Undulations, Steric Interaction and Cohesion of Fluid Membranes (*).

W. Helfrich and R.-M. Servuss

*Institut für Theorie der kondensierten Materie
and Institut für Atom- u. Festkörperphysik, Freie Universität Berlin,
Arnimallee 14, D-1000 Berlin 33, B.R.D.*

Summary. — The theory of undulations of fluid membranes is reviewed and in some parts extended. The functional dependences of the steric interaction of undulating membranes are derived in a new way from simple physical arguments. Discussing the competition between steric repulsion and van der Waals attraction, one finds that membranes which usually separate (*e.g.* giant egg lecithin vesicles) should cohere if under lateral tension. The contours of two cohering vesicles observed when egg lecithin was swelling are analysed to show that the net energy of cohesion can be extremely small ($\leqslant 10^{-5}$ erg cm^{-2}).

PACS. 87.20. – Membrane biophysics.

1. – Introduction.

Fluid membranes such as lecithin bilayers in water undergo out-of-plane fluctuations, also called undulations. These can be strong enough to be visible in a microscope if little or no lateral tension acts on the membrane. A single lecithin bilayer forming a giant vesicle is a good example.

Since membranes are two-dimensional structures, undulations give rise to some interesting properties which are often linked with a divergence as the

---

membrane area becomes infinite. Equally interesting is the behaviour of a pair of parallel membranes and of multilayer systems. The mutual collisions of undulating membranes produce a repulsive steric interaction which may overcome their van der Waals attraction.

In the present paper we first review the phenomenological theory of curvature elasticity and list the very few experimental data available. Undulations and their effects are then discussed in detail, some of them new. A novel theory of the steric interaction of fluid membranes is given next. It permits a very direct derivation of all functional dependences, but is poor in predicting the strength of interaction. Finally, we turn to the competition of steric repulsion and van der Waals attraction. While lecithin vesicles in water usually do not cohere, new experiments [1] have shown that cohesion can be « turned on » by an osmotically induced lateral tension. Here we consider some theoretical problems of vesicle cohesion and separation. In particular, it is argued that lateral tension should always lead to the cohesion of infinite parallel membranes. The contours of two cohering vesicles in a photograph are analysed to demonstrate that the cohesion energy can be surprisingly small.

2. – Fluid membrane curvature elasticity.

The phenomenological formula [2] for the curvature elastic-energy density per unit area of a fluid membrane may be written as

$$(1) \qquad\qquad g = \tfrac{1}{2}\varkappa(c_1 + c_2 - c_0)^2 + \bar\varkappa c_1 c_2 .$$

Here $c_1 = 1/R_1$ and $c_2 = 1/R_2$ are the principal curvatures, R_1 and R_2 being the principal radii of curvature. The spontaneous curvature c_0 is, in general, nonzero whenever the two sides of the membrane are unequal. There may be differences in lipid concentration and composition or in the aqueous media facing an otherwise symmetric bilayer. (Monolayers are asymmetric by definition.) The sum of curvatures, $c_1 + c_2$, and the Gaussian curvature $c_1 c_2$ are associated with different elastic moduli, $\varkappa$ and $\bar\varkappa$, of dimension erg. Equation (1) is the usual quadratic approximation. It is invariant with respect to an interchange of c_1 and c_2, as it must be, and contains all linear and quadratic invariants of this type, which is another requirement.

Equation (1) was used to derive a second-order differential equation for the shape of axisymmetric vesicles by means of the usual Euler-Lagrange formalism [2]. What makes the result special is the nonnegligible role of stresses that are quadratic functions of the principal curvatures. The differential

[1]   R. M. SERVUSS and W. HELFRICH: in preparation.
[2]   W. HELFRICH: *Phys. Lett. A*, **43**, 409 (1973).

equation was applied to calculate theoretical shapes of red blood cells [3] and artificial vesicles [4].

For the following it is important to note that the $\bar{\varkappa}$-term drops out of all shape equations unless they involve membrane edges. This agrees with the fact that the integral of Gaussian curvature over a closed surface is a topological quantity, depending solely on the genus of the surface (Gauss-Bonnet theorem). Dealing only with closed vesicles or theoretically infinite membranes, we can henceforth omit the nilpotent $\bar{\varkappa}$-term. We remark that the modulus $\bar{\varkappa}$ of Gaussian curvature influences the fusion of bilayers and monolayers, *i.e.* the presence or absence of passages, pores and other connective « point defects » [5]. Some of the cubic lyotropic liquid crystals mentioned by CHARVOLIN [6] and of the microemulsions analysed by TAUPIN [7] in their papers at this meeting may be cases in which it cannot be disregarded.

