

Geometry of lipid vesicle adhesionR. Capovilla^{1,*} and J. Guven^{2,†}¹*Departamento de Física, Centro de Investigación y de Estudios Avanzados del IPN, Apartado Postal 14-740, 07000 México, DF, Mexico*²*Instituto de Ciencias Nucleares, Universidad Nacional Autónoma de México, Apartado Postal 70-543, 04510 México, DF, Mexico*

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The adhesion of a lipid membrane vesicle to a fixed substrate is examined from a geometrical point of view. This vesicle is described by the Helfrich Hamiltonian quadratic in the mean curvature; it interacts by contact with the substrate, with an interaction energy proportional to the area of contact. We identify the constraints on the geometry at the boundary of the shared surface. The result is interpreted in terms of the balance of the force normal to this boundary. No assumptions are made either on the symmetry of the vesicle or on that of the substrate. The strong bonding limit as well as the effect of curvature asymmetry on the boundary are discussed.

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I. INTRODUCTION

Geometrical models provide a surprisingly robust phenomenological description of the equilibria of physical membranes [1–5]. The Hamiltonian that describes the membrane is constructed as a sum of geometrical scalars; in particular, lipid membrane vesicles are well approximated by one that is quadratic in the mean curvature [6–8]. Such models can also be extended to model adhesion between vesicles or between a vesicle and a rigid substrate [9–11], processes that are increasingly relevant to biophysics. (Two reviews are Refs. [12,13].) In this paper, we examine one important aspect of this problem, the geometry of the contact boundary, which, surprisingly, does not appear to have been examined in any generality.

To model the interaction one can exploit, as for an isolated membrane, the geometrical scalars characterizing the surface of contact as well, perhaps, as its boundary. As such, this is not a model of the adhesion of individual molecules to specific sites on the membrane, a task that lies beyond the scope of this continuum description.

In its simplest form, which is the one we consider, the interaction Hamiltonian is proportional to (minus) the area of contact. The energy associated with the boundary of the contact region is ignored. Axially symmetric configurations have been studied thoroughly in this “ideal” context [11,14]. In Ref. [15], the adhesion of “linear” vesicles in two dimensions was considered. More recently, in Refs. [16,17] and [18] perturbation theory has been developed in the strong bonding limit, in which the bending energy itself is small compared to that of adhesion. Nonaxially symmetric configurations of an adhering vesicle under the effect of gravity were studied in Ref. [19] using numerical techniques. We note that a more realistic treatment of adhesion considering chemically structured or rough surfaces has been provided in Ref. [20].

For definiteness, we will assume that one of the interacting surfaces is a fixed substrate, although it is simple to relax

this restriction. We will *not*, however, assume that this surface is flat. More significantly, we relax the assumption that the vesicle geometry is axially symmetric. In previous axially symmetric work the geometric origins of the boundary conditions are not clear, because the technique is tailored so finely to the symmetry; nor is it clear to what extent they will survive the relaxation of symmetry. This is a less than desirable situation in a model that is intrinsically geometric to begin with. Of course, one is also interested in geometries that are not axially symmetric: to mention just one context where this would be the case, we note that all configurations with a negative area difference appear to be inconsistent with axial symmetry [21]. Indeed, it may also be energetically favorable for an initially axially symmetric vesicle to adhere to a substrate in a manner that breaks its original symmetry.

Our first approach will be to search for minima of the energy. To do this, we will exploit the geometrical framework introduced recently to describe lipid membranes [22], and extended to accommodate edge effects in Ref. [23]. The extension to adhering geometries introduces its own subtleties due to potential discontinuities at the boundary of contact: the energy is stationary only when appropriate constraints on the vesicle geometry are satisfied on this boundary. Our treatment of the problem is divided into three parts. To establish our bearings, we begin in Sec. II with a rederivation of the Young equation for a liquid droplet where the bonding to the wall competes with the surface tension of the drop. In Sec. III, we consider lipid vesicles described by the Helfrich Hamiltonian. Discontinuities at the boundary of the contact region are discussed in Sec. III A. In Sec. III B, establishing contact with the recent work in this direction, we study the strong bonding limit in which the bending energy is ignored but any asymmetry between the layers is accounted for. In this limit, discontinuities at the boundary of the contact region are not smoothed; a nonvanishing contact angle does not imply a divergent energy. Finally, in Sec. IV we consider the general case. The finiteness of the curvature energy necessarily eliminates an angle of contact between the vesicle and the substrate; stationary energy completely fixes the curvature at the boundary. This generalizes the situation for axially symmetric shapes, where as is well known, the curvature is completely fixed at the boundary [11]: the

*Electronic address: capo@fis.cinvestav.mx

†Electronic address: jermal@nuclecu.unam.mx

vesicle radius of curvature normal to the line of contact is inversely proportional to the square root of the bond strength, the tangential radius as well as the potentially non-vanishing off-diagonal curvature are both completely fixed by the substrate geometry. We demonstrate that the boundary condition is not modified by a curvature asymmetry. In Sec. V, we use the expressions for the internal stress tensor in a lipid membrane developed in Ref. [22], to provide a surprisingly simple interpretation of the boundary condition in terms of the balance of forces at the boundary for a flat substrate. We end with some brief conclusions.

