is reasonable for the more rigid cell membrane. The last value ($\tau_f \sim 720$ μsec) was difficult to interpret. It may be due to the lower temperature ($T = 27°$ C) or greater elastic modulus. More likely our theory is not applicable to the later stages of membrane breakdown, where a statistical mechanism of pore expansion and fusion is operating (Abidor et al., 1979; Pastushenko et al., 1979; Chizmadzhev et al., 1979).

Discussion

We have presented a viscoelastic model of electric breakdown of lipid bilayers and cell membranes, which predicts results in agreement with the experimental data of Benz and Zimmermann (1979). It cannot explain the last stages of mechanical breakdown of lipid bilayers as observed by Abidor et al. (1979), where another mechanism is operating (Chizmadzhev, Arakelyan & Pastushenko, 1979).

This model is an extension of the electromechanical model of membrane breakdown (Crowley, 1973; Zimmermann et al., 1974), taking into account the surface tension and viscosity of the membrane. For this reason it is able to describe two important phenomena: (1) the decreasing membrane stability with decreasing membrane surface tension, and (2) the time course of the membrane breakdown. It is now well established that the stability of lipid bilayers considerably decreases under the influence of surface-active substances. A simple explanation of this fact can be given, based on Eq. (11). It can be seen that the critical potential U_c is proportional to the surface tension σ to the power $\frac{1}{4}$. Hence, it is possible, when decreasing the surface tension, to reach the preexisting membrane potential, after which the membrane will break. The dependence ($U \sim \sigma^{\frac{1}{4}}$) is not strong enough to allow very easy membrane breakdown under the influence of different surfactant species, but not weak enough to prevent it if the surface tension is very low.

The ability to describe the initial stage of membrane breakdown, which is now generally accepted to be the formation of pores (in the membrane) is very important. The reversible membrane breakdown is a rather fast process (times usually of the order of 10 μsec), which was studied (*see* the excellent reviews of Zimmermann and coworkers (Zimmermann et al., 1981, Zimmermann & Vienken, 1982)) very extensively in recent years using precise experimental techniques. The pore expansion and fusion, which leads to the mechanical breakdown of the membrane, is a slower process (times of the order of 10 to 100 μsec and up) (Abidor et al., 1979) and can be described by the theory of Chizmadzhev and collaborators (1979). As can be seen from Fig. 3 (curve 4) our model fails to fit the experimental data for large times (τ above 1 msec). In addition, it predicts a value of 0.5 V for the critical potential for this case, which is inconsistent with the experimental observations. For large potentials, which correspond to very short times (τ smaller than 100 nsec), the fit between the theory and the experiment is also poor (*see* Fig. 3, curves 2 and 3). As pointed out by Zimmermann et al. (1981) and Zimmermann and Vienken (1982) another effect, usually due to the ability of individual ions to move through the membrane at high electric fields, can be significant at high potentials and short charging times. However, the result that the membranes remain in the high conductance state for some time after breaking cannot be understood using this mechanism, if the membrane thickness does not change (Benz & Zimmermann, 1980).

Based on the viscoelastic mechanism present-

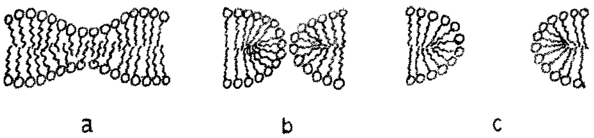

Fig. 4. Possible stages of electric field-induced membrane breakdown: (*a*) growing of the surface shape fluctuations, (*b*) molecular rearrangements, leading to a membrane discontinuity, and (*c*) pore expansion, which can result in an irreversible membrane breakdown

ed here, it is convenient to divide the process of electric field-induced membrane breakdown into three stages (*see* Fig. 4): (1) Growing of the membrane shape fluctuations (Fig. 4*a*), (2) Molecular rearrangements leading to a discontinuity of the membrane (Fig. 4*b*) and (3) Expansion of the pore resulting in the mechanical breakdown of the membrane (Fig. 4*c*).