Experimental data are still very scarce. They were mostly obtained with egg lecithin which is probably a rather poor standard due to its variable composition [8]. The elastic modulus of the sum of curvatures was found from the bending fluctuations of tubular vesicles to be

$$(2) \qquad \varkappa = (2.3 \pm 0.3) \cdot 10^{-12} \text{ erg}$$

for egg lecithin membranes at room temperature [9]. PETROV *et al.* [10] reported an estimate of $\bar{\varkappa}$ for egg lecithin and a few other phospholipids, interpreting freeze-fracture photographs of aqueous multilayer systems of Kléman *et al.* [11]. Their rough value for all materials is

$$\bar{\varkappa} \approx 1 \cdot 10^{-12} \text{ erg} .$$

While PETROV *et al.* surmise that $\bar{\varkappa}$ becomes negative at higher water content,

[3] H. J. DEULING and W. HELFRICH: *Biophys. J.*, **16**, 861 (1976).
[4] H. J. DEULING and W. HELFRICH: *J. Phys. (Paris)*, **37**, 1335 (1976).
[5] W. HELFRICH: *Physics of Defects*, Les Houches Summer School, Session XXXV, edited by R. BALIAN, M. KLÉMAN and J. P. POIRIER (Amsterdam, 1981), p. 715.
[6] J. CHARVOLIN: *Nuovo Cimento D*, **3**, 3 (1984).
[7] C. TAUPIN: *Nuovo Cimento D*, **3**, 62 (1984); P. G. DE GENNES and C. TAUPIN: *J. Phys. Chem.*, **86**, 2294 (1982).
[8] This was seen in studies of its diamagnetic susceptibility. F. SCHOLZ, E. BOROSKE and W. HELFRICH: *Magnetic anisotropy of lecithin membranes*, poster presented at the « Meeting on Lyotropics and Related Fields » held in Rende, Cosenza, September 13-18, 1982, to be published elsewhere.
[9] R. M. SERVUSS, W. HARBICH and W. HELFRICH: *Biochim. Biophys. Acta*, **436**, 900 (1976); R. M. SERVUSS and E. BOROSKE: *Chem. Phys. Lipids*, **27**, 57 (1980).
[10] A. G. PETROV, M. O. MITOV and A. DERZHANSKI: *Phys. Lett. A*, **65**, 374 (1978).
[11] M. KLÉMAN, C. E. WILLIAMS, M. J. COSTELLO and T. GULIK-KRZYWICKI: *Philos. Mag.*, **35**, 33 (1977).

we feel that theoretical arguments ([12]) and the observation of passages ([13]) favour $\bar{\varkappa} > 0$ for the single egg lecithin bilayer in excess water. The spontaneous curvature c_0 was found to be small but variable in vesicles obtained by the swelling of lecithin in water ([14]). It can be made very large if one induces by osmosis ([15]) a lipid imbalance between the monolayers of vesicle membranes. The bilayer edge energy was also measured. TAUPIN et al. ([16]) studied small vesicles of dipalmitoyl lecithin and of egg lecithin, finding $\gamma = 0.65 \cdot 10^{-6}$ erg cm^{-1}. HARBICH and HELFRICH ([17]) determined $\gamma = 2 \cdot 10^{-6}$ from the shape of electrically opened giant vesicles of egg lecithin.

3. – Undulations of a single membrane.

Small enough undulations of a single fluid membrane can be completely described by the displacements $u(\boldsymbol{r})$ from a plane, say the (x, y)-plane, so that $\boldsymbol{r} = (x, y)$ and $u = z$. Such « well-behaved » undulations have been studied in earlier papers ([18-20]), where most of the formulae of this section can be found. All calculations further presuppose

$$(3) \qquad\qquad |\text{grad } u| = \text{tg } \varphi \ll 1 \,,$$

φ being the tilt angle of the membrane with respect to the (x, y)-plane.

The undulations $u(\boldsymbol{r})$ can be decomposed into modes. For a quadratic piece of membrane of area A we have, with periodic boundary conditions, in terms of real waves,

$$(4a) \qquad\qquad u(\boldsymbol{r}) = \sum_{\boldsymbol{q}}{}' (a_{\boldsymbol{q}} \cos \boldsymbol{q}\boldsymbol{r} + b_{\boldsymbol{q}} \sin \boldsymbol{q}\boldsymbol{r}) \,,$$

or, in terms of complex waves,

$$(4b) \qquad\qquad u(\boldsymbol{r}) = \sum_{\boldsymbol{q}} u_{\boldsymbol{q}} \exp [i\boldsymbol{q}\boldsymbol{r}] \qquad\qquad \text{with } u_{-\boldsymbol{q}} = u_{\boldsymbol{q}}^{*} \,,$$

([12]) S. MARČELJA: unpublished.

([13]) W. HARBICH, R. M. SERVUSS and W. HELFRICH: Z. Naturforsch. Teil A, **33** 1013 (1978).

