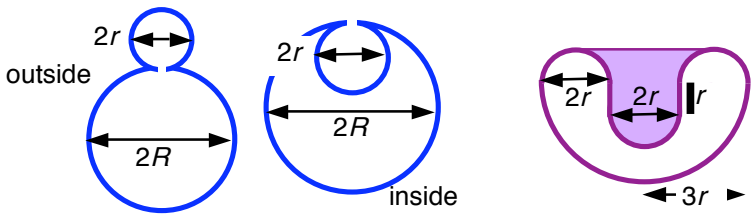
PHYS 4xx Whole 2 - Vesicles and the human erythrocyte

Lecture continues (including equations) from Whole 1.

What effect does a non-zero value for C_o have on the configuration energy? First, it introduces a length scale C_o^{-1}. For example, the bending energy of a spherical shell with radius r is $8\pi\kappa_b(1 - rC_o/2)^2 + 4\pi\kappa_G$ at $C_o \neq 0$. The first term vanishes at $r = 2/C_o$, with the result that the spherical shell with the lowest deformation energy has a particular size at $C_o \neq 0$. This conclusion is true for arbitrary shapes, meaning that the bending energy is a function of cell shape *and* size at $C_o \neq 0$. In addition, the sign of C_o influences the favored shape, as we can see by considering the two axisymmetric shells:



(a) (b)

The doublet shape on the left has curvatures $1/r$ in the small bud and $1/R$ in the main body, whereas the extreme stomatocyte to its right has $-1/r$ in the cavity and $1/R$ on the exterior surface. As a result, the bending energies are simply

$$E_{outside} = 8\pi\kappa_b[\,(1 - rC_o/2)^2 + (1 - RC_o/2)^2\,] + 4\pi\kappa_G \qquad (3a)$$

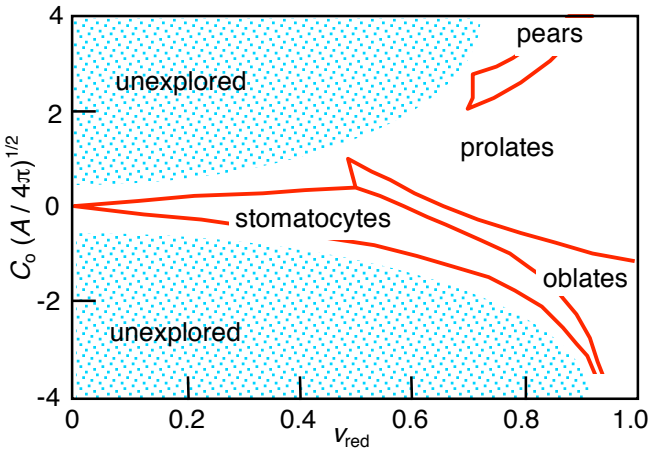
$$E_{inside} = 8\pi\kappa_b[\,(1 + rC_o/2)^2 + (1 - RC_o/2)^2\,] + 4\pi\kappa_G, \qquad (3b)$$

where the labels refer to the position of the smaller shell and where the energy of the neck has been neglected. Let's take RC_o and rC_o to be the same for both configurations, meaning that the shells have the same areas but different enclosed volumes. The difference in their energies is then

$$E_{outside} - E_{inside} = -16\pi\kappa_b(r/R)RC_o, \qquad (4)$$

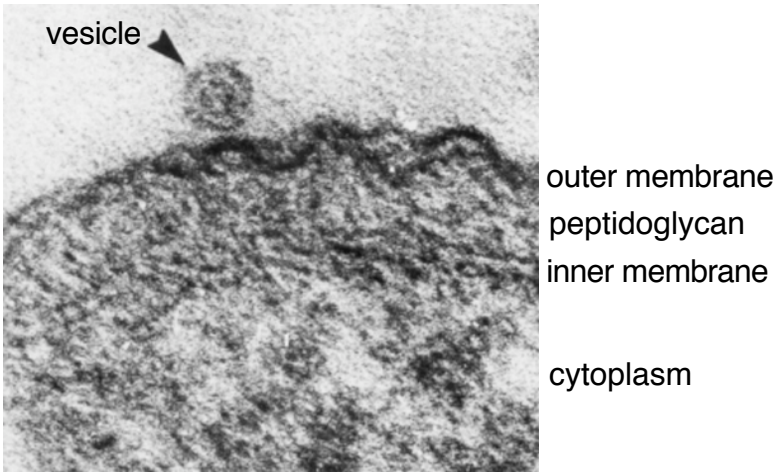
indicating that the doublet configuration is favored ($E_{outside} < E_{inside}$) if $C_o > 0$ and the stomatocyte shape is favored if $C_o < 0$. In other words, negative values of C_o favor shapes with regions of negative curvature.

