Out-of-Plane Fluctuations of Lipid Bilayers

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It is shown that out-of-plane fluctuations of two-dimensonally fluid membranes may lead to a decrease in effective area and affect stretching elasticity.

There is a growing interest in the study of monolamellar lipid bilayer vesicles. They can be produced[1] in various sizes, the diameters ranging from a few 100 Å to a few mm, and represent the simplest models for biological cells and vesicles.

Lipid bilayer membranes are often regarded as two-dimensional fluids: The best known examples are lecithin bilayers at temperatures where the hydrocarbon chains are in the molten state. The shape of such vesicles is thought to be controlled by the curvature elasticity of the membrane whenever the enclosed volume is smaller than what is required for the formation of a sphere. The curvature-elastic energy density per area can be written as[2]

$$g = (1/2)\,\varkappa\,(c_1 + c_2 - c_0)^2$$

where c_1 and c_2 are the two principal curvatures ($c = 1/\text{radius}$), c_0 a spontaneous curvature which may arise if the two sides of the membrane are different or facing different media, and $\varkappa$ the elastic modulus of curvature.

On the basis of liquid-crystalline curvature elasticity one expects $\varkappa \approx K\,b \approx 5 \times 10^{-13}$ erg. Here $K \approx 10^{-6}$ dyn is the typical value of the bulk modulus of liquid crystals and $b = 5 \times 10^{-7}$ cm the typical thickness of bilayers. Similar values for $\varkappa$ are obtained from a specific molecular model of lecithin membranes (S. Marčelja, private communication). The smallness of the elastic modulus casts some doubt on the shape stability of monolamellar bilayer vesicles, especially since they sometimes appear irregular under the microscope (and red blood cells exhibit the so-called flicker phenomenon). We wish to show in the present note that the estimated elastic moduli (there are no experimental numbers yet) are indeed close to a critical limit.

Let us consider a squared piece of membrane of area A, parallel to the x, y axes of a cartesian coordinate system. We disregard the edge energy which may tend to close it. For $c_0 = 0$ the bilayer will be essentially flat except for thermal out-of-plane fluctuations $z\ (x, y)$ causing a certain bumpiness. We are interested in the ensuing relative change in area, $\Delta A/A$, the effective area $A + \Delta A$ being defined as the projection of the roughened surface onto the x, y plane. The true area A is assumed to remain constant.

In order to calculate $\Delta A/A$ we consider sinusoidal fluctuation modes. Their density as obtained from periodic boundary conditions in two-dimensional $\boldsymbol{q}$ space ($\boldsymbol{q}$ = wave vector) is given by $A/(2\,\pi)^2$. The mean square curvature of each mode is

$$\overline{c^2} = k_{\mathrm{B}}\,T/A\,\varkappa$$

with k_{B} being Boltzmann's constant and T absolute temperature. For the associated displacement we have

$$\overline{z^2(q)} = \overline{c^2}/q^4\,.$$

The change of effective area due to one mode is

$$\delta A(q) = -\tfrac{1}{2}\,\overline{z^2}\,q^2\,A = -\frac{k_{\mathrm{B}}\,T}{2\,\varkappa\,q^2}\,.$$

The total relative change may be approximated by the integral

$$\frac{\Delta A}{A} = -\frac{A}{(2\,\pi)^2}\int_{\pi/\sqrt{A}}^{\pi/a} \frac{\delta A(q)}{A}\,2\,\pi\,q\,\mathrm{d}q = -\frac{k_{\mathrm{B}}\,T}{4\,\pi\,\varkappa}\ln\frac{\sqrt{A}}{a}$$

where a is the distance between adjacent lipid molecules.

Inserting $k_{\mathrm{B}}\,T = 4 \times 10^{-14}$ erg (room temperature) and $\varkappa = 5 \times 10^{-13}$ erg we have

$$\frac{\Delta A}{A} = -6 \times 10^{-3}\ln\frac{\sqrt{A}}{a}\,.$$

As an example we take $a = 5$ Å and $\mathrm{A} = 150\ \mu\mathrm{m}^2$ (area of red blood cell membrane), and obtain $\Delta A/A = -0.06$. Obviously the change in effective area should be quite small, but it may matter in sensitive experiments and for small $\varkappa$. We note that the derivation is valid only for $-\Delta A/A \ll 1$. The area reduction is more important for even larger vesicles. However, their shape can be shown to be very easily perturbed, *e. g.* by a small density difference between the inner and outer media, unless it is spherical and stabilized by an internal osmotic excess pressure. The latter will suppress long-wavelength out-of-plane fluctuations by the induced lateral stress σ.

It may be of general interest to examine the effect of a stress $\sigma > 0$ on out-of-plane fluctuations. Their strength is now given by the relation

$$\tfrac{1}{2}\,\varkappa\,\overline{c^2}\,A - \delta A\ (q)\,\sigma = \tfrac{1}{2}\,k_{\mathrm{B}}\,T$$

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which leads to

$$\delta A(q) = -\tfrac{1}{2}\,\frac{k_B T}{\varkappa\, q^2 + \sigma}\,.$$

With $q = 10^5\ \mathrm{cm}^{-1}$ and $\varkappa = 5 \times 10^{-13}$ erg a lateral stress makes itself felt for $\sigma \gtrsim 5 \times 10^{-3}\ \mathrm{dyn\,cm}^{-1}$. Integration yields

$$\frac{\Delta A}{A} = -\frac{k_B T}{4\pi\varkappa} \ln \sqrt{\frac{\dfrac{\pi^2}{a^2} + \dfrac{\sigma}{\varkappa}}{\dfrac{\pi^2}{A} + \dfrac{\sigma}{\varkappa}}}\,.$$

This expression is to be added to the relative area change due to regular stretching and may be associated with an apparent weakening of stretching elasticity at small σ. The effective $\varkappa$ is not influenced by out-of-plane fluctuations in our approximation. (At given effective area and curvature, any increase in true area is exactly compensated by a decrease in true mean curvature.)

[1] See, *e. g.*, M. P. Sheetz and S. I. Chan, Biochemistry **11,** 4573 [1972]; D. Papahadjopoulos, W. J. Vail, K. Jacobson, and G. Poste, Biochim. Biophys. Acta **394,** 483 [1975].

[2] W. Helfrich, Z. Naturforsch. **28 c,** 693 [1973].