II. SURFACE TENSION DOMINATED MODEL

It is worthwhile to first review the adhesion of a drop of liquid of fixed volume onto a surface. Here the focus is on the competition between the surface tension of the liquid and the attraction between the liquid surface and the substrate. The former tends to reduce the surface area of the drop; the latter to increase the area of contact. The energy is given as a sum of three terms

$$F = \mu A - w A_{\text{contact}} - p(V - V_0). \quad (1)$$

The energy associated with the constant surface tension μ of the drop is proportional to its total surface area A ; that associated with adhesion is proportional to (minus) the area of contact A_{contact} between the drop and the substrate. The parameter w is the attractive contact potential. The third term involving the Lagrange multiplier p implements the volume constraint fixing the enclosed drop volume V at the value V_0 .

The equilibrium drop configurations are those at which the energy (1) is stationary. The problem posed here differs from the standard isoperimetric problem in that the area at different positions on the surface gets weighted according to whether or not it lies in the contact region, which itself is determined by the outcome of the variational problem. Indeed the contact surface might be weighted negatively. For physically realistic parameters, however, an equilibrium is realized. The energy is always bounded from below.

In equilibrium, the curvature of the drop's surface will suffer a discontinuity along the boundary C of the contact region. We parametrize the embedding of the free surface of the droplet in three-dimensional space as follows: $\mathbf{x} = \mathbf{X}(\xi^a)$, and the substrate $\mathbf{x} = \tilde{\mathbf{X}}(\tilde{\xi}^a)$, $a = 1, 2$. The energy is a functional both of \mathbf{X} for the free surface and $\tilde{\mathbf{X}}$ for the region of contact. They coincide on C , $\mathbf{X} = \tilde{\mathbf{X}}$. See Fig. 1. We now recast the first two terms appearing in F as (A_{free} is the area of the free surface)

$$\begin{aligned} \mu A - w A_{\text{contact}} &= \mu A_{\text{free}} + (\mu - w) A_{\text{contact}} \\ &= \mu \int_{\text{free}} d^2 \xi \sqrt{\gamma} + (\mu - w) \int_{\text{contact}} d^2 \tilde{\xi} \sqrt{\tilde{\gamma}}. \end{aligned} \quad (2)$$

Here γ is the determinant of the metric γ_{ab} induced on the free surface given by $\gamma_{ab} = \mathbf{e}_a \cdot \mathbf{e}_b$, where $\mathbf{e}_a = \partial_a \mathbf{X}$ are vectors tangent to the surface. Similar definitions hold for the

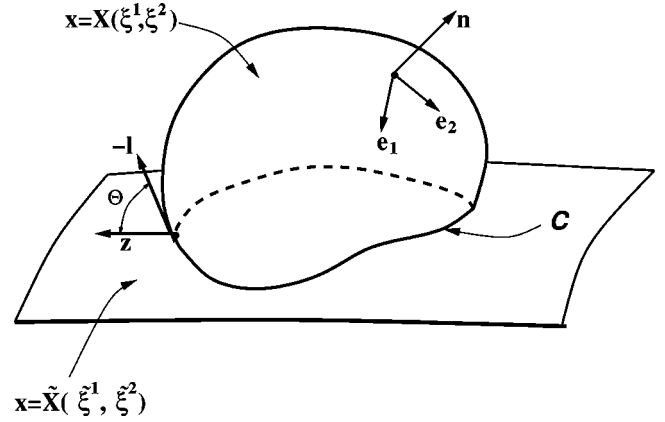


FIG. 1. Definition of the quantities used in the description of the geometry of adhesion.

geometrical quantities, indicated with a tilde, associated with the substrate. Note that the boundary C may possess disconnected components.