The "phase diagram" for vesicle shapes at non-zero C_o has been partially explored (Seifert *et al.*, 1991; Miao *et al.*, 1991):

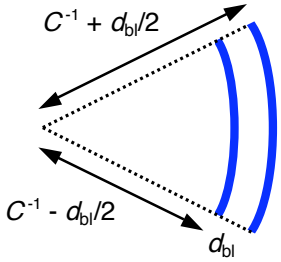


The shapes along the $C_o = 0$ line were shown above, with the narrow domain of oblates visible at $v_{red} \sim 0.6$. Having regions of negative curvature, stomatocytes are more favored at negative C_o; in contrast, prolate ellipsoids and pears (doublets with smooth necks) are favored at large positive C_o.

The spontaneous curvature model does not recognize that the two leaflets may be mechanically decoupled. Consider the inner and outer leaflets of the small vesicle in:



The lipid head groups in the outer leaflet form a spherical shell whose diameter is roughly double that of the inner shell of lipid headgroups. If the leaflets of this vesicle were mechanically coupled, such that they contained the same number of lipids, then the outer leaflet would have only a quarter the number of lipids per unit area as the inner leaflet, clearly a high-stress situation.



The difference in area of the leaflets ΔA can be written in a two-dimensional representation, so that it is easily incorporated into the spontaneous curvature model. Consider first the two arcs of a circle displayed in Fig. 10.12 (in bold) separated by a distance d_{bl} and having a common center of curvature; the curvature of the mid-line between the arcs is defined as C. By geometry, the ratio of the outer arc length to the inner one is just $(1 + Cd_{bl}/2)/(1 - Cd_{bl}/2) \approx 1 + Cd_{bl}$. The same result holds in an orthogonal direction, so that the ratio of the corresponding outer and inner areas is just $A_{outer}/A_{inner} = (1 + C_1 d_{bl})\cdot(1 + C_2 d_{bl}) \approx 1 + C_1 d_{bl} + C_2 d_{bl}$, where C_1 and C_2 are the principal curvatures. Thus, the difference between the areas of the outer and inner boundaries of a membrane segment (of area dA) is approximately $(C_1 d_{bl} + C_2 d_{bl})dA$, and the total area difference, integrated over the surface, is

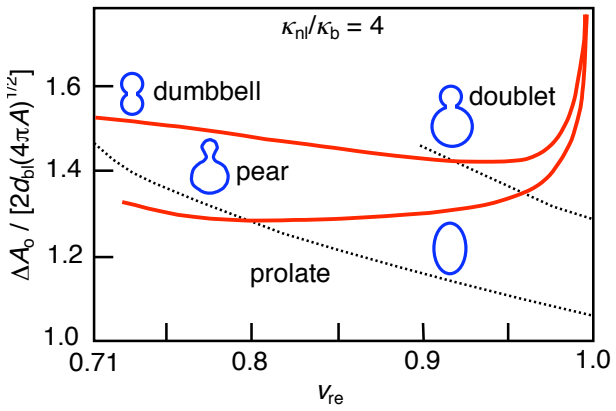
$$\Delta A \approx d_{bl} \int (C_1 + C_2)\mathrm{d}A. \qquad (5)$$

The energy associated with the leaflet area difference is proportional to the (square of the) *deviation* of ΔA from its unstressed value ΔA_o. The bending energy of the spontaneous curvature and area difference contributions can be parametrized as

$$E = (\kappa_b/2) \int (C_1 + C_2 - C_o)^2 \,\mathrm{d}A + \kappa_G \int C_1 C_2 \,\mathrm{d}A + (\kappa_{nl}/2)\cdot(\pi / A d_{dl}^2)\cdot(\Delta A - \Delta A_o)^2, \qquad (6)$$

which is referred to as the ADE model (for *area difference elasticity*). The constant κ_{nl} is a non-local bending resistance, carrying units of energy, and can be related to the area compression modulus of the leaflets. One measurement of κ_{nl} (Waugh *et al.*, 1992) and estimates of κ_{nl} from the underlying bilayer deformation (Miao *et al.*, 1994) argue that κ_{nl}/κ_b is of order unity.

It can be shown that the set of stationary shapes in the ADE model (pears, ellipsoids, dumb-bells etc.) is the same as the spontaneous curvature approach (see Miao *et al.*, 1994); however, the energy of a given configuration will vary according to the values of C_o, κ_{nl}/κ_b etc. Thus, the phase diagram will be different from one model to the next. A section of the phase diagram for $\kappa_{nl}/\kappa_b = 4$ at $C_o = 0$ is:



One can see how the area of the outer leaflet increases with respect to the inner leaflet as the shape changes from prolate ellipsoids to pears to multiplets at fixed volume.

Once the characteristics such as C_o and ΔA have been determined for a specific cell, other shapes can be both predicted and compared against experiment. For example, the predicted shapes in the ΔA model reproduce the observed ones very well over the very narrow temperature range 43.8 to 44.1 ^oC; (Berndl *et al.*, 1990; see also Käs and Sackmann, 1991)