Instability and Deformation of a Spherical Vesicle by Pressure

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The infinitesimal stability of a spherical vesicle (closed membrane) is studied as a function of the pressure difference between the outer and inner media. It is found that above some threshold pressure the spherical vesicle can be deformed into a shape associated with lth-order spherical harmonics. The comparison with numerical examples calculated previously by Deuling and Helfrich shows good agreement. Some applications to red blood cells are discussed.

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Theoretical investigations of vesicles (closed membranes), in the beginning, were devoted to the explanation of the shapes of red blood cells. Those cells possess a well-known biconcave-discoid shape under normal physiological condition. They can recover their initial shape after deformation when the external forces that produce the shape change are removed. Various attempts have been made to explain this peculiar shape but failed,[1] as they required changes of membrane area in the transition from sphere to disk (elastic rubber models), or predicted shapes which are dumbbell-like and not to be observed (curvature elasticity model, but without spontaneous curvature).

In view of these difficulties, Helfrich[2] has discussed the bending elasticity of fluid membranes as formed by lipids and proposed that the shapes of vesicles and, perhaps, red blood cells represent minima of the curvature energy

$$F=\tfrac{1}{2}k_c\oint(c_1+c_2-c_0)^2ds+\Delta p\int dv+\lambda\oint ds, \quad (1)$$

where k_c is the elastic constant and c_1, c_2, and c_0 are the two principal curvatures and the spontaneous curvature, respectively. The latter serves to describe the asymmetry of the membrane or its environment and to treat shape transitions of red blood cell by chemical agents.[3] The Lagrange multipliers Δp and λ take account of the constraints of constant volume and area, $\Delta p=p_0-p_i$ is the osmotic pressure difference between outer and inner media, and λ a tensile stress. Instead of the last term of Eq. (1), Jenkins[4] introduced a local area constraint by $\oint\gamma ds$, where γ is a Lagrange function varying with position. But in the following we show that this does not affect the results.

Various solutions of

$$\delta F=0, \quad (2)$$

under the condition of rotational symmetry, have been numerically investigated by Jenkins[4] and earlier by Deuling and Helfrich.[5,6] Among the solutions there are shapes strikingly similar to observed red blood cell shapes, but their stability has not been checked thoroughly.

Recently, Peterson[7–10] has studied in detail the problem of the stability of membrane shapes. But it is not completely clear that these results about stability are correct. For example, in the spherical limit,[10] Peterson parametrized shapes near the sphere $r=r_0$ as slightly distorted spheres,

$$r=r_0+\epsilon Y_{lm}, \quad (3)$$

where Y_{lm} is a spherical harmonic, and derived

$$\delta F=\tfrac{1}{2}k_c(\epsilon/r_0)^2[l(l+1)-2][l(l+1)-6]. \quad (4)$$

Equation (4) means that, firstly, δF is independent of c_0 and, secondly, $l=1,2$ satisfy $\delta F=2$ so that the vesicle can wander freely in a multidimensional space of energetically equivalent configurations. However, Helfrich[2] has suggested earlier that any infinitesimal deformation of a spherical vesicle corresponding to higher Legendre polynomials than P_2, i.e., Y_{20}, would require larger pressure differences than the threshold value for ellipsoidal deformations, which is

$$\Delta p_c=(2k_c/r_0^3)(6-c_0r_0). \quad (5)$$

In other words, the stability of a spherical vesicle depends on Δp, c_0, and r_0. So there seems to be a puzzle.

In this Letter we try to provide a clear answer to this problem. On the basis of detailed analytic calculations,[11] we have obtained general stability conditions for spherical vesicles. They indicate a branching phenomenon of deformations under pressure: Any infinitesimal deformations corresponding to spherical harmonics higher than Y_{lm} would require a pressure difference larger than the threshold value

$$\Delta p_l=(2k_c/r_0^3)[l(l+1)-c_0r_0] \quad (l=2,3,\ldots). \quad (6)$$

Obviously, Eq. (5) is included in Eq. (6) as the special case of $l=2$. Comparing (6) with the numerical examples calculated previously by Deuling and Helfrich,[6] we find beautiful agreement of the pressures. Some applications of Eq. (6) to red blood cells are discussed.