([14]) W. HARBICH, H. J. DEULING and W. HELFRICH: J. Phys. (Paris), **38**, 727 (1977).

([15]) E. BOROSKE, M. ELWENSPOEK and W. HELFRICH: Biophys. J., **34**, 95 (1982).

([16]) C. TAUPIN, M. DVOLAITZKY and C. SAUTEREY: Biochemistry, **14**, 4771 (1975).

([17]) W. HARBICH and W. HELFRICH: Z. Naturforsch. Teil A, **34**, 1063 (1979).

([18]) W. HELFRICH: Z. Naturforsch. Teil C, **30**, 841 (1975).

([19]) F. BROCHARD and J. F. LENNON: J. Phys. (Paris), **36**, 1035 (1975).

([20]) F. BROCHARD, P. G. DE GENNES, P. PFEUTY: J. Phys. (Paris), **37**, 1099 (1976).

where $\boldsymbol{q} = (2\pi/A^{\frac{1}{2}})(m, n)$, m and n being natural numbers. The restricted summation in (4a) denoted by $\sum'$ means that only one of two opposite wave vectors $\boldsymbol{q}$ is taken into account. This may be achieved by summing only over a half-plane of wave vectors. The contributions of opposite wave vectors in (4b) add up to one real sinusoidal wave of variable phase.

The curvature elastic energy associated with such a pair of modes is given by

$$(5a) \qquad \frac{1}{4}A\varkappa q^4(a_q^2 + b_q^2),$$

or

$$(5b) \qquad \frac{1}{4}A\varkappa q^4|2u_q|^2.$$

We are dropping vector notation as a flat fluid membrane is isotropic in its plane (if the molecules are parallel to the layer normal). In the following we need, for the undulating membrane, the difference between the area projected on the (x, y)-plane and the true area. It is per unit area of the (x, y)-plane

$$(6) \qquad \cos\varphi - 1 \approx -\varphi^2/2 \approx -(\text{tg }\varphi)^2/2 \qquad \text{for } \varphi \ll 1,$$

where φ is the local angle which the membrane makes with the plane. This yields for the decrease of effective or projected area per pair of modes

$$(7a) \qquad (\Delta A)_q = -\frac{1}{4}Aq^2(a_q^2 + b_q^2),$$

or

$$(7b) \qquad (\Delta A)_q = -\frac{1}{4}Aq^2|2u_q|^2.$$

In the presence of lateral tension σ, there is a free energy associated with ΔA_q which is, of course,

$$(8) \qquad \sigma(\Delta A)_q.$$

The mean square amplitudes of the modes can be obtained from the equipartition theorem. The mean energy of deformation per pair of modes being kT, we find immediately

$$(9a) \qquad \langle a_q^2 \rangle = \langle b_q^2 \rangle = \frac{2kT}{A(q^4\varkappa + q^2\sigma)},$$

or

$$(9b) \qquad \langle|u_q|^2\rangle = \frac{kT}{A(q^4\varkappa + q^2\sigma)}.$$

We are now ready to calculate some effects of fluid membrane undulations. Let us start with the total decrease in effective membrane area. Replacing

the sum by an integral,

$$(10) \qquad \sum_{\boldsymbol{q}} \to \frac{A}{(2\pi)^2} \int 2\pi q \, \mathrm{d}q \,,$$

and using (9) leads to the total decrease

$$(11) \qquad \left(\frac{\Delta A}{A}\right)_{\sigma=0} \approx -\frac{kT}{4\pi\varkappa} \ln \frac{A^{\frac{1}{2}}}{a}$$

for the special case $\sigma = 0$. In deriving the approximate formula (11) we use simplified cut-offs. The lower limit of integration is chosen to be $\pi/A^{\frac{1}{2}}$, so that a very small square or rather disk of this radius representing the point $\boldsymbol{q} = 0$ is left out in the $\boldsymbol{q}$ plane. The upper limit is taken to be π/a, where a is the spacing of the amphiphilic molecules or of the hydrocarbon chains if there is more than one in a molecule.

As an example, we compute $\Delta A/A$ for $\varkappa = 2 \cdot 10^{-12}$ erg, $a = 5$ Å and $A = 150$ $\mu\mathrm{m}^2$, the area of the red-blood-cell membrane. The result whose amount represents the fraction of area « absorbed » by undulations, most of them microscopically unresolvable, is 0.015. The value is not impressive. However, it would be ten times larger if $\varkappa$ were ten times smaller, as certain experiments ([19]) suggest for the red-blood-cell membrane. In our numerical example, $\Delta A/A$ could reach the « critical limit » of unity ([18]) for $\varkappa = 3 \cdot 10^{-14}$ erg. This value and its derivation are somewhat similar to an estimate concerning the feasibility of microemulsions ([7]).

