

Theory of vesicle budding

This article has been downloaded from IOPscience. Please scroll down to see the full text article.

1990 J. Phys.: Condens. Matter 2 SA329

(<http://iopscience.iop.org/0953-8984/2/S/051>)

View [the table of contents for this issue](#), or go to the [journal homepage](#) for more

Download details:

IP Address: 129.252.86.83

The article was downloaded on 27/05/2010 at 11:17

Please note that [terms and conditions apply](#).

Theory of vesicle budding

W Wiese and W Helfrich

Institut für Theoretische Physik, Freie Universität Berlin, Arnimallee 14, D-1000 Berlin 33, Federal Republic of Germany

Received 9 July 1990

Abstract. The formation of a small daughter vesicle from a large mother vesicle is considered, the two being connected by a narrow constriction. This budding is achieved by either decreasing the enclosed volume or increasing the membrane spontaneous curvature of a nearly spherical vesicle while the other quantity and the membrane area are constant. The activation energy of the discontinuous transition is identified and found to decrease to zero as the respective parameter change progresses.

The shape of non-spherical vesicles formed by a fluid membrane in water is usually thought to be controlled by the bending rigidity, including the spontaneous curvature, and the constraints of fixed enclosed volume and membrane area [1]. While the general differential equation for equilibrium shapes is of fourth order in the displacement of the membrane [2], axisymmetric equilibrium shapes obey a second-order differential equation for an angle as a function of a single variable. This special equation has been used to calculate red blood cell shapes [3, 4], to predict a variety of stable and unstable equilibrium shapes of vesicles [1] and to propose a model of cell division with a sphere splitting into two smaller spheres of equal size [5]. Very recently, the question of whether or not vesicles adhere to an attractive wall has been treated in the same terms [6].

In the following we wish to deal with a problem known as budding in cell biology, i.e. the creation of a small daughter vesicle from a large mother vesicle, involving a narrow constriction and, eventually, fission. The considerations are again limited to rotationally symmetric shapes.

In general, shape calculations start from the variational *ansatz*

$$\delta \oint [\frac{1}{2}k_c g(c_1 + c_2 - c_0)^2 dA + \Delta p V + \lambda A] dA = 0.$$

Here $g = \frac{1}{2}k_c(c_1 + c_2 - c_0)^2$ is the bending elastic energy per unit area of membrane, k_c being the bending rigidity. c_1 and c_2 are the principal curvatures, and c_0 the spontaneous curvature. The constraints of constant enclosed volume V and membrane area A enter (1) with the Lagrange multipliers Δp and λ which are the difference between the outside and inside pressure and the lateral membrane tension, respectively.

Restricting ourselves to axisymmetric shapes, we may express the principal curvatures along a meridian and tangential to a parallel, respectively, by

$$c_m = \cos \psi (d\psi/dx) \quad c_p = (\sin \psi)/x.$$

Here x is the distance from the polar axis and ψ is the angle that the membrane makes

with the plane tangent to the north pole. (ψ runs from 0 at the north pole to π at the south pole, so that the curvatures are positive for a sphere.) A transformation of the resulting second-order differential equation for $\psi(x)$ leads to the set of first-order differential equations used in the computer calculations [1, 3–5]:

$$\begin{aligned} dc_m/ds &= \pm(1 - fc_p^2)^{-1/2} \{c_p[(c_p - c_0)^2 - c_m^2] + 2(\lambda/k_c)c_p + \Delta p/k_c\} \\ &\quad - 2(1 - fc_p^2)(c_m - c_p)/f \\ dc_p/ds &= \pm 2(1 - fc_p^2)^{1/2}(c_m - c_p)/f \\ df/ds &= \pm 4(1 - fc_p^2)^{1/2} \end{aligned}$$

where $f = x^2$ and the new independent variable s , ranging from 0 to 1, is the fraction of the membrane area between the north pole and the parallel. (The signs in front of the derivatives are plus at the north pole and change at each equator.)

We consider budding in two simple situations corresponding to possible experiments. The membrane area is assumed constant in both of them. In one case, the vesicle volume is decreased from its maximum, which is the sphere, at a fixed positive spontaneous curvature. In the other case, the volume is fixed at a value not much below its maximum while the spontaneous curvature is increased from zero. Both times the final state of lowest energy is the bud, i.e. a small sphere (daughter) in equilibrium with a large sphere (mother) to which it is connected by a constriction of ideally infinitesimal size.