The total time of membrane breakage can be represented as a sum of the times corresponding to each stage. The theory presented here describes the first stage, and, rigorously taken, it is valid up to a local thickness change 2ζ of the order of $0.1\,h$ (linear stability analysis). However, by analogy to similar phenomena well known in the colloid chemistry, as rupture of foam, wetting, and emulsion films, and as shown by the present calculations, because of the small driving force (due to the small thickness change), the time of growth of the surface fluctuation can be rather long ($\sim\mu$sec). By increasing the fluctuation amplitude, and respectively decreasing the membrane thickness, the driving force, due to the electrical field, rapidly (nonlinearly) increases. This results in fast molecular rearrangements, leading to discontinuity of the membrane (Fig. 4*b*). Different molecular pictures of this process can be imagined, but it is still not clarified. One of the reasons is the very short duration of this stage. As pointed out by Benz and Zimmermann (1980), the membrane breakdown itself lasts on the order of nanoseconds.

The last stage can be described by the phenomenological, statistical theory of Chizmadzhev and coworkers (1979). It usually takes milliseconds and more.

Finally, we would like to emphasize on possible extensions of the present theory:

1) This concerns the dynamic properties of the membrane material. The general three-element model used in this work can be considered in detail when appropriate experimental data are available. Another important question is the mechanical and electrical anisotropy of the membrane.

2) The medium, surrounding the membrane, can possess viscoelastic properties.

3) Short wavelengths can contribute to the membrane rupture.

4) The presence of other membranes (or other particles) may significantly change the membrane stability.

5) The influence of external constraints. One important example is osmotic pressure, resulting in an increase of membrane tension. A simple formula for this case is presented in Appendix C.

6) The tangential mobility of membrane surfaces.

Our theoretical and experimental investigations are now in progress on these questions as on others, concerning the fundamental problem of the stability of membrane systems.

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Appendix A

Derivation of the General Dispersion Equation for the Three-Element Viscoelastic Model

As usually accepted in the linear stability analysis, let us assume that all the quantities in Eqs. (1)-(5) can be represented as

$$\begin{matrix} p \\ \tau_{rz} \\ u_r \\ u_z \\ \zeta_A \\ \zeta_B \end{matrix} = \begin{matrix} p_f \\ \tau_{rz} \\ u_{rf} \\ u_{zf} \\ \zeta_{Af} \\ \zeta_{Bf} \end{matrix} \quad \exp(\omega t) \qquad \text{(A1)}$$

where p_f, r_{rz}, u_{rf}, u_{zf}, ζ_{Af} and ζ_{Bf} are functions of r and z, independent on the time t. The substitution of Eq. (A1) into Eqs. (1)-(5) yields

$$\partial p_f/\partial r = \partial \tau_{rzf}/\partial z \qquad \text{(A2)}$$

$$\partial p_f/\partial z = 0 \qquad \text{(A3)}$$

$$\nabla_r u_{rf} + \partial u_{zf}/\partial z = 0 \qquad \text{(A4)}$$

$$(1+\omega\mu/G_o)\tau_{rzf} = [G+\mu\omega(1+G/G_o)]\,\partial u_{rf}/\partial z \qquad \text{(A5)}$$

$$p_f + \Pi'\zeta_f = -\sigma_A \Delta_r \zeta_{Af} = -\sigma_B \Delta_r \zeta_{Bf} \qquad \text{(A6)}$$

where we have used the relation $\dot{u}_r = \partial u_r/\partial t = \omega u_r$ and have introduced the total fluctuation amplitude $\zeta_t = \zeta_A + \zeta_B$ ($\zeta_t = \zeta_f \exp(\omega t)$). The boundary conditions for u_{rf} and u_{zf} are

$$u_{rf} = 0 \qquad \text{at } z = H_A, -H_B \qquad \text{(A7)}$$

$$u_{zf} = \zeta_{Af,Bf} \qquad \text{at } z = H_A, -H_B \qquad \text{(A8)}$$

where we have used Eq. (7) and have introduced the distances H_A and H_B from an arbitrary plane $z=0$ to the both surfaces (*see* Fig. 1). The substitution of τ_{rzf} from Eq. (A5) into Eq. (A2), the subsequent integration on z, using Eq. (A3) and the boundary conditions (Eq. (A7)) leads to an expression for the radial displacement u_{rf}. The substitution of this expression into the continuity equation (A4) and the subsequent integration on z, using the boundary conditions (Eq. (A8)), yields

$$\zeta_f = -h^3 \Delta_r p_f/\gamma; \qquad \gamma = [G+\mu\omega(1+G/G_o)]/(1+\mu\omega/G_o). \qquad \text{(A9)}$$