To derive the equations describing the equilibrium shape of a droplet, let us consider a variation of the embedding of the free surface, $\mathbf{X} \rightarrow \mathbf{X} + \delta \mathbf{X}$. We let \mathbf{n} to denote the unit normal to the free surface. We decompose the displacement with respect to the spatial basis adapted to this surface, $\{\mathbf{e}_a, \mathbf{n}\}$: $\delta \mathbf{X} = \Phi^a \mathbf{e}_a + \Phi \mathbf{n}$. We have for the corresponding variation of the induced metric $\delta_X \gamma_{ab} = 2K_{ab} \Phi + \nabla_a \Phi_b + \nabla_b \Phi_a$. The normal deformation is proportional to the extrinsic curvature tensor, $K_{ab} = \mathbf{e}_b \cdot \partial_a \mathbf{n}$. The mean extrinsic curvature is $K = K_{ab} \gamma^{ab}$. The tangential deformation is the Lie derivative of γ_{ab} along the vector field Φ^a ; ∇_a is the covariant derivative compatible with γ_{ab} .

On the boundary C , the fixed substrate constrains $\delta \mathbf{X}$ to lie along the contact region. We will ignore this for the moment, treating $\delta \mathbf{X}$ as though it were unconstrained on C . Then variation of A_{free} gives

$$\delta_X A_{\text{free}} = \int_{\text{free}} dA K \Phi + \int_C ds l^a \Phi_a. \quad (3)$$

Here l^a is the outward pointing normal to C on the free surface; s is arclength along C . We also have that the variation of the enclosed volume is

$$\delta_X V = \int_{\text{free}} dA \Phi. \quad (4)$$

Remote from C only the normal projection of the variation Φ plays a role in determining the equilibria of the droplet. This is generally true regardless of the model.

For this model, the free surface satisfies $\mu K = p$, as follows from the first term in Eq. (3), together with Eq. (4). Note that there is no boundary term associated with the normal deformation Φ . This contrasts with the tangential deformation whose only net physical effect is to induce a displacement of the boundary.

The boundary deformation we have described is not free: the variation $\delta \mathbf{X}$ on C is constrained to lie tangent to the

substrate. Without loss of generality, we can also assume that it is normal to the boundary C , so that

$$\delta\mathbf{X} = \Phi_0 \tilde{\mathbf{z}}, \quad (5)$$

where $\tilde{\mathbf{z}}$ is the outward unit normal to C on the substrate (see Fig. 1). We then have for the integrand appearing in the boundary term in Eq. (3), $l^a \Phi_a = \mathbf{l} \cdot \delta\mathbf{X} = \mathbf{l} \cdot \tilde{\mathbf{z}} \Phi_0$, where $\mathbf{l} = l^a \mathbf{e}_a$ is the surface vector l^a treated as a spatial vector. The boundary contribution to the variation of the free surface $\delta_X A_{\text{free}}$ is then

$$\delta_X A_{\text{free}} = \int_C ds \mathbf{l} \cdot \tilde{\mathbf{z}} \Phi_0. \quad (6)$$

We now consider the variation of the area of contact A_{contact} . The deformation $\delta\mathbf{X}$ of the free surface will induce a variation in A_{contact} through the boundary that they share,

$$\delta_X A_{\text{contact}} = \int_C ds \Phi_0, \quad (7)$$

which is a two-dimensional analog of Eq. (4). Note that the substrate need not be planar. We can now read off the total boundary contribution to the variation $\delta_X F$, with F given by Eqs. (1) and (2). In equilibrium, we require that

$$\int_C ds [\mu \mathbf{l} \cdot \tilde{\mathbf{z}} + (\mu - w)] \Phi_0 = 0 \quad (8)$$

for an arbitrary Φ_0 . We therefore conclude that

$$w = \mu(1 + \mathbf{l} \cdot \tilde{\mathbf{z}}). \quad (9)$$

Defining the contact angle Θ by $\cos \Theta = -\mathbf{l} \cdot \tilde{\mathbf{z}}$, this expression reproduces the well known Young equation.

III. LIPID VESICLE ADHESION

A lipid membrane is modeled by the Helfrich bending energy

$$F_b = \alpha \int dA K^2. \quad (10)$$

For definiteness, we will focus on either of two variants of the model: in both versions the enclosed volume and the total surface area are fixed; in the spontaneous curvature model, K is replaced by $K - K_0$ in Eq. (10) where the constant K_0 is the spontaneous curvature; in the bilayer couple model, the area difference, proportional to the integrated mean curvature

$$M = \int dA K, \quad (11)$$

is also fixed [21]. Thus we construct the constrained energy,

$$F = F_b - w A_{\text{contact}} + \mu(A - A_0) + \beta(M - M_0) - p(V - V_0). \quad (12)$$

Here μ is now the Lagrange multiplier associated with the area constraint; likewise β is that associated with the area difference constraint.