Permitting nonvanishing lateral tension, we obtain from standard tables for the change in effective area the integral

$$(12) \qquad \left(\frac{\Delta A}{A}\right)_{\sigma>0} = -\frac{kT}{8\pi\varkappa} \ln \frac{\pi^2/a^2 + \sigma/\varkappa}{\pi^2/A + \sigma/\varkappa} \,,$$

which, in the range

$$(13) \qquad \varkappa \frac{\pi^2}{A} \ll \sigma \ll \varkappa \frac{\pi^2}{a^2} \,,$$

simplifies to

$$(14) \qquad \left(\frac{\Delta A}{A}\right)_{\sigma>0} = -\frac{kT}{8\pi\varkappa} \ln \frac{\varkappa\pi^2}{\sigma a^2} \,.$$

Taking the same numbers for $\varkappa$, A and a as in the last section, we may replace (13) by

$$(15) \qquad 10^{-5} \text{ dyn cm}^{-1} \ll \sigma \ll 10^4 \text{ dyn cm}^{-1} \,.$$

Accordingly, eq. (14) seems to be a good approximation in most cases of practical interest (see below). Fluid membranes of lecithin and other lipids, usually prepared as black lipid membranes, are known to rupture at tensions of the order of a few dyn cm^{-1} [21].

Equations (12) or (14) complement the ordinary elastic response governed by the elastic modulus of membrane stretching, λ. The total elastic response of a fluid membrane to stretching may be written as

$$(16) \qquad \left(\frac{\Delta A}{A}\right)_{\sigma > 0} = \frac{kT}{8\pi\varkappa} \ln \frac{\sigma a^2}{\varkappa\pi^2} + \frac{1}{\lambda}\,\sigma\,.$$

Forming the derivative of $\Delta A/A$ with respect to σ and using

$$\frac{\mathrm{d}g_s}{\mathrm{d}\sigma} = \sigma\,\frac{\mathrm{d}(\Delta A/A)_\sigma}{\mathrm{d}\sigma}$$

leads to the elastic energy of stretching per unit area:

$$(17) \qquad g_s = \frac{kT}{8\pi\varkappa}\,\sigma + \frac{1}{2\lambda}\,\sigma^2 + \text{const}\,.$$

The range of validity of this simple equation consisting of terms linear and quadratic in σ and containing neither a nor A is restricted by inequality (15) and the obvious condition $\sigma > 0$.

The stretching elasticity of egg lecithin vesicle membranes was recently measured by KWOK and EVANS [22] to be

$$(18) \qquad \lambda = (140 \pm 16)\ \text{dyn cm}^{-1}$$

at room temperature. Lateral tensions were produced by the sucking action of a pipette on the vesicle. The undulatory part of stretching elasticity has not been considered and could explain some irregularities observed at low tensions. Inserting moduli (2) and (18) into (17), we can compute the crossover tension σ_{eq}, where both terms of (17) contribute equally to $\mathrm{d}g_s/\mathrm{d}\sigma$:

$$(19) \qquad \sigma_{eq} = 0.11\ \text{dyn cm}^{-1}\,.$$

As KWOK and EVANS measured up to the tension of rupture between 3 and 4 dyn cm^{-1}, their value of λ is probably correct.

[21] See, *e.g.*, H. T. TIEN: *Bilayer Lipid Membranes* (New York, N. Y., 1974), p. 40.
[22] R. KWOK and E. EVANS: *Biophys. J.*, **35**, 637 (1981).

The microscopic visibility of undulations depends on their strength. Their mean square amplitude is given by

$$(20) \qquad \langle u^2 \rangle = \tfrac{1}{2} \sum_q{}' \left(\langle a_q^2 \rangle + \langle b_q^2 \rangle \right) = \sum_q \langle |u_q|^2 \rangle \,,$$

which, in the special case $\sigma = 0$, becomes

$$(21) \qquad \langle u^2 \rangle = \frac{kT}{2\pi\varkappa} \int\limits_{q_{min}}^{q_{max}} \frac{\mathrm{d}q}{q^3} \,,$$

where use has been made of (9) and (10). The integral diverges rapidly at its lower limit. With

$$q_{min} = \frac{\pi}{A^{\frac{1}{2}}} \,, \quad q_{max} = \frac{\pi}{a} \,,$$

the limits of integration adopted in deriving (11), we obtain

$$(22) \qquad \langle u^2 \rangle = \frac{kT}{4\pi\varkappa} \frac{A}{\pi^2} \,,$$

provided that $A \gg a^2$. Only the longest wave-lengths contribute significantly to $\langle u^2 \rangle$. Note that

$$(23) \qquad \langle u^2 \rangle^{\frac{1}{2}} \sim A^{\frac{1}{2}} \,,$$

which means that the r.m.s. amplitude scales with the length of the edge of the considered square piece of membrane. This implies that the undulations of relaxed vesicles ($\sigma = 0$) are essentially scale invariant.