Osmotic shrinkage of vesicles is known to transform spheres into other shapes which usually are flaccid, undergoing strong fluctuations [7]. (We disregard here any effect of water permeation on spontaneous curvature [8].) A change in spontaneous curvature at fixed volume can in principle be achieved by exchanging the outer aqueous medium for another solution at constant osmotic pressure.

Two spheres connected by an infinitesimal constriction, which may have to be enforced, are in mechanical equilibrium at those values of Δp and λ which satisfy the normal force balance [2]

$$k_c(c_0/R_i^2)(2 - c_0R_i) - \Delta p - 2\lambda/R_i = 0$$

simultaneously for both spherical radii R_i ($i = 1, 2$). The double spheres are (mechanically) stable equilibrium shapes only if the constriction remains infinitesimal in the absence of the constraint. We do not expect this to be the case, but the true equilibrium shapes approximated by the double spheres should have narrow constrictions, which we could not compute, and will be lower in energy. Interestingly, these double spheres are a class of shapes by themselves, i.e. they do not tend to one of the usual deformation modes represented by Legendre polynomials as the volume of the large sphere asymptotically approaches its maximum value $(4\pi/3)R_0^3$ with $R_0 = (A/4\pi)^{1/2}$.

In order to deal with budding through volume reduction we compare the bending elastic energies of three classes of shapes. They are the double spheres, the symmetric shapes ranging from the sphere via prolate ellipsoids to dumbbells, and the asymmetric shapes changing from incipient buds (with three equators) via pears to eggs before merging in the symmetric shapes. The ellipsoids and the asymmetric shapes are calculated equilibrium shapes. Two examples of the latter are shown in figures 1 and 2. The bending energies E are plotted versus the volume for $c_0R_0 = 8$ in figure 3. The ellipsoids are the states of lowest energy where they are nearly spherical. They become unstable where the third line representing the pears, etc. merges into theirs as may be seen by the following argument. The locus of the pears, like that of the double spheres, represents two equilibrium shapes, the thinner ends pointing either up or down. The pears, etc.

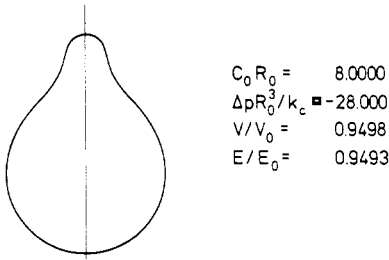


Figure 1. An incipient bud (unstable) with some of its parameters.

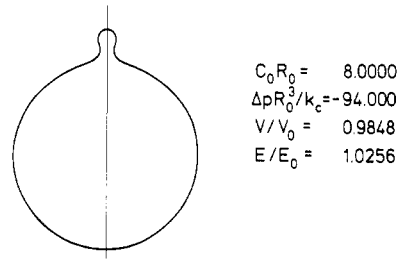


Figure 2. A pear-like shape (unstable) with some of its parameters.

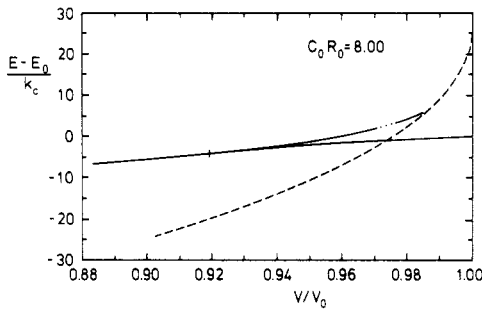


Figure 3. Energies in units of k_c as functions of the relative volume for $c_0 R_0 = 8$, where $V_0 = (4\pi/3)R_0^3$ and $E_0 = 2\pi k_c(2 - c_0 R_0)^2$. The top curve represents unstable asymmetric shapes, covering the range where they could be computed. Its dotted part is the border region between incipient buds (three equators, on the right) and pears (one equator, on the left) which was not accessible to calculation. The short vertical line marks the merging of the asymmetric shapes into the symmetric shapes. The ellipsoids start from the sphere ($V/V_0 = 1$) and are stable before being joined by the unstable shapes. Double spheres with infinitesimal constrictions are represented by the third curve. The stable equilibrium shapes for which they substitute must be even lower in energy. Their curve may merge and annihilate with that of the unstable asymmetric shapes on the right of the region where the latter were obtainable. The bud forms as one goes from right to left.