A. Discontinuities resolved

In the simple model discussed in Sec. II there is no energy penalty associated with discontinuities along the contact boundary C . However, both the intrinsic and extrinsic curvature will suffer a discontinuity along C . When the curvature of the vesicle contributes to its energy, such a discontinuity will generally result in a singularity in the energy. Because this singular contribution has support on C , it is no longer valid to decompose the energy into two parts, $F = F_{\text{free}} + F_{\text{contact}}$.

This point is well illustrated by considering an axially symmetric surface. Cylindrical polar coordinates $\{\rho, z, \varphi\}$ are introduced on R^3 ; constant φ curves on the surface are parametrized by arclength ℓ . The surface is then described completely once $\rho = R(\ell)$ is specified. The extrinsic curvature tensor consistent with axial symmetry is

$$K_{ab} = \ell_a \ell_b K_\ell + (\gamma_{ab} - \ell_a \ell_b) K_R, \quad (13)$$

where the scalars K_ℓ and K_R are the two principal curvatures, and ℓ^a is the outward pointing unit normal to the circle of fixed ℓ , $\ell^a = (1, 0)$. We identify the scalar curvature $\mathcal{R} = 2 \det K = 2K_\ell K_R$, and $K = K_\ell + K_R$. Now let θ be the angle that the tangent to a curve of fixed φ makes with the positive x axis. The principal curvatures are then given by

$$K_\ell = \theta', \quad K_R = \frac{\sin \theta}{R}. \quad (14)$$

The prime denotes a derivative with respect to ℓ . We have for the integrated mean curvature

$$M = 2\pi \int d\ell R \left(\theta' + \frac{\sin \theta}{R} \right). \quad (15)$$

Suppose that θ suffers a discontinuity Θ on the circle at $\ell = \ell_0$, so that $\theta(\ell) \approx \Theta H(\ell - \ell_0)$, where H is the step function. There is a finite contribution from this circle given by

$$\int_C dA K = 2\pi \int_{\ell_0 - \epsilon}^{\ell_0 + \epsilon} d\ell \theta' R = 2\pi R(\ell_0) \Theta. \quad (16)$$

The mean curvature is thus integrable across the discontinuity. In general we have the decomposition

$$M = \int_{\text{drop}/C} dA K - \int_C ds \arccos(\mathbf{l} \cdot \tilde{\mathbf{z}}) \quad (17)$$

with $\cos \Theta = -\mathbf{l} \cdot \tilde{\mathbf{z}}$, and where the notation for the normals is that introduced in Sec. II.

We note that the Gauss-Bonnet invariant for a vesicle of spherical topology can likewise be decomposed

$$\int_{\text{drop}/C} dA \mathcal{R} + 2 \int_C ds \Delta \kappa = 8\pi, \quad (18)$$

where $\Delta \kappa = \tilde{\kappa} - \kappa_{\text{free}}$ is the discontinuity in the geodesic curvature of C . For an axially symmetric vesicle, the value of the latter term is $2\pi \cos \Theta$. (An analogous decomposition of the Hilbert-Einstein action arises in the study of the dynamics of thin shells in general relativity [24].) As long as the adhering vesicle remains intact, the Gauss-Bonnet invariant will not play a role in adhesion. Though each of the two components appearing in Eq. (18) will behave nontrivially under deformation of the surface, their sum will not change.

The geometric invariant K^2 does possess a singularity at a curvature discontinuity. We note that this singularity is identical to that arising from the alternative quadratic invariant, $K_{ab}K^{ab}$. This is because the Gauss-Codazzi equation, $\mathcal{R} = K^2 - K_{ab}K^{ab}$, identifies their difference as the scalar curvature \mathcal{R} that according to Eq. (18) picks up a finite contribution at a discontinuity. In an axially symmetric geometry the troublesome term in the bending energy is θ'^2

$$\int dA K^2 \approx 2\pi \int d\ell R \theta'^2 + \dots \quad (19)$$

The θ'^2 term appearing in the integrand gives rise to a δ function squared singularity across the boundary. To eliminate the corresponding divergence in the energy, we *do* require $\Theta = 0$. The surface must be differentiable across C . It is straightforward to bootstrap this axially symmetric analysis to the general case by introducing Gaussian normal coordinates adapted to the boundary. In general, we require that $\Theta = 0$ or $\tilde{\mathbf{z}} = -\mathbf{l}$.

