Electronic Supporting Information for:

Gaussian curvature directs the distribution of spontaneous curvature on bilayer membrane necks

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1 Elastic lipid bilayer with one type of curvature-inducing protein

In this section, we present a brief derivation of the generalized shape equation based on local stress balance. This approach, developped in details in[38,42,43], results in an equivalent model to the one obtained by the variationnal consideration[35,37,44]. We then express specialize the model to minimal surfaces, and propose a relationship between spontaneous curvature and protein density. Finally we discuss the need for a multi-protein model.

1.1 Equilibrium model of elastic surfaces by local force balance

The equation of mechanical equilibrium of an elastic surface ω subject to a lateral pressure p can be written in the compact form

$$\mathbf{\Sigma}^{\alpha}_{;\alpha} + p\mathbf{n} = \mathbf{0}\,, \tag{S1.1}$$

where $\mathbf{\Sigma}^{\alpha}$ are the stress vectors and $\mathbf{n}$ is the unit normal to the local surface. Greek indices range over $1,2$, and if repeated, are summed over this range. Semicolon identifies covariant differentiation with respect to the metric $a_{\alpha\beta} = \mathbf{a}_\alpha \cdot \mathbf{a}_\beta$ where $\mathbf{a}_\alpha = \mathbf{r}_{,\alpha}$ are the tangent vectors and $\mathbf{r}(\theta^\alpha)$ is the parametrization of the position field. The commas refer to partial derivatives with respect to the surface coordinates θ^α. With these definitions, the normal vector is given by $\mathbf{n} = (\mathbf{a}_1 \times \mathbf{a}_2)/\mid \mathbf{a}_1 \times \mathbf{a}_2 \mid$. In Eq. S1.1, the differential operation represents the surface divergence defined as $\mathbf{\Sigma}^{\alpha}_{;\alpha} = (\sqrt{a})^{-1}(\sqrt{a}\mathbf{\Sigma}^{\alpha})_{,\alpha}$ where $a = \det(a_{\alpha\beta})$. In surface theory, a manifold is described the metric $a_{\alpha\beta}$ defined above, and the curvature tensor given by $b_{\alpha\beta} = \mathbf{n}\cdot\mathbf{r}_{,\alpha\beta}$.

For an elastic membrane whose energy surface density per unit mass depends on the metric and curvature only $F(a_{\alpha\beta}, b_{\alpha\beta}; \theta^\alpha)$, the stress vectors involved in the local force balance (Eq. S1.1) can be written as[42]

$$\mathbf{\Sigma}^{\alpha} = \mathbf{T}^{\alpha} + S^{\alpha}\mathbf{n}\,. \tag{S1.2}$$

Here the tangential stress vectors are

$$\mathbf{T}^{\alpha} = T^{\beta\alpha}\mathbf{a}_\beta \quad \text{with} \quad T^{\beta\alpha} = \Sigma^{\beta\alpha} + b^{\beta}_{\mu} M^{\mu\alpha}\,, \tag{S1.3}$$

and the components of the normal stress vectors are

$$S^{\alpha} = -M^{\alpha\beta}_{;\beta}\,, \tag{S1.4}$$

where $b^{\beta}_{\alpha} = a^{\beta\lambda}b_{\lambda\alpha}$. The components of the stress vectors depends on the energy density as[42]

$$\Sigma^{\alpha\beta} = \rho\left(\frac{\partial F}{\partial a_{\alpha\beta}} + \frac{\partial F}{\partial a_{\beta\alpha}}\right) \text{ and } M^{\alpha\beta} = \frac{\rho}{2}\left(\frac{\partial F}{\partial b_{\alpha\beta}} + \frac{\partial F}{\partial b_{\beta\alpha}}\right), \tag{S1.5}$$

where ρ the surface mass density of the membrane. The tangential and normal local force balances can now be obtained by introducing Eqs. S1.2, S1.3, and S1.4 into Eq. S1.1, resulting in

$$T^{\beta\alpha}_{;\alpha} - S^{\alpha}b^{\beta}_{\alpha} = 0 \quad \text{and} \quad S^{\alpha}_{;\alpha} + T^{\beta\alpha}b_{\beta\alpha} + p = 0\,, \tag{S1.6}$$

where we made use of the Gauss and Weingarten equations[82] $\mathbf{a}_{\alpha;\beta} = b_{\alpha\beta}\mathbf{n}$ and $\mathbf{n}_{,\alpha} = -b^{\beta}_{\alpha}\mathbf{a}_\beta$ respectively.

