**PHYS 4xx Whole 1 - Vesicles and the human erythrocyte**

Mechanically simple cells often adopt smooth symmetrical shapes such as the familiar biconcave disc of the red blood cell, or the spherocylinder of some bacteria.

In panel (a), a bud is appended to a nearly spherical shell whose enclosed volume is not far below the maximum allowed by the surface area. The configurations in panel (b) have volumes well below their maximum values; these shapes are not ellipsoidal, and display both positive and negative curvature along meridians running from pole to pole.

(a)   (b)
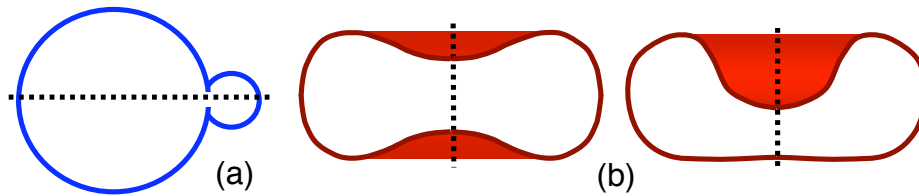
Within the spontaneous curvature model for membrane bending, the deformation energy of a spherical shell is $E_{\text{sphere}} = 4\pi(2\kappa_b + \kappa_G)$ if $C_o = 0$. How does this energy change as the spherical shell is distorted, with a resulting loss of volume at fixed surface area? Consider two configurations, the spherocylinder and the pancake, as representative of prolate and oblate shapes.

(a)   (b)
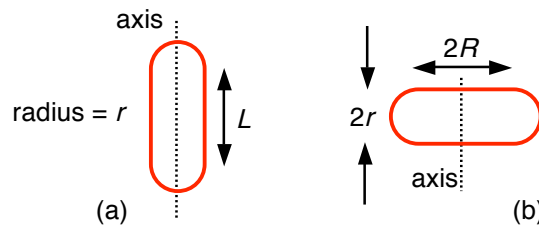
These shapes are described by length parameters r, R, and L, and have energies

$$E_{\text{spherocylinder}} = 8\pi\kappa_b + \pi\kappa_b(L/r) + 4\pi\kappa_G \tag{1a}$$
$$E_{\text{pancake}} = \pi\kappa_b(8 + \pi R/r) + 4\pi\kappa_G \qquad (R/r \gg 1), \tag{1b}$$

when $C_o = 0$. Eq. (1b) is an approximation valid for $R/r \gg 1$.

Displayed below are the energies of the two representative shapes compared with E_{sphere}, as in $\Delta E_{\text{pancake}} = E_{\text{pancake}} - E_{\text{sphere}}$, where the exact result is used for the pancake energy, not Eq. (1b). The volume is quantified by the unitless combination v_{red}

$$v_{\text{red}} = 6\sqrt{\pi}\, V/A^{3/2}, \tag{2}$$

which equals unity for a sphere. When $C_o = 0$, Eqs. (1) do not depend on the absolute size of the shell, only on the ratios L/r and R/r; hence, ΔE is unique for each v_{red} when $C_o = 0$.
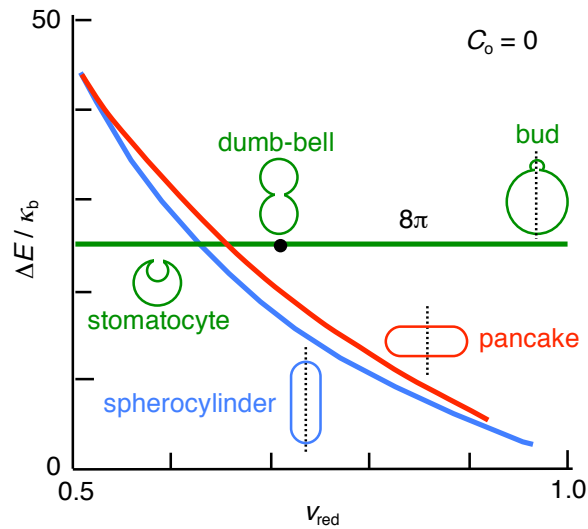
The spherocylinder is energetically favored over the pancake in the volume range $0.6 < v_{red} < 1$. However, the energies reverse as v_{red} passes below 0.5, with the pancake becoming the favored shape of the two for $v_{red} < 0.5$.

Also displayed is the energy of two touching spheres joined by a narrow neck with $E_{doublet} \sim 16\pi\kappa_b + 4\pi\kappa_G$, an approximation valid at $C_o = 0$ for two shells joined externally as a bud or internally as a pocket. Fourcade *et al.* (1994) have shown that the bending energy of the neck region may not be important because the principal curvatures have opposite sign (resulting in a small mean curvature). With $\Delta E_{doublet}/\kappa_b \sim 8\pi$, the energy of these configurations is independent of v_{red}; the reduced volume of the stomatocyte shape can range from 0 to 1, but the doublets obey $1/\sqrt{2} \leq v_{red} < 1$. Higher multiplet states with n externally connected spheres can attain lower values of v_{red} (down to $1/\sqrt{n}$) at the cost of adding another $8\pi\kappa_b$ to the bending energy for each new sphere, at vanishing C_o. Shapes with small buds are clearly not favored.

The figure predicts that, of the shapes considered, the prolate spherocylinder is favored for $v_{red} > 0.63$ and the extreme stomatocyte (internal cavity) is favored for $v_{red} < 0.63$. However, these shapes may not be true energy minima. Softening the curves may raise or lower the energy of the configurations, and affect which shape has the lowest energy. Numerical searches have been performed within the spontaneous curvature model, and others, for the true minimal energy states. A selection of shapes from one such search at $C_o = 0$ as a function of v_{red} are (Seifert *et al.*, 1991):

stomatocyte   oblate   prolate

0.3   0.591   0.592   0.651   0.652   0.8   0.95
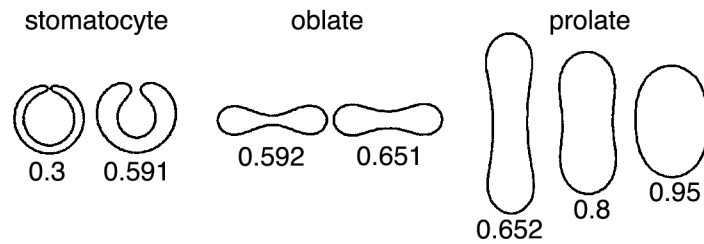
Although similar to our approximate boundary between stomatocytes and prolates at v_{red} = 0.63, the numerical results yield a narrow range of reduced volume around $0.59 \leq v_{red} \leq 0.65$ where the oblate shapes have the lowest energy. Further, these shapes are not ellipsoidal but rather biconcave, like the red blood cell.