Bending energy of a toroidal pore: comparing different solutions

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1 Intro

The bending energy of a membrane with negligible thickness is given by the Helfrich bending energy:

$$G_b = \frac{K_b}{2} \int dS(\kappa_1 + \kappa_2 + \kappa_s)^2 \tag{1}$$

where κ_1 and κ_2 are the principal curvatures for the membrane surface and κ_s is the membrane's spontaneous curvature. [1] This can be equivalently written as

$$G_b = \frac{K_b}{2} \int dS \left(\frac{1}{R_1} + \frac{1}{R_2} + \kappa_s \right)^2 \tag{2}$$

Though it is now known that membrane fusion pores have a minimum energy conformation of an ellipse rotated about a central axis [2], modeling the pore as a toroid provides a useful maximum energy starting point. I use the following coordinate system and variables defined in fig. 1 to do so. Note that R_0 and R_1 are constant, but R_2 is a function of z since it is the radius of curvature for the circumferential rings on the torus's inner surface swept out by a full rotation about the z axis.

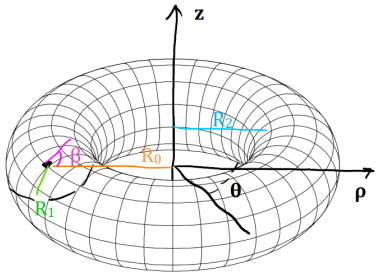

Figure 1: Coordinates and variables used to define the torus. Note that R_1 is constant while R_2 is a function of z. Unless stated otherwise, $z = 0$ will be set to be the inferiormost edge of the torus. The torus midplane is thus at $z = R_1$.

2 My solution

To make the analysis easier, fig. 1 has been reframed as a cross-section in fig. 2. To simplify things, I'll assume that $\kappa_s = 0$ in this section.
For the first step, R_2 can be be easily found in terms of β.

$$R_2 = R_0 - R_1 cos(\beta) \tag{3}$$

The angle β can be found via simple trigonometry.

$$\beta = arcsin(\frac{R_1 - z}{R_1}) \tag{4}$$

Thus, we can restate equation 3 in terms of z as

$$R_2 = R_0 - R_1 cos\left(arcsin\left(\frac{R_1 - z}{R_1}\right)\right) = R_0 - R_1\sqrt{1 - \frac{R_1 - z}{R_1}} \tag{5}$$

where the square-root equality is valid for $z \leq R_1$.

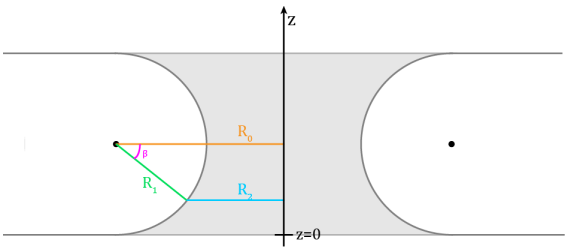

Figure 2: Cross section of the toroidal fusion pore using the same coordinates as defined in fig. 1. The thin black lines represent an infinitely thin membrane, gray area represents the pore lumen, and the white area represents space external to the fusing membranes. The z axis is the axis of rotational symmetry, and the various quantities shown in 1 are depicted here in cross-section.

Using our derived R_2, we can now solve for the pore's Helfrich bending energy by plugging eq. 5 into eq. 2.
To solve this numerically, I'll use the G_b *per unit area*:

$$G_b^{area} = \frac{K_b}{2}\left(\frac{1}{R_1} + \frac{1}{R_0 - R_1 cos(arcsin(\frac{R_1 - z}{R_1}))}\right)^2 \tag{6}$$

For each z, an infinitesimally thin ring's energy is then found.

$$G_b^{ring} = 2\pi R_1 G_b^{area} \tag{7}$$

Finally, we get the total pore energy by integrating over z:

$$G_b = \int G_b^{ring} dz \tag{8}$$

I don't think there's an analytic solution to eq 5. I couldn't figure out how to integrate even R_2 alone by hand; the $cos[arcsin((R_1 - z)/R_1)]$ version seemed unapproachable while the square-root equivalent produced an endless chain when I tried integration by substitution. Mathematica was unable to solve it either: it gave just spat the inputted integral back out when I gave it the square-root version and got hung up for >5 min (on my Surface Pro 4) computing the nested trig function version.

3 Markin, *et al.*'s solution

Markin *et al.* [3] developed a different solution to the bending energy of a toroidal membrane in 1984 that has been widely used since then. Their general solution was derived for a hemifusion stalk, but it can also be applied to a fusion pore given the analogous geometries. (Note that their original solution was for membranes of non-zero thickness, but thickness terms will be ignored since the equations are not altered significantly by neglecting it.) They too start with the Helfrich bending energy 2. However, our approaches appear to differ in two major ways: a) they find R_2 via a completely different method and b) they solve for the *change* in bending energy between the toroidal state and a preceding intermediate rather just the toroidal bending energy. The latter is simple enough to adjust for by dropping the terms applying to the initial bending energy. The derivation for curvatures around the pore circumference is not so easy to account for.
They define their initial principal curvature, the "meridional curvature", as $\kappa_m = -1/R_1$ - identical to my treatment. Rather than using trigonometry to find R_2 though, they reference an identify from Pogorelov [4] to define the "parallel curvature" function, κ_p around the pore circumference:

$$\kappa_p + R_2 \frac{d\kappa_p}{dR_2} = \kappa_m \tag{9}$$

This looks like a linear approximation to me, but I can't find any copies of the source article. In any case, the torus midplane serves as a boundary condition for κ_p since at the midplane ($z = R_1$) $\kappa_p = R_0 - R_1$. They then "solve" eq 9 (I don't know how they defined κ_p to be able to take its derivative) and insert the definition of κ_m to get