Practically, the free energy density is sometimes given as a function of the mean curvature H and Gaussian curvature K. These are related to the metric and curvature by

$$H = \frac{1}{2}a^{\alpha\beta}b_{\alpha\beta}\,, \quad K = \frac{1}{2}\varepsilon^{\alpha\beta}\varepsilon^{\lambda\mu}b_{\alpha\lambda}b_{\beta\mu}\,, \tag{S1.7}$$

where $a^{\alpha\beta} = (a_{\alpha\beta})^{-1}$ is the dual metric, and $\varepsilon^{\alpha\beta}$ is the permutation tensor defined by $\varepsilon^{12} = -\varepsilon^{21} = 1/\sqrt{a}$, $\varepsilon^{11} = \varepsilon^{22} = 0$. According to the definitions S1.7, the free energy density per unit mass can be re-written in terms of the mean and Gaussian curvature $F(H,K;\theta^\alpha)$. Furthermore, lipid membranes are essentially incompressible (see assumption 3 above). This leads us to introduce a Lagrange multiplier $\gamma(\theta^\alpha)$ to ensure that the local area dilatation $J = 1$, or equivalently, to constraint the constant surface density ρ of the membrane. Consequently we can define the surface energy density of the membrane as follows

$$F(\rho, H, K; \theta^\alpha) = \bar{F}(H,K;\theta^\alpha) - \frac{\gamma(\theta^\alpha)}{\rho}\,, \tag{S1.8}$$

and when introducing the surface energy per unit area $W(\rho,H,K;\theta^\alpha) = \rho\bar{F}(H,K;\theta^\alpha)$, the components of the stress vectors (Eqs. S1.5) can be written as[42]

$$\Sigma^{\alpha\beta} = (\lambda + W)a^{\alpha\beta} - (2HW_H + 2KW_K)\,a^{\alpha\beta} + W_H\tilde{b}^{\alpha\beta} \tag{S1.9}$$

$$M^{\alpha\beta} = \frac{1}{2}W_H a^{\alpha\beta} + W_K\tilde{b}^{\alpha\beta} \tag{S1.10}$$

where $\lambda(\theta^\alpha) = -[\gamma(\theta^\alpha) + W(H,K;\theta^\alpha)]$, and $\tilde{b}^{\alpha\beta} = 2Ha^{\alpha\beta} - b^{\alpha\beta}$ is the cofactor of the curvature. The subscripts H and K refer to the partial derivative of the energy with respect to the indicated variable. The Lagrange multiplier γ has a mechanical interpretation of surface pressure and is not a material property of the surface[38,43]. λ can be interpreted as the surface tension based on comparisons with edge conditions on a flat surface[38].

Finally, introducing Eqs. S1.9 and S1.10 into Eqs. S1.3 and

S1.4, we can rewrite the normal and tangential force balances (Eqs. S1.6) as

$$\Delta\left(\frac{1}{2}W_H\right)+(W_K)_{;\alpha\beta}\tilde{b}^{\alpha\beta}+W_H(2H^2-K)+2H(KW_K-W) = p+2\lambda H\,, \quad \text{(S1.11)}$$

and

$$-(\gamma_{,\alpha}+W_K K_{,\alpha}+W_H H_{,\alpha})\,a^{\beta\alpha}=\left(\frac{\partial W}{\partial\theta^\alpha}\,|_{\exp}+\lambda_{,\alpha}\right)a^{\beta\alpha}=0\,, \quad \text{(S1.12)}$$

where $\Delta(\cdot)=(\cdot)_{;\alpha\beta}a^{\alpha\beta}$ is the surface Laplacian (or Beltrami operator), and $\partial(\cdot)/\partial\theta^\alpha\,|_{\exp}$ is the explicit derivative with respect to θ^α.

Eqs. S1.11 and S1.12 are the general shape equation and incompressibility condition for an elastic surface with free energy per unit area $W(\rho,H,K;\theta^\alpha)$. In the following we specialize it to the case of lipid membranes by specifying the form of the free energy.

1.2 Elastic lipid bilayers with non-constant spontaneous curvature

The most common model of lipid membranes is the Helfrich energy[33]. This can be extended to account for the entropic contribution of membrane-bound proteins to the areal free-energy functional such as

$$W(\sigma,H,K;\theta^\alpha)=A(\sigma)+k(\theta^\alpha)[H-C(\sigma)]^2+k_G(\theta^\alpha)K\,, \quad \text{(S1.13)}$$

Here $A(\sigma)$ is the contribution of the membrane-bound proteins to the free energy and σ is the surface density of proteins. $k(\theta^\alpha)$ and $k_G(\theta^\alpha)$ are the bending and Gaussian moduli respectively, considered to be surface coordinate dependent. $C(\sigma)$ is the spontaneous (mean) curvature, which is determined by the local membrane composition, say the surface density of a curvature-inducing protein σ. We will propose later a possible relationship for $C(\sigma)$. While it is certainly possible to propose explicit functions of $A(\sigma)$ and $C(\sigma)$ on the protein density (see[75] for discussion on $A(\sigma)$, and[45,77] for specific examples) we will for now retain their general form.