We will also need $\langle u^2 \rangle$ for $\sigma \neq 0$. The general integral of (9) may be taken from tables; it is, for $A \gg a^2$,

$$(24) \qquad \langle u^2 \rangle = \frac{kT}{4\pi\sigma} \ln \left(1 + \frac{\sigma}{\varkappa q_{min}^2} \right) .$$

If $\sigma/\varkappa q_{min}^2 \ll 1$, we return to (22). In the opposite case eq. (24) simplifies to

$$(25) \qquad \langle u^2 \rangle = \frac{kT}{4\pi\sigma} \ln \frac{\sigma}{\varkappa q_{min}^2} \,.$$

4. – Steric interaction of undulating membranes.

Undulations make parallel fluid membranes bump into each other, thus causing a repulsive interaction. We call the interaction steric as it is basically

an excluded-volume effect. The statistical mechanics of steric interaction in multilayer systems was treated in some detail in an earlier paper [23]. Here we will only derive the functional dependence of the effect, using simple physical arguments, but paying little attention to numerical factors.

For this purpose we consider a single fluid membrane under vanishing lateral tension between parallel rigid plates. The mean square amplitude of undulations of a *free* membrane diverges strongly with its area according to (22). Let $\pm d$ be the separations of the plates from the (x, y)-plane. We then have

$$(26) \qquad\qquad -d \leqslant u(\boldsymbol{r}) \leqslant d .$$

Restricting $u(\boldsymbol{r})$ to this interval at only one point $\boldsymbol{r}_0$ in the (x, y)-plane would result in

$$(27) \qquad\qquad \langle u^2(\boldsymbol{r}_0) \rangle = d^2/3$$

and complicated expressions for other $\boldsymbol{r}$. Restricting $u(\boldsymbol{r})$ everywhere to the interval between the plates and exciting only one mode, of the type $\sin q_x x \cdot \sin q_y y$, would give $\langle a_q^2 \rangle = d^2/3$ for the amplitude and

$$(28) \qquad\qquad \langle u_q^2(\boldsymbol{r}) \rangle = d^2/12 ,$$

if the average over all $\boldsymbol{r}$ is taken. As previously [23], we assume the mean square displacement of a membrane between rigid plates, which can be excited in all its modes but obeys (26), to be the geometric mean of the two limits (27) and (28), *i.e.* we write as an approximation

$$(29) \qquad\qquad \langle u^2(\boldsymbol{r}) \rangle = d^2/6 .$$

Inserting (29) into (22) and solving for A leads to

$$(30) \qquad\qquad A_{\mathrm{sq}} = \frac{2\pi^3}{3} \frac{\varkappa d^2}{kT} .$$

The area is called A_{sq} because now we imagine the membrane to be divided into squares of size A_{sq}. It seems plausible to regard the motions of each square as being practically independent of those of the other squares. We may then treat each square as a particle of a one-dimensional ideal gas. Kinetic gas theory tells us that the average force exerted by such a particle on the boundaries of an interval $2d$ is $kT/2d$, regardless of the particle mass and other details. From this simple argument we deduce for the pressure P caused by the undulating

---

[23] W. HELFRICH: *Z. Naturforsch. Teil A*, **33**, 305 (1978).

membrane on either plate $P = kT/2\,d A_{sq}$. Together with (30) this leads to

$$(31) \qquad\qquad P = \frac{3}{4\pi^3}\,\frac{(kT)^2}{\varkappa d^3}\;.$$

Integration over d yields the energy of interaction per unit area of membrane with either plate

$$(32) \qquad\qquad \frac{\Delta G_{st}}{A} = \frac{3}{8\pi^3}\,\frac{(kT)^2}{\varkappa d^2}\;.$$

The dependence of the steric interaction on d, $\varkappa$ and kT is the same as was found before ([22]).

However, the earlier extensive calculations yielded for the numerical factor in (32) the value of 3/32 for a membrane between rigid plates, which is much larger than $3/8\pi^3$. The discrepancy seems to be due mostly to the crudeness of the above estimate of the area density of « independent » membrane pieces. The more reliable result for a multilayer system of fluid membranes was ([22])

$$(33) \qquad\qquad \frac{\Delta G_{st}}{A} = \frac{3\pi^2}{128}\,\frac{(kT)^2}{\varkappa d^2}\;.$$

It was argued that taking mode-mode correlation into account should increase the theoretical strength of steric interaction by about a factor 2. In the following we are interested in the interaction between two fluid membranes belonging to different vesicles. The steric interaction of undulating membranes may be stronger for a pair than for a multilayer system. This is because in the system there are as many pairwise interactions as membranes, while with a single pair the undulations of two membranes have to be restricted by one pairwise interaction. The difference may be up to another factor of 2. Therefore, we think

$$(34) \qquad\qquad \frac{\Delta G_{st}}{A} = \frac{(kT)^2}{\varkappa d^2}$$

to be at present the best approximation for the case in question.