The integration of the second equality in Eq. (A6) on r and using the condition for lack of a singularity at $r=0$ and that $\zeta_A = \zeta_B = 0$ at the membrane boundaries ($r=R$, R being the membrane radius) gives

$$\zeta_f = \zeta_{Af} + \zeta_{Bf} = (1+\sigma_B/\sigma_A)\zeta_{Bf} = (1+\sigma_A/\sigma_B)\zeta_{Af}. \qquad \text{(A10)}$$

The substitution of Eq. (A10) and of p_f from Eq. (A6) into Eq. (A9) and using the representation $\zeta_f = 2\zeta_o J_o(kr)$, ζ_o being an initial amplitude and $J_o(kr)$-Bessel's function of first kind, zero order ($\Delta_r J_o(kr) = -k^2 J_o(kr)$), we obtain the dispersion equation (8).

Appendix B

Derivation of the Expression for the Membrane Breakdown Time

Let us suppose that the membrane will break when the two surfaces touch each other, i.e., when $2\zeta = h$ (for the case of symmetrical membranes, where $\sigma_A = \sigma_B$). The amplitude $\zeta = \zeta_A = \zeta_B$ can be represented as

$$\zeta = \zeta_o \exp(\beta t), \qquad \text{(B1)}$$

where the part, which depends on the radial coordinate $r(J_o(kr))$, is taken at its maximum value ($J_o(0)=1$). Assuming that the shape perturbation starts to grow from $t=0$ and the breaking occurs when $t=\tau$ and $2\zeta = h$, we obtain

$$\tau = \alpha/\beta, \qquad \alpha = \ln(h/2\zeta_o), \qquad \text{(B2)}$$

which coincides with that expression, which is used to get Eq. (10).

Another approximate expression for α can be obtained if we take into account that our analysis is linear and, consequently, valid for $\zeta/h = \varepsilon$, where ε is a small number. In addition, let us assume that, because of the strong increase of the external or intermolecular forces (Π) with decreasing the local thickness $h - 2\zeta$ (this is a necessary condition for the membrane breakdown), the time of shape perturbation growing at $\zeta/h > \varepsilon$ is much smaller than the time of the linear growing and therefore can be neglected. Then, the time of membrane breaking will be

$$\tau = \alpha_n/\beta, \qquad \alpha_n = \ln(\varepsilon h/2\zeta_o). \tag{B3}$$

Because of the logarithmic dependence of α_n on ε, the proportionality factor α is not significantly affected from ε and for estimates can be used in the form of Eq. (B2). In any case, the general rule is that, because of making other approximations, α is to be taken of the order of unity.

Appendix C

Effect of the Membrane Tension

Let us suppose that the membrane tension T is equivalent of acting at an additional pressure equal to $T/(h+\zeta_t)$, where $\zeta_t = \zeta_A + \zeta_B$. Then the dynamic pressure p in the membrane can be calculated by adding a new term, resulting from the expansion in series with respect to small ζ_t/h: $T/(h+\zeta_t) - T/h = -T\zeta_t/h^2$, in Eq. (5)

$$p + \Pi'\zeta_t + T\zeta_t/h^2 = -\sigma_A \Delta_r \zeta_A = -\sigma_B \Delta_r \zeta_B. \tag{C1}$$

It can be seen from Eq. (C1) that, in the disjoining pressure approach and for the linear stability analysis, the influence of the membrane tension is equivalent to an additional "disjoining pressure" equal to $-T/h$. Hence, all the formulae obtained in this paper can be extended to account for the membrane tension simply by replacing Π' with $\Pi' + T/h^2$. For example, the expression for the breaking time under the influence of electrical fields (Eq. (10)) will transform to

$$\tau = \alpha(\mu/G)/(\varepsilon_m^2 \varepsilon_o^2 U^4/24\sigma G h^3 + T^2/\sigma G h - 1). \tag{C2}$$

It follows from Eq. (C2) that the increase of the membrane tension T will result in a decrease of the critical potential and the breaking time. In addition, the membrane can be broken only by the action of the membrane tension (at $U=0$). The preliminary estimates, based on Eq. (C2), are in line with the basic experimental observations. Now in progress is our experimental and theoretical work, where the membrane tension effect will be examined in detail, based on a generalization of Eq. (C2) and compared with other work on this phenomenon. Particularly, we will attempt to develop a rigorous theory of membrane breakdown under the action of external forces which stretch the membrane.