The shape equation for lipid membrane with protein and space dependent moduli is obtained by introducing the free energy density (S1.13) into Eq. (S1.11), resulting in

$$\Delta[k(H-C)]+2H\Delta k_G-(k_G)_{;\alpha\beta}b^{\alpha\beta}+2k(H-C)(2H^2-K) +2H(k_GK-W(\sigma,H,K;\theta^\alpha))=p+2\lambda H\,. \quad \text{(S1.14)}$$

The incompressibility for lipid membranes is obtained similarly, introducing (S1.13) into the Eq. (S1.12)

$$\nabla\lambda=-W_\sigma\nabla\sigma-\nabla k(H-C)^2-\nabla k_G K\,, \quad \text{(S1.15)}$$

where $(\cdot)_\sigma=\partial(\cdot)/\partial\sigma$ is the partial derivative with respect to σ, and $\nabla(\cdot)=(\cdot)_{,\alpha}a^{\alpha\beta}$ is the surface gradient. One can recognize W_σ as the chemical potential of the membrane protein, and given Eq. (S1.13), we have

$$W_\sigma=A_\sigma-2k(H-C)C_\sigma\,. \quad \text{(S1.16)}$$

Eqs. S1.14 and S1.15 describe the equilibrium configuration of lipid membrane subject to heterogeneous spontaneous curvature induced by proteins. An additional constraint related to the area incompressibility of the membrane requires the lipid velocity field ($\mathbf{u}=u^\alpha\mathbf{a}_\alpha+w\mathbf{n}$) to satisfy[45]

$$u^\alpha_{;\alpha}=2Hw\,. \quad \text{(S1.17)}$$

Although models for lipid flow within biological membranes have been proposed[38,43,46,75], such description is out of the scope of this study. Provided a lipid velocity field satisfying Eq. S1.17, and suitable boundary conditions, the system given by the coupled equations S1.14 and S1.15 fully describes the equilibrium configuration of a lipid membrane subject to a static distribution of curvature-inducing proteins.

1.3 Static distribution of curvature-inducing protein on minimal surfaces

In this section, we specialize the system of Eqs. S1.14 and S1.15 to minimal surfaces, and examine the associated restrictions on the Lagrange multiplier field λ and velocity field u^α.

Before to proceed, it is useful to clarify what are the imposed and the unknown quantities in our model. Traditionally, one seeks to compute the shape of the membrane for a given distribution of spontaneous curvature and boundary conditions. This is often done by formulating the shape equation and incompressibility condition within a certain parametrization. For instance, within the Monge parametrization one would aim to compute the height of the membrane $h(x,y)$ with respect to a reference plane at every point, while in axisymetric coordinates one would solve for the distance to the axis of symmetry $r(z)$. In our case however, we consider the *inverse problem*, that is to say, we seek to compute the distribution of spontaneous curvature for a given shape of the membrane and boundary conditions. Independently of the approach, the spontaneous curvature $C(\sigma)$ is interpreted physically as resulting form the distribution of curvature-inducing proteins (or lipids) of areal density σ on the membrane. We illustrate our 'inverse problem' approach by choosing minimal surfaces as the imposed membrane shape. We further demonstrate the applicability of our model by solving on catenoid-like necks, which are minimal surfaces that have been extensively used as models for the study of fusion/fission intermediate.