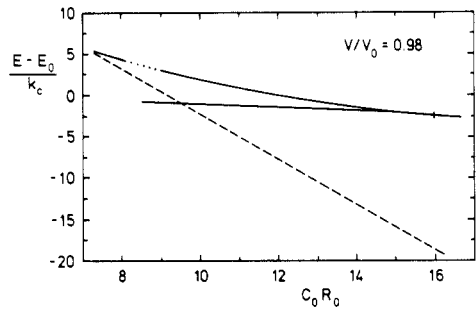


Figure 4. Energies in units of k_c as functions of spontaneous curvature for $V/V_0 = 0.98$. For details see figure 3, but reverse sides. The bud forms as one goes from left to right.

must be unstable shapes so that the merger of two ‘ridges’ with the ‘valley’ of the ellipsoids results in a single extremum of the energy which then has to be a ‘ridge’. The topographical reasoning should hold despite the infinite dimensionality of configurational space.

In an experiment starting from the sphere, the vesicle should first become an ellipsoid as the volume is decreased at constant spontaneous curvature. There will be a spontaneous transformation into the bud at the volume where the ellipsoid becomes unstable. The same transition may take place before this point is reached by means of thermal activation. The activation energies can be read for each volume from the plot in figure

3. This is because the topmost curve represents 'ridges' or, more precisely, 'passes' of the bending energy in configurational space. The two classes of asymmetric shapes are likely to be absent above a certain volume where they join and annihilate each other. A similar situation arises in connection with invaginated red blood cell shapes [1, 4]. The energies are plotted in units of k_c which for typical biological model membranes is of the order of $10k_B T$.

The same three classes of shapes are involved in the budding from an ellipsoid of constant volume and surface area while the variable parameter is spontaneous curvature. The situation is especially simple as the double sphere keeps its form and the ellipsoid changes shape only little with c_0 . The energies of the three shapes are plotted versus $c_0 R_0 \geq 0$ in figure 4 for the volume $V = 0.98(4\pi/3)R_0^3$. The interpretation of the plot is analogous to that of the preceding figure, allowing again for spontaneous and activated transitions from the ellipsoid to the bud.

Our theory of budding, and in particular the assignment of stability or instability to the shapes invoked, is based on the assumption that there are no other equilibrium shapes of lower bending energy. This seems to be correct for $c_0 R_0 = 8$ if one considers the energies of weakly excited deformation modes represented by spherical harmonics (see, e.g., [2]) because for a given volume the ellipsoid is the spherical harmonic mode of lowest energy. The inclusion of shapes without rotational symmetry should not affect these arguments.

The eventual fission of the daughter from the mother vesicle cannot be described by an elastic theory. Casual observations with egg yolk phosphatidylcholine (EYPC) membranes indicated that separation can be triggered very easily, e.g. by touching the cover slide of a sample cell [9]. Moreover, there is evidence that certain biological model membranes, notably EYPC bilayers, change their topology in the absence of any stresses as a function of temperature [10].

Acknowledgments

We thank H J Deuling for his advice on the calculations. We are grateful to Ou-Yang Zhong-can for stimulating discussions when we were starting this work, and to M A Peterson for a preprint dealing with invaginated shapes. This work was supported by the Deutsche Forschungsgemeinschaft through SFB 312.

References

- [1] Deuling H J and Helfrich 1976 *J. Physique* **37** 1335
- [2] Ou-Yang Zhong-can and Helfrich W 1989 *Phys. Rev. A* **39** 5280
- [3] Deuling H J and Helfrich W 1976 *Biophys. J.* **16** 861
- [4] Svetina S and Zeks B 1989 *Eur. Biophys. J.* **17** 101
- [5] Verhas J 1988 *Liq. Cryst.* **3** 1183
- [6] Seifert U and Lipowsky R 1990 *Phys. Rev. A* at press
- [7] Evans E and Sackmann E 1988 private communications
- [8] Boroske E, Elwenspoeck M and Helfrich W 1981 *J. Biophys.* **34** 95
- [9] Harbich W unpublished results
- [10] Harbich W and Helfrich W 1990 *Chem. Phys. Lipids* **55** 191