5. – Competition between steric repulsion and van der Waals attraction.

The most interesting feature of the steric interaction of undulating membranes is its long range. In this respect it surpasses all other repulsive interactions between membranes. Hydration forces ([24]) are known to drop off ex-

---

([24]) S. MARČELJA and N. RADIC: *Chem. Phys. Lett.*, **42**, 129 (1976).

ponentially and so do electrostatic ones ([25]) sufficiently far from the membrane. The characteristic lengths are roughly 2 Å in the first case and between a few Å and 1 μm in the second one. As was pointed out earlier ([23]), steric interaction can compete in range and strength with van der Waals attraction. In dealing with the latter it is preferable to consider tensions, *i.e.* negative pressures, rather than free energies per unit area because the power law of van der Waals forces depends on separation d. The stress varies as $1/d^3$ for small spacings where adjacent membranes act on each other like half-spaces. As d becomes much larger than the membrane thickness and finally reaches the region of retardation, the power law changes to $1/d^6$. For a rigid multilayer system of alternating lipid and water, NINHAM and PARSEGIAN ([26]) calculated the dependence of tension on d, obtaining, for small d,

$$(35) \qquad (G)_{\mathrm{vdW}}/A = -1.4 \cdot 10^{-15}/d^2 \,,$$

or, more appropriately,

$$(36) \qquad -P_{\mathrm{vdW}} = 2.8 \cdot 10^{-15}/d^3 \,.$$

van der Waals interaction has also been studied experimentally for many phospholipid membranes ([27]). The strength found for egg lecithin ([28]) at room temperature is about half the theoretical value (36). This happens to be roughly equal in magnitude to the theoretical strength of steric interaction as computed from (34), $\varkappa = 2 \cdot 10^{-12}$ erg and $kT = 4 \cdot 10^{-14}$ erg.

Let us now discuss some details of the competition between steric repulsion and van der Waals attraction, in order to predict the behaviour of a pair of fluid membranes in various circumstances. If the lateral tension is zero and both interactive forces vary as $1/d^3$, one of two states should be stable: either complete cohesion with $d = 0$, or complete separation with $d = \infty$. Actually, this case is unrealistic for a number of reasons. They are, among others,

   i) the faster drop of van der Waals forces at larger distances,

   ii) the usual predominance of hydration forces at small distances preventing close contact, and

   iii) especially for very small $\varkappa$, a breakdown of our general assumption (3) that the angle φ is small ([7]).

([25]) A. C. COWLEY, N. FULLER, R. P. RAND and V. A. PARSEGIAN: *Biochemistry*, **17**, 3163 (1978).
([26]) B. W. NINHAM and V. A. PARSEGIAN: *J. Chem. Phys.*, **53**, 3398 (1970).
([27]) R. P. RAND: *Ann. Rev. Biophys. Bioeng.*, **10**, 277 (1981). These results, including those of ref. ([28]), are probably not in conflict with ours as they were obtained with disordered dispersions.
([28]) D. M. LE NEVEU, R. P. RAND and V. A. PARSEGIAN: *Nature (London)*, **259**, 601 (1976).

For lecithin membranes only the first two corrections are important. (In particular, the $1/d^2$ dependence of steric interaction need not be questioned.) Bound states may then be expected to permit slight fluctuations of local membrane spacing. Moreover, at a certain ratio of the strengths of steric repulsion and van der Waals attraction, there may be two stable states, one bound and the other totally separated. We remark that it is helpful in the present context to consider only the relative displacement $u_2(\boldsymbol{r}) - u_1(\boldsymbol{r})$ of the two membranes rather than the individual displacements. In this way the problem of two undulating membranes of modulus $\varkappa$ is reduced to that of one membrane of modulus $\varkappa/2$ in front of a rigid wall.

Experiments ([1]) have shown that vesicles do not cohere unless their membranes are under a lateral tension σ. For the very small tensions which had to be used in these studies the energy of cohesion appeared to drop with decreasing σ. This raises the question whether lateral tension will always induce cohesion, at least if the membrane areas involved are infinitely extended. Arguments similar to those employed in deriving steric interaction for $\sigma = 0$ provide an answer. Putting $q_{\min}^2 = \pi^2/A_{\mathrm{sq}}$, we obtain from (25)

$$(37) \qquad\qquad \langle u^2 \rangle = \frac{kT}{4\pi\sigma} \ln \frac{\sigma A_{\mathrm{sq}}}{\varkappa\pi^2} \,.$$