Minimal surfaces are characterized by the property that the mean curvature vanishes pointwise ($H=0$ everywhere on the membrane). Furthermore, as a first approximation, we consider membranes with isotropic mechanical properties (k and k_G are constants). Accordingly, in the absence of transmembrane pressure, the shape equation S1.14 reduces to a variable-coefficient Helmhotz equation for the spontaneous curvature

$$\Delta C(\sigma)-2KC(\sigma)=0\,. \quad \text{(S1.18)}$$

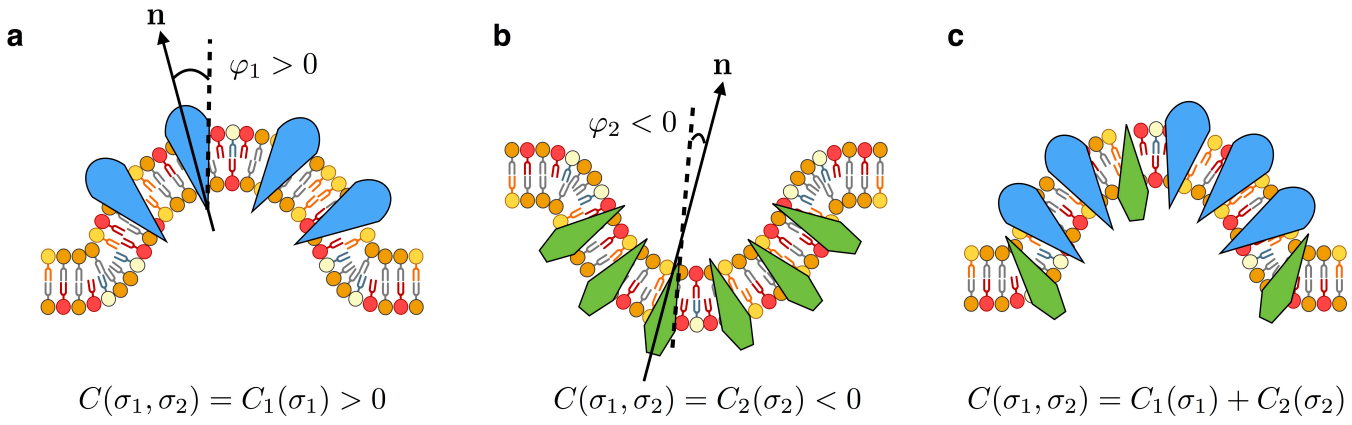

Fig. S1 Schematic representation of curvature-inducing proteins with conical shape on a lipid membrane. (a) Proteins with positive angle φ induce positive spontaneous curvature. (b) Proteins with a negative angle φ induce negative spontaneous curvature. (c) The value of the spontaneous curvature is the a combination of the local protein composition.

Both the energetic contribution of the proteins $A(\sigma)$ and the local Lagrange multiplier λ are now absent from the shape equation S1.18, therefore uncoupling them from the incompressibility condition. Yet, any solution of Eq. S1.18 is restricted to the condition that the balance equation S1.15 with S1.16 is satisfied. For minimal surfaces, these later equations reduce to

$$\nabla\lambda = -\left[A(\sigma)_\sigma + 2kC(\sigma)C(\sigma)_\sigma\right]\nabla\sigma\,. \tag{S1.19}$$

Using the identities $\nabla A(\sigma) = A(\sigma)_\sigma\nabla\sigma$ and $\nabla\left[C(\sigma)^2\right] = 2C(\sigma)C(\sigma)_\sigma\nabla\sigma$, this can be simplified to

$$\nabla\lambda = -\nabla[A(\sigma) + kC(\sigma)^2]\,, \tag{S1.20}$$

from which we get λ as a function of $A(\sigma)$ and $C(\sigma)$ apart from a constant λ_0, such that

$$\lambda = -[A(\sigma) + kC(\sigma)^2] + \lambda_0\,. \tag{S1.21}$$

Equation S1.21 is the admissibility condition for the Lagrange multiplier field λ.

1.4 Relationship between protein density and spontaneous curvature

Here we propose an explicit relationship between the spontaneous curvature and the distribution of curvature-inducing proteins.

One protein model Let us consider a pointwise protein surface density on the membrane $\sigma(\theta^\alpha)$. The goal of this section is to propose an expression for $C(\sigma)$. Note that we consider proteins only for ease of visualization, but our model can be as easily applied to spontaneous curvature-inducing lipids or nano-objects instead of proteins.

A convenient way to think about the relationship between spontaneous curvature and protein density, is in terms of the insertion of a conical shape transmembrane protein with its axis of revolution directed along the surface normal (see Fig. S1). Following this representation, the point value of $C(\sigma)$ will depend on (i) the angle of the cone (φ), (ii) the lipid-protein specific moietic interactions (κ), and (iii) the local density of protein (σ). It should be noted that in this model, we neglect any thickness variation or lipid tilt resulting from the insertion of the proteins in the lipid bilayer. Although experimental observations seem to support point (iii) [10,19], to our knowledge, no explicit relation between C and σ has been reported based on experimental data. Consequently, we consider a simple expression for the spontaneous curvature of the form [45]

$$C(\sigma) = \kappa\varphi\sigma\,. \tag{S1.22}$$

This form ensures that the induced spontaneous curvature vanishes in the case of cylindrical embedded proteins ($\varphi = 0$), and assumes that a same type of conical protein inserted from one or the other lipid leaflet will have φ of opposite sign, and therefore produce a spontaneous curvature of opposite sign. It should be noted that this expression does not account for protein-protein interaction, and therefore should be considered only in a dilute regime, outside of any saturation effect.