Theoretically, the membrane of a vesicle may be described as a closed surface in Euclidean three space given by vectors $\mathbf{Y}(u,v)$, depending on the two real parameters u and v. From Eqs. (1) and (2), we have derived[11] the equilibrium-shape equation as

$$\Delta p - 2\lambda H + 4k_c(H + \tfrac{1}{2}c_0)(H^2 - K - \tfrac{1}{2}c_0 H) + 2k_c \Delta H = 0, \quad (7)$$

where H and K are the mean curvature and Gaussian curvature defined (in dealing with a sphere, c_1^{-1} and c_2^{-1} are taken to be the radius of the sphere) by

$$H = -\tfrac{1}{2}(c_1 + c_2), \quad K = c_1 c_2, \quad (8)$$

and Δ is the Laplace-Beltrami operator on the surface defined as

$$\Delta = (1/\sqrt{g})\partial_i(g^{ij}\sqrt{g}\,\partial_j). \quad (9)$$

Here

$$g_{ij} = \partial_i \mathbf{Y} \cdot \partial_j \mathbf{Y}, \quad g^{ij} = (g_{ij})^{-1}, \quad g = \det(g_{ij}), \quad (10)$$

with $\partial_1 = \partial_u$ and $\partial_2 = \partial_v$.

First, one can find the equation

$$\Delta p + 2dH + 2k_c' H(H^2 - K) + k_c' \Delta H = 0 \quad (11)$$

derived by Jenkins [Ref. 4, Eq. (2.35)] as a special example of Eq. (7) with $c_0 = 0$, $d = -\lambda$, and $k_c' = 2k_c$. This shows that it makes no difference whether the area constraint is global or local.

It is obvious that a sphere is always a solution of Eq. (7) if its radius satisfies the following equation:

$$\Delta p r_0^3 + 2\lambda r_0^2 - k_c c_0 r_0(2 - c_0 r_0) = 0, \quad (12)$$

which is the same as Eq. (47) in Ref. 2. To study the stability of the sphere, we consider the slightly distorted spheres

$$r = r_0 + \sum a_{lm} Y_{lm}, \quad (13)$$

where $l \geq 1$ and $m = -l, -l+1, \ldots, l$. With a lengthy calculation,[11] we have obtained their deformation energy as follows:

$$\delta F = \sum |a_{lm}|^2 \{A r_0^2 - B l(l+1) + k_c [l(l+1)]^2 / 2r_0^2\}, \quad (14)$$

where

$$A = \tfrac{1}{2}\Delta p r_0^{-1} + k_c c_0 r_0^{-3},$$
$$B = \tfrac{1}{4}\Delta p r_0 + \tfrac{1}{2} k_c (2 + c_0 r_0) r_0^{-2}. \quad (15)$$

From Eqs. (14) and (15), we find that the coefficients $|a_{jm}|^2$ for $1 < j \leq l$ in Eq. (14) will be negative when

$$\Delta p > \Delta p_l, \quad (16)$$

where Δp_l are defined by Eq. (6). Obviously, in this case, nonzero a_{jm} will reduce the curvature energy. In other words, a deformation corresponding to higher spherical harmonics than Y_{lm} can occur. The case of $l = 1$ means only the trivial translation of the sphere, and physical deformations begin only at $l = 2$. Accordingly, we have $\delta F = 0$ for $l = 1$.