$$\kappa_p = -\frac{1}{R_1} + \frac{R_0}{r}\frac{1}{R_2} \tag{10}$$

To find the change in bending energy between the toroidal form and some rotationally symmetric precursor, they start with the expression

$$G_b = 2\pi K_b[\int dS(\kappa_p + \kappa_m - 2\kappa_s)^2 - \int dS(2\kappa_0 - 2\kappa_s)^2] \tag{11}$$

where κ_s is again the spontaneous curvature and κ_0 is the identical principal curvatures of the precursor. (I don't understand what happened to the factors before the integral.) When substituting our definitions of κ_m and κ_p into eq 11, Markin *et al*'s final integral expression becomes

$$\begin{aligned} G_b &= 2\pi K_b\{\int dS\left[\left(-\frac{1}{R_1}+\frac{R_0}{r}\frac{1}{R_2}\right)+\left(-\frac{1}{R_1}\right)-2\kappa_s\right]^2-\int dS(2\kappa_0-2\kappa_s)^2\} \\ &= 2\pi K_b\{\int dS\left[\frac{R_0}{r}\frac{1}{R_2}-\frac{2}{R_1}\right]^2-\int dS(2\kappa_0-2\kappa_s)^2\} \end{aligned} \tag{12}$$

Since we're only interested in the toroidal bending energy, we can ignore the second integral term. If we also assume that $\kappa_s = 0$, we thenobtain

$$G_b = 2\pi K_b\int dS\left[\left(-\frac{1}{R_1}+\frac{R_0}{r}\frac{1}{R_2}\right)+\left(-\frac{1}{R_1}\right)\right]^2 = 2\pi K_b\int dS\left[\frac{R_0}{r}\frac{1}{R_2}-\frac{2}{R_1}\right]^2 \tag{13}$$

I did not attempt to compute either of these integrals myself because I'm really not sure how to do so without first solving for R_2 the way I did in my own approach (ie parametrizing it to the central axis). However, this is the solution that Markin *et al* [3] get for eq 12:

$$\begin{aligned} G_b =& 2\pi K_b\left[\left[\left(\frac{2}{R_1}+2\kappa_s\right)^2-(4\kappa_0-2\kappa_s)^2\right]*\left[\frac{\pi}{2}R_1(R_0+h)-R_1^2\right]\right. \\ &-\pi r\left(\frac{2}{R_1}+2\kappa_s\right)\frac{R_0+h}{R_1} \\ &\left.+\frac{2}{R_1}\frac{(R_0+h)^2}{\sqrt{(R_0-R_1+h)(R_1+h+R_0)}}arctan\left(\sqrt{\frac{R_1+h+R_0}{R_0-R_1+h}}\right)\right] \end{aligned} \tag{14}$$

Unfortunately, they don't outline any of the steps taken to solve this integral, so I don't know what they did here. Markin *et al* [3] then assume that R_1 is constant and equal to the membrane thickness (ie that the membranes are separated by a distance less than their thickness) and that κ_0 is negligible. This yields

$$G_b = 2\pi K_b\left[2\kappa_s h[\pi(\epsilon+2)-4]+2\frac{(\epsilon+2)^2}{\sqrt{(\epsilon+2)^2-1}}arctan\left(\sqrt{\frac{\epsilon+3}{\epsilon+1}}\right)-4\right] \tag{15}$$

where $\epsilon \equiv \frac{R_0-R_1}{h}$.
Kozlov *et al* [5] appear to modify (though I don't know how) eq 15 to the form

$$G_b = \pi K_b\left[2\kappa_s[\pi(R_0+\delta)-4R_1]+\frac{2}{R_1}\frac{(R_0+\delta)^2}{\sqrt{(R_0-R_1+\delta)(R_0+R_1+\delta)}}arctan\left(\sqrt{\frac{R_0+R_1+\delta}{R_0-R_1+\delta}}\right)\right] \tag{16}$$

where $\delta = h/2$. Finally, we can assume that $h = 0$ as Chizmadzhev *et al* do [6] to get

$$G_b = \pi K_b\left[2\kappa_s[\pi R_0-4R_1]+\frac{2}{R_1}\frac{R_0^2}{\sqrt{(R_0-R_1)(R_0+R_1)}}arctan\left(\sqrt{\frac{R_0+R_1}{R_0-R_1}}\right)\right] \tag{17}$$

It's a bit difficult for me to extricate what parts of eqs 15, 16, & 17 are from subtracting off the initial precursor's bending energy just by inspection. However, this is clearly quite different form from my own solution, and I suspect that at least part of it has to do with our different definitions for the circumferential curvature - ie eq 5 vs eq 10.

References

[1] Helfrich W. Elastic Properties of Lipid Bilayers: Theory and Possible Experiments. *Z Naturforsch C.* 1973; 28(11):693-703.

[2] Jackson MB. Minimum Membrane Bending Energies of Fusion Pores. *J Membr Biol.* 2009 Oct; 231(2-3):101-115.

[3] Markin VS, Kozlov MM, Borovjagin VL. On the Theory of Membrane Fusion. The Stalk Mechanism. *Gen Physiol Biophys.* 1984; 5:361-377.

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[5] Kozlov MM, Leikin SL, Chernomordik LV, Markin VS, and Chizmadzhev YA. Stalk mechanism of vesicle fusion. *Eur Biophys J.* 1989; 17:121-129.

[6] Chizmadzhev YA, Cohen FS, Shcherbakov A, Zimmerberg J. Membrane mechanics can account for fusion pore dilation in stages. *Biophys J.* 1995; 69(6):2489-2500.