A limitation of the model in its current form is that the spontaneous curvature is the result of only one type of protein. As a consequence, $C(\sigma)$ can only be either positive everywhere, or negative everywhere, but cannot change sign from one point of the membrane to the other. This is in contradiction with our results on the determination of spontaneous curvature on catenoid-shaped necks. The minimal set of proteins to allow the spontaneous curvature to have positive and negative values is two, and this case is considered next.

Two proteins model We propose that the local protein density results from a minimal set of two proteins $\sigma = \{\sigma_1, \sigma_2\}$. All the results below can be easily generalized to a set of N proteins. As a first approximation, we assume that the spontaneous curvature is a linear combination of the spontaneous curvatures induced by each individual proteins $C(\sigma_1,\sigma_2) = C_1(\sigma_1) + C_2(\sigma_2)$. Similarly to the one protein model (Eq. S1.22), we assume a linear relationship between spontaneous curvature and protein density, such that

$$C_i(\sigma_i) = (\kappa_i\varphi_i)\sigma_i\,, \tag{S1.23}$$

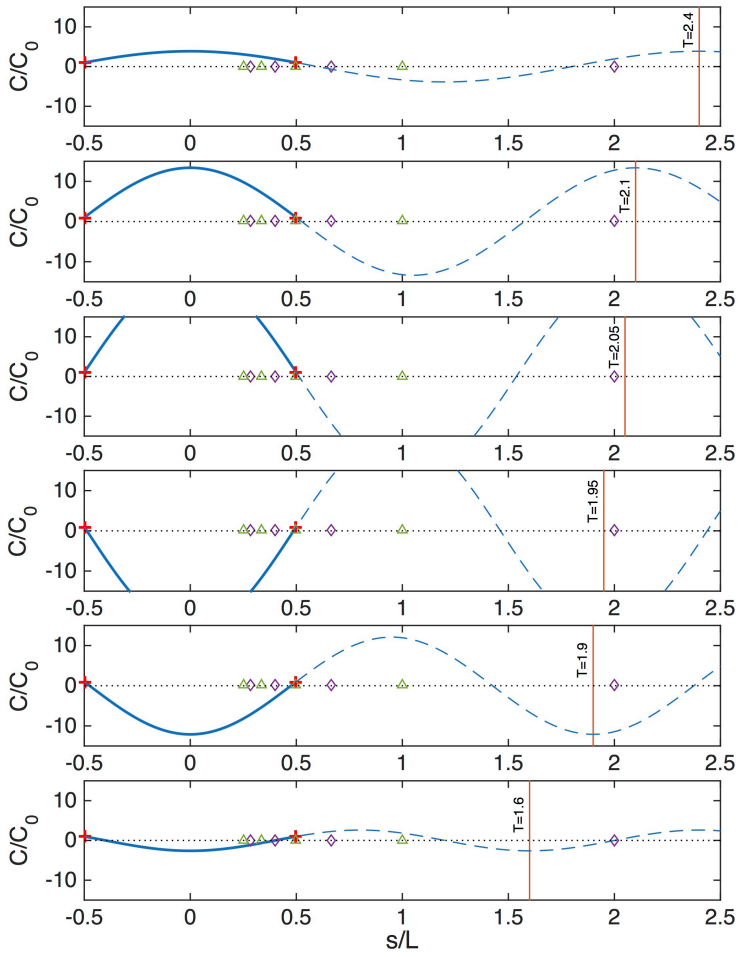

Fig. S2 The switch-like behavior in spontaneous curvature observed for catenoids can be conceptually understood with a simple oscillator. The solution of a simple harmonic oscillator (Eq. S2.3) with $C_1 = C_0$ depends on the oscillator period $T = -\pi/K$. Decreasing values of the oscillator period correspond to increasing values of K, and therefore decreasing values of the neck radius. C diverges for $T^*/L = 2/(1+2n)$ (marked by purple diamonds), and changes mode for $T^*/L = 1/(1+n)$ (indicated by green triangles).

where κ_i is a positive constant representing the lipid/protein specific hydorphobic interactions, and φ_i is the angle made by the meridian of the conic protein with the surface normal (see Fig. S1). Note that in order for the total spontaneous curvature $C(\sigma_1,\sigma_2)$ to have either positive or negative values, the angles of the two proteins needs to have opposite signs ($\varphi_1\varphi_2 < 0$).