The stability considerations indicate an interesting branching phenomenon of the instability and deformation of the sphericles. Jenkins[4] predicted the same phenomenon on the basis of Eq. (11), which he linearized, and he also found it in his numerical calculations for $l = 2, 3$ and $c_0 = 0$. However, for larger l and $c_0 \neq 0$, it has not been checked. Fortunately, there is no need to do it afresh. More than ten years ago, Deuling and Helfrich[6] calculated a large variety of rotationally symmetric shapes of vesicles. Among them the three types of contours having triangular, pentagonal, and heptagonal cross sections, respectively (cf. Figs. 5, 6, and 7 in Ref. 6) are examples of the deformation of nearly spherical vesicles. Using their data ($c_0 r_0 = -8.0$ and $1.43 \leq \Delta p/\Delta p_c \leq 1.70$, and $\Delta p/\Delta p_c = 2.7$ and 4.40, respectively), we make a check as shown in Table I and find that the deformations correspond exactly to the models of $l = 3$, 5, and 7, respectively. It is well known that the spherical harmonics Y_{l0} are rotationally symmetric about the polar axis, i.e., cross sections of the shape along the axis will show some lth-polygon symmetry. This is why the three contours have triangular, pentagonal, and heptagonal cross sections, respectively. The agreement of the pressures between theory and numerical calculation is beautiful.

The observed changes in the shape of red blood cells may provide other examples. The so-called[12] triconcave and quadriconcave red cells produced by hypotonic media (see Figs. 105–107 in Ref. 12) may be the deformations associated with $l = 3$ and 4, respectively. And, in a sense, the normal red blood cell, the so-called discocyte, represents a branch of $l = 2$ because of its biconcave shape. A calculated contour of this type is shown in Fig.

TABLE I. Comparison of theory with numerical examples calculated by Deuling and Helfrich (Ref. 6). Here $c_0 r_0 = -8.0$ and $\Delta p/\Delta p_c$ are taken from Ref. 6, Δp_l and Δp are calculated according to Eqs. (5) and (6). We take $2k_c/r_0^3$ as the unit of pressure.

l	Δp_l	$\Delta p/\Delta p_c$	Δp	Cross section	Figure No. in Ref. 6
2	14				
3	20	1.43–1.70	16.0–23.8	Triangular	5
4	28				
5	38	2.7	37.8	Pentagonal	6
6	50				
7	64	4.40	61.6	Heptagonal	7

3(a) of Ref. 6. Here $c_0 r_0 = -2.0$ and $\Delta p / \Delta p_c = 0.955$ satisfy the model for $\Delta p_c = \Delta p_2$ as given by Eqs. (5) and (6). These equations also predict that the deformation may be induced by a change of c_0 under the constraint $\Delta p =$const. The so-called glass effect[12] of red blood cells, which become echinocytic when they are near a glass rod (see Fig. 100 in Ref. 12), seems to have this origin: Glass may increase the value of the spontaneous curvature c_0 by its chemical effect and, therefore, cause l of Eq. (6) to be increased at a constant pressure difference between the outer and inner medium of the cell. As a result, the deformations represent spherical harmonics of very high order. However, the shapes may also be influenced by the shear elasticity of the red-cell membrane.

In summary, our discussion shows that the pressure is an important parameter in our understanding of the stability and deformation of spherical vesicles. This may have physiological significance. The good agreement with previous numerical calculations confirms our theoretical prediction.

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[1]W. Helfrich and H. J. Deuling, J. Phys. (Paris), Colloq. Suppl. 3 **36**, C1-327 (1975).

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

[3]W. Helfrich, Z. Naturforsch. **29c**, 510 (1974).

[4]J. T. Jenkins, J. Math. Biol. **4**, 149 (1977).

[5]H. J. Deuling and W. Helfrich, Biophys. J. **16**, 861 (1976).

[6]H. J. Deuling and W. Helfrich, J. Phys. (Paris) **37**, 1335 (1976).

[7]M. A. Peterson, J. Math. Phys. **26**, 711 (1985).

[8]M. A. Peterson, J. Appl. Phys. **57**, 1739 (1985).

[9]M. A. Peterson, Mol. Cryst. Liq. Cryst. **127**, 159 (1985).

[10]M. A. Peterson, Mol. Cryst. Liq. Cryst. **127**, 257 (1985).

[11]The detail will appear in a full paper by the present authors. Equation (6) can also be derived from the equation used in a paper on the effective rigidity of spherical vesicle: W. Helfrich, J. Phys. (Paris) **47**, 321 (1986).

[12]M. Bessis, *Living Blood Cells and Their Ultrastructure* (Springer-Verlag, Berlin, 1973).