The new equation shows that $1/A_{\mathrm{sq}}$ is an exponentially decreasing function of $\langle u^2 \rangle$. From the derivation of (25) we know that it is valid only for $\sigma A_{\mathrm{sq}}/\varkappa\pi^2 \gg 1$, which is easily seen to correspond to $\langle u^2 \rangle \gg kT/4\pi\sigma$. As before, we use now the proportionality (29) between $\langle u^2 \rangle$ and d^2 and equate $1/A_{\mathrm{sq}}$ to the particle density of a fictitious gas producing the repulsive pressure. Both relations should still apply if we do not insist on exact values for the numerical factors. Accordingly, an exponential drop of the repulsive force with d^2 may be expected above a certain mean spacing of the two undulating membranes. Below this spacing σ is negligible. Since the negative pressure of van der Waals interaction is larger in amount than some constant times $1/d^6$, attraction will always exceed repulsion beyond a certain spacing. In other words, lateral tension should induce the cohesion of infinite membranes repelling each other in its absence. It seems also clear that the net energy of cohesion representing a balance of attraction and repulsion can be made arbitrarily small by decreasing σ.

Figure 1 serves to demonstrate a case of very weak cohesion. Onionlike structures such as the one seen there in phase contrast microscopy are found frequently when egg lecithin swells in water. We are interested in the (rarely observed) attachment of a tubular vesicle to the outside of one of the onion skins. Both membranes were most likely unilamellar, the tube was seen to undulate, while the sphere appeared rather rigid. Let us now compare a typical elastic energy of a closed vesicle (the topological term can again be omitted)
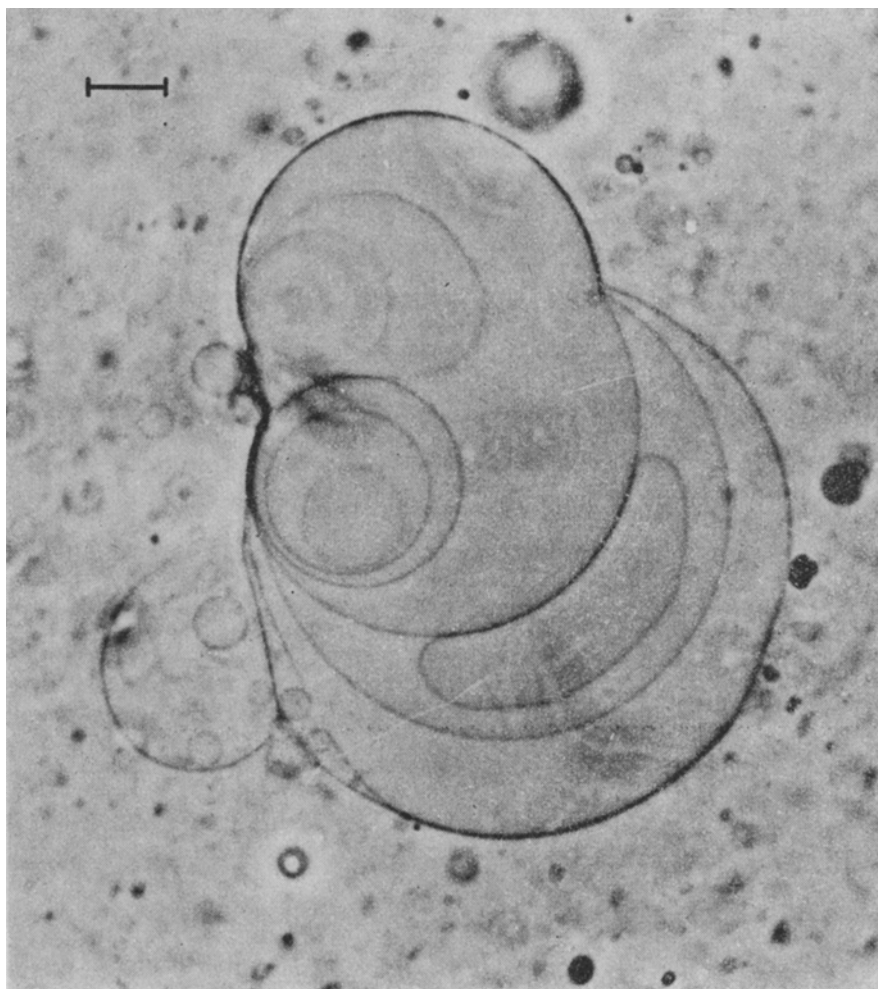
Fig. 1. – Onionlike vesicular structure of egg lecithin in water seen under a phase contrast microscope. A tubular vesicle is attached to the outside of an onion skin. The bar represents 10 µm.

to the maximum energy due to membrane contact. Using $\varkappa = 2 \cdot 10^{-12}$ erg, we have for a spherical vesicle the elastic energy

$$8\pi\varkappa = 5 \cdot 10^{-11} \text{ erg} .$$

With $\sigma_c = 2 \cdot 10^{-2}$ erg cm^{-2}, the value determined on multilayer systems of egg lecithin [28] and the probable area of contact estimated from fig. 1, $A_c = 100$ µm², we have the contact energy

$$\sigma_c A_c \approx 2 \cdot 10^{-8} \text{ erg} .$$

The latter energy is much larger than the former. If this were true, we would expect a much stronger deformation of the tubular vesicle producing a larger area of contact than that seen in the figure. Therefore, we may conclude that in this particular case $\sigma_c \ll 1 \cdot 10^{-2}$ erg cm^{-2}.