With these forms in effect, Eqs. S1.18 and S1.21 can be expressed directly as a function of the protein densities. The shape equation thus reduces to

$$\Delta(\kappa_1\varphi_1\sigma_1 + \kappa_2\varphi_2\sigma_2) - 2K(\kappa_1\varphi_1\sigma_1 + \kappa_2\varphi_2\sigma_2) = 0\,, \qquad \text{(S1.24)}$$

subject to the admissibility condition for λ

$$\lambda = -[A(\sigma_1,\sigma_2) + k(\kappa_1\varphi_1\sigma_1 + \kappa_2\varphi_2\sigma_2)^2] + \lambda_0\,. \qquad \text{(S1.25)}$$

In the case where the two proteins have the same physical properties, but are inserted on either side of the membrane ($\kappa_1 = \kappa_2 = \kappa$, and $\varphi_1 = -\varphi_2 = \varphi$, we can define the effective protein density $\tilde{\sigma} = \sigma_1 - \sigma_2$ which satisfies

$$\Delta\tilde{\sigma} - 2K\tilde{\sigma} = 0\,, \qquad \text{(S1.26)}$$

and

$$\lambda = -[A(\sigma_1,\sigma_2) + k(\kappa\varphi\tilde{\sigma})^2] + \lambda_0\,. \qquad \text{(S1.27)}$$

2 Simple Oscillator Analogy

In order to study the behavior of Eq. S1.18 in simplified conditions, let us consider the case where K is a constant. In one-dimension, Eq. S1.18 can be written as

$$\frac{d^2C}{ds^2} = -\omega^2 C\,, \qquad \text{(S2.1)}$$

where $\omega^2 = -2K$ is a positive constant, and $s \in [-L/2; L/2]$. This is the equation of a simple harmonic oscillator of period $T = 2\pi/\omega = \pi\sqrt{-2/K}$, which has for general solution

$$C(s) = A\cos(\omega s) + B\sin(\omega s)\,, \qquad \text{(S2.2)}$$

A and B being constants determined by the boundary conditions. With boundary conditions $C(-L/2) = C_0$ and $C(L/2) = C_1$ the solution is

$$C(s) = \frac{C_0 + C_1}{2\cos(\omega L/2)}\cos(\omega s) - \frac{C_0 - C_1}{2\sin(\omega L/2)}\sin(\omega s)\,. \qquad \text{(S2.3)}$$

From Eq. S2.3 we have that the value of C at the neck ($s=0$) is

$$C(0) = \frac{C_0 + C_1}{2\cos(\omega L/2)} \,, \tag{S2.4}$$

which diverges for $\omega^* = (\pi + 2n\pi)/L$, where $n \in \mathbb{N}$. Or in terms of the oscillator period, the solution diverges for

$$T^* = \frac{2L}{1+2n} \,. \tag{S2.5}$$

Eq. S2.3 is plotted in Fig. S2 for various periods T. The value of C within the interval $[-L/2; L/2]$ is positive for $T > T^*(n=1)$, and negative below. To decrease the oscillator period is conceptually equivalent to increase the absolute value of K, or to decrease the neck radius of the catenoid. For a catenoid, the Gaussian curvature at the neck is $K(s=0) = -1/r_n^2$. Taking $\omega^2 = 2/r_n^2$, the positive value of the neck radius for which the spontaneous curvature diverges is

$$r_n^* = \frac{\sqrt{2}L}{\pi(1+2n)} \,. \tag{S2.6}$$

For $n=0$, we have $r_n^*/L \simeq 0.45$. From Eq. S2.6, it is clear that the value of the critical neck radius is independent of the boundary conditions.

3 Direct solution of the shape equation

In this section we verify that the solution for the spontaneous curvature obtained on catenoid-shaped neck does produce catenoid by following the "direct" approach. The shape equation for an isotropic membrane is

$$\Delta[k(H-C)] + 2k(H-C)(H^2 - K + HC) = p + 2H(\lambda + A) \,, \tag{S3.1}$$

with the incompressibility condition that can be written as

$$\nabla(\lambda + A) = 2k(H-C)C_\sigma \nabla\sigma \,. \tag{S3.2}$$

3.1 Axisymmetric parametrization

We write the equilibrium equations of the membrane in axisymmetric coordinates. We therefore define a surface of revolution that is described in the coordinate basis $(\mathbf{e}_r, \mathbf{e}_\theta, \mathbf{k})$ by

$$\mathbf{r} = r(s)\mathbf{e}_r + z(s)\mathbf{k} \,, \tag{S3.3}$$

where s is the arclength along the curve, $r(s)$ is the radius to the axis of revolution, and $z(s)$ is the elevation from a reference plane. Since $r(s)^2 + z(s)^2 = 1$, it is convenient to define the angle ψ such that

$$\mathbf{a}_s = \cos\psi\mathbf{e}_r + \sin\psi\mathbf{k} \quad \text{and} \quad \mathbf{n} = -\sin\psi\mathbf{e}_r + \cos\psi\mathbf{k} \,, \tag{S3.4}$$

are the tangent and normal vectors to the curve respectively. It follows that the surface can be parametrized as

$$r'(s) = \cos\psi \,, \tag{S3.5}$$

$$z'(s) = \sin\psi \,, \tag{S3.6}$$

where $(\cdot)' = d(\cdot)/ds$. We can now write the tangential and transverse principal curvatures as

$$\kappa_1 = \psi' \quad \text{and} \quad \kappa_2 = r^{-1}\sin\psi \,, \tag{S3.7}$$

respectively, and the mean and Gaussian curvatures as

$$H = \frac{\kappa_1 + \kappa_2}{2} = \frac{\psi' + r^{-1}\sin\psi}{2} \tag{S3.8}$$

$$K = \kappa_1\kappa_2 = H^2 - (H - r^{-1}\sin\psi)^2 \,, \tag{S3.9}$$

respectively. Eq. S3.8 provides the differential equation for ψ, which can be rearranged as

$$r\psi' = 2rH - \sin\psi \,. \tag{S3.10}$$

Eq. S3.1 is a second order partial differential equation. In order to simplify its resolution, we define Λ as

$$\Lambda = r\,[k(H-C)]' \,, \tag{S3.11}$$

allowing to write the shape equation (Eq. S3.1) as a first order differential equation for the mean curvature

$$H' = r^{-1}\Lambda + C' \,. \tag{S3.12}$$

Using the relation $\nabla(H-C) = r^{-1}[(H-C)']' = r^{-1}(rL)'$, into Eq. S3.1, we get a differential equation for Λ

$$r^{-1}\Lambda' = \frac{p}{k} + 2H\left[(H-C)^2 + \frac{\lambda + A}{k}\right] - 2[H-C]\left[H^2 + (H - r^{-1}\sin\psi)^2\right] \,. \tag{S3.13}$$

Finally, Eq. S3.2 becomes

$$[\lambda + A]' = 2k(H-C)C' \,. \tag{S3.14}$$

The full system is composed of Eqs. S3.5, S3.6, S3.10, S3.12, S3.13, and S3.14, and must be completed with 6 boundary conditions. For a domain defined as $s \in [0, L/2]$, we set

$$\begin{aligned} &r(0) = r_n \,, && r(L/2) = r_n\cosh[z(L/2)/r_n] \,, \\ &z(0) = 0 \,, && z(L/2) = r_n\mathrm{asinh}[L/2/r_n] \,, \\ &\psi(0) = \pi/2 \,, && \psi(L/2) = \mathrm{asin}[1/\sqrt{1 + (L/2/r_n)^2}] \,, \end{aligned} \tag{S3.15}$$

where we used Eq. S3.9 to determine $\psi(L/2)$.

3.2 Dimensionless system

Based on the length scales introduced in the main text, L and C_0, we define the axisymmetric dimensionless variables as

$$\begin{aligned} &\bar{s} = s/L \,, \quad \bar{r} = r/L \,, \quad \bar{z} = z/L \,, \quad \bar{H} = HL \,, \quad \bar{C} = C/C_0 \,, \quad \bar{l} = \Lambda L \,, \\ &\bar{\lambda} = (\lambda + A)L^2/k \,, \quad \bar{p} = pL^3/k \,, \quad \bar{K} = KL^2 \,, \quad \bar{k}_G = k_G/k \,. \end{aligned} \tag{S3.16}$$