A rough upper limit of the lateral tension σ can be obtained from the fact that the usual undulations of vesicle walls seemed hardly suppressed in the tubular vesicle. According to (24) this suggests

$$\frac{\sigma}{\varkappa q_{\min}^2} \leqslant 1 \; .$$

With $q_{\min} \approx 2\pi/L$, $L = 100$ μm ($=$ length of tube) and again $\varkappa = 2 \cdot 10^{-12}$ erg we compute

$$\sigma \leqslant 8 \cdot 10^{-5} \text{ dyn cm}^{-1} \; .$$

Moreover, the lateral tension or at least a lower limit for it can also be deduced from the contour of the tubular vesicle which merges smoothly with that of the sphere. Imagining for the moment a membrane that is curved only near the area of contact and practically flat elsewhere, we can write for the energy density in the curved region

$$(38) \qquad g = \frac{1}{2}\varkappa \left(\frac{\mathrm{d}\Psi}{\mathrm{d}s}\right)^2 + \sigma(1 - \cos\Psi) \; .$$

Here s measures the length of a path on the membrane which starts at and is normal to the rim of the contact area, while Ψ is the local angle the path makes with its asymptote. Applying the Euler-Lagrange formalism to (38) gives the « shape » equation

$$(39) \qquad \frac{\mathrm{d}^2\Psi}{\mathrm{d}s^2} = \frac{\sigma}{\varkappa}\sin\Psi \; ,$$

which, for small Ψ, can be approximated by

$$(40) \qquad \frac{\mathrm{d}^2\Psi}{\mathrm{d}s^2} = \frac{\sigma}{\varkappa}\Psi \; .$$

The quantity $(\varkappa/\sigma)^{\frac{1}{2}}$ is a new coherence length. An upper limit for it of ca. 1 μm may be read from fig. 1 if allowance is made for a superimposed constant curvature. Thus we obtain the lower limit

$$\sigma \gtrsim 2 \cdot 10^{-4} \text{ dyn cm}^{-1} \; .$$

The agreement between upper and lower limit is satisfactory. However, more photographs and a more extensive mathematical analysis would be needed to arrive at a reliable value for σ.

Our aim here is to show that σ_c can be much smaller than $2 \cdot 10^{-2}$ dyn cm^{-1}. The cohesion energy is related to the lateral tension through

$$\sigma_c = (1 - \cos \Psi_0) \sigma,$$

where Ψ_0 is the contact angle or, with smooth merging, the angle the asymptote makes with the contact area near the rim. From the estimated $\sigma \approx 1 \cdot 10^{-4}$ dyn cm^{-1} and $\Psi_0 \approx 30°$ as taken from the photograph we thus obtain $\sigma_c \leqslant 1 \cdot 10^{-5}$ erg cm^{-2}. Figure 1 and similar observations also suggest that stretching one of two egg lecithin membranes may suffice to induce cohesion between them. This seems to provide experimental evidence that the steric repulsion of freely undulating membranes is only slightly stronger than their van der Waals attraction.

● RIASSUNTO (*)

La teoria delle ondulazioni delle membrane dei fluidi è rivista ed estesa in alcune parti. Si derivano le dipendenze funzionali dell'interazione sterica delle membrane ondulate in un nuovo modo da semplici argomenti fisici. Discutendo la competizione tra repulsione sterica e attrazione di Van der Waals, si trova che membrane che di solito separano (per esempio, grandi vescicole di lecitina dell'uovo) dovrebbero aderire se sottoposte a tensione laterale. I contorni di due vescicole contigue osservate quando la lecitina dell'uovo si sta rigonfiando mostrano che l'energia netta di coesione può essere estremamente piccola ($\leqslant 10^{-5}$ erg cm^{-2}).

Неровности, стерическое взаимодействие и когезия жидких мембран.

Резюме (*). — Анализируется теория неровностей жидких мембран. Из простых физических аргументов выводятся функциональные зависимости стерического взаимодействия волнистых мембран. Рассматривая конкуренцию между стерическим отталкиванием и притяжением Ван дер Ваальса, получается, что мембраны, которые обычно разделяют, должны связывать при поперечном напряжении. Анализируются контуры двух связанных пузырьков и показывается, что суммарная энергия сцепления может быть чрезвочайно малой ($\leqslant 10^{-5}$ эрг см$^{-2}$).