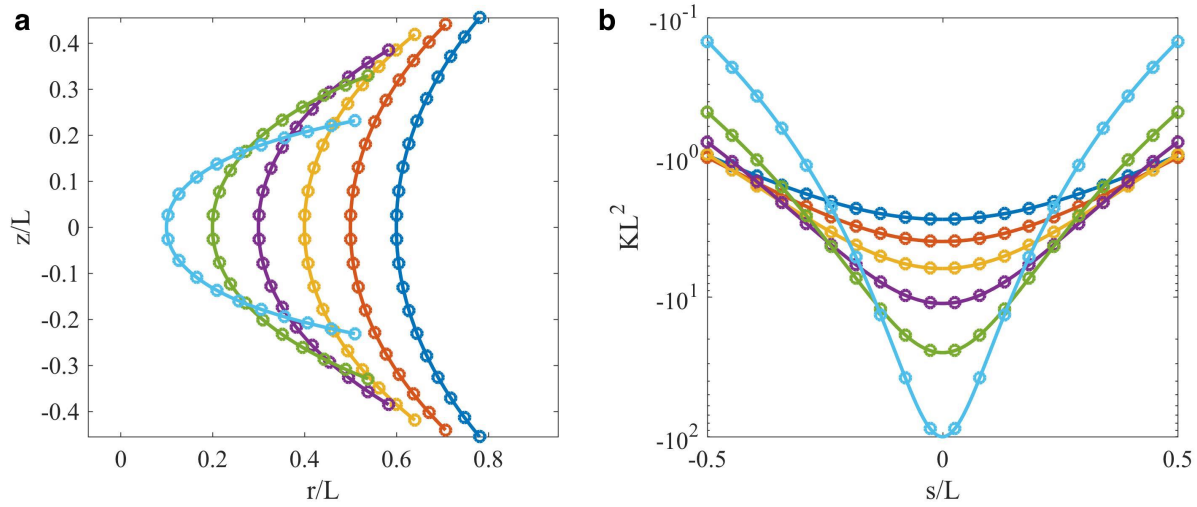

Fig. S3 Direct solution of the shape equation subject to the distribution of spontaneous curvature from Fig. 3(c). Symbols are exact values for a catenoid, solid lines are computation results. (a) Shape of the neck, and (b) Gaussian curvature.

The dimensionless system then becomes

$$\begin{aligned} &\bar{r}' = \cos\psi\,, \quad \bar{z}' = \sin\psi\,, \quad \bar{r}\psi' = 2\bar{r}\bar{H} - \sin\psi\,, \\ &\bar{H}' = \bar{r}^{-1}\bar{l} + \bar{C}'\,, \quad \bar{\lambda}' = 2(\bar{H}-\bar{C})\bar{C}'\,, \\ &\text{and}\ \ \bar{r}^{-1}\bar{l}' = \bar{p} + 2\bar{H}\left[(\bar{H}-\bar{C})^2 + \bar{\lambda}\right] \\ &\qquad\qquad -2(\bar{H}-\bar{C})\left[\bar{H}^2 + (\bar{H}-\bar{r}^{-1}\sin\psi)^2\right]\,, \end{aligned} \tag{S3.17}$$

with the boundary conditions

$$\begin{aligned} &\bar{r}(0) = \bar{r}_n\,, && \bar{r}(0.5) = \bar{r}_n \cosh[\bar{z}(0.5)/\bar{r}_n]\,, \\ &\bar{z}(0) = 0\,, && \bar{z}(0.5) = \bar{r}_n \operatorname{asinh}[0.5/\bar{r}_n]\,, \\ &\psi(0) = \pi/2\,, && \psi(0.5) = \operatorname{asin}[1/\sqrt{1+(0.5/\bar{r}_n)^2}]\,, \end{aligned} \tag{S3.18}$$

where $\bar{r}_n = r_n/L$.

3.3 Numerical implementation and results

With the aim to verify that the distribution of spontaneous curvature obtained through the inverse problem produces a catenoid-shaped membrane, we chose a different numerical method for the direct computation. Therefore, we solved the system with a custom made code in Matlab® (Mathworks, Natick, MA), utilizing the built-in boundary value problem solver *bvp4c*. The values for the distribution of spontaneous curvature was extracted from the data shown in Fig. 3(c) using a spline interpolation to obtain the value of C between the initial mesh-points. Then the system of Eqs. S3.17 with the boundary conditions S3.18 was solved on an initial mesh of $1,000$ equidistant points. To obtain convergence, the solver was allowed to increase the number of mesh-points up to $100,000$. The relative and absolute tolerances were set to 10^{-4} and 10^{-7} respectively.

Solution for the direct computations of the shape equation are presented in Fig. S3. Both the shape and the Gaussian curvature fit closely the ones of a perfect catenoid. This results confirm that the distribution of spontaneous curvature obtained through the inverse approach minimizes the energy of a catenoid-shaped structure subject to the the above boundary conditions.