B. Strong bonding limit

Before addressing the full problem, let us consider the strong bonding limit, $\alpha \ll wA$. At lowest order the bending energy F_b is ignored in Eq. (12), and the variational problem reduces to the minimization of the contact energy subject to the three constraints. (In this section, we will use the language appropriate to the bilayer couple model.) Whereas Θ necessarily vanishes on the contact boundary for the Helfrich Hamiltonian, it need not vanish in this limit.

Let us first consider the variational problem on the free surface of the vesicle. Under a tangential deformation of this surface any scalar function \mathcal{F} , and in particular, $\mathcal{F} = \mu + \beta K$, transforms as a divergence that is transferred to the boundary,

$$\delta_{\parallel} \int_{\text{free}} dA \mathcal{F} = \int_C ds l_a \Phi^a \mathcal{F}. \quad (20)$$

This is because $\delta_{\parallel} \mathcal{F} = \Phi^a \partial_a \mathcal{F}$. The details of \mathcal{F} are irrelevant. Since Φ_a is constrained to lie tangent to the contact region, from Eq. (5), with $\mathcal{F} = \mu + \beta K$, we have then

$$\delta_{\parallel} \int_{\text{free}} dA (\mu + \beta K) = \int_C ds (\mu + \beta K) \mathbf{l} \cdot \tilde{\mathbf{z}} \Phi_0. \quad (21)$$

Note that this expression reduces to Eq. (6) when $\mu = 1, \beta = 0$.

We now examine a normal deformation of the free surface. The Euler-Lagrange equation that determines the local vesicle equilibrium shape is obtained by demanding that the energy be stationary with respect to normal deformations of the free surface. Its derivation within the present framework has been discussed in detail elsewhere [22]. Let us focus on the normal deformation of the new ingredient with respect to the model discussed in Sec. II appearing in Eq. (12), which is M . We consider the contributions from the free surface, C and the contact region as given by Eq. (17) separately. We begin with M_{free} . We have

$$\delta_{\perp} M_{\text{free}} = \int_{\text{free}} dA \mathcal{R} \Phi - \int_C ds \nabla_{\perp} \Phi. \quad (22)$$

We have used $\delta_{\perp} K = -\nabla^2 \Phi - K^{ab} K_{ab} \Phi$, as well as the Gauss-Codazzi equation, and $\nabla_{\perp} = l^a \nabla_a$ denotes the derivative along \mathbf{l} . It is now straightforward to read off the bulk Euler-Lagrange equation,

$$\mu K + \beta \mathcal{R} = p. \quad (23)$$

Note that this equation is second order in derivatives.

To proceed with the determination of the boundary conditions, we need to identify the independent unconstrained variation at the interface. We identify these as $\Phi_0 = \tilde{\mathbf{z}} \cdot \delta \mathbf{X}$ and its derivative along $\tilde{\mathbf{z}}$, $\tilde{\nabla}_{\perp} \Phi_0$. We will, however, continue to use $\nabla_{\perp} \Phi_0$ to denote $\mathbf{l} \cdot \tilde{\mathbf{z}} \tilde{\nabla}_{\perp} \Phi_0$. We note that the normal deformation at the boundary, using Eq. (5) is

$$\Phi = \mathbf{n} \cdot \delta \mathbf{X} = \mathbf{n} \cdot \tilde{\mathbf{z}} \Phi_0, \quad (24)$$

and on the boundary C , its normal derivative is

$$\begin{aligned} \nabla_{\perp} \Phi &= \nabla_{\perp} (\mathbf{n} \cdot \tilde{\mathbf{z}} \Phi_0) \\ &= (\mathbf{n} \cdot \tilde{\mathbf{z}}) \nabla_{\perp} \Phi_0 + \Phi_0 \tilde{\mathbf{z}} \cdot \nabla_{\perp} \mathbf{n} + \Phi_0 \mathbf{n} \cdot \nabla_{\perp} \tilde{\mathbf{z}} \\ &= (\mathbf{n} \cdot \tilde{\mathbf{z}}) \nabla_{\perp} \Phi_0 + (\mathbf{l} \cdot \tilde{\mathbf{z}}) [K_{\perp} + (\mathbf{l} \cdot \tilde{\mathbf{z}}) \tilde{K}_{\perp}] \Phi_0, \end{aligned} \quad (25)$$

where we have defined $K_{\perp} = K^{ab} l^a l^b$, and $\tilde{K}_{\perp} = \tilde{K}_{ab} \tilde{z}^a \tilde{z}^b$. We have used the fact that $\mathbf{n} \cdot \nabla_{\perp} \tilde{\mathbf{z}} = (\mathbf{l} \cdot \tilde{\mathbf{z}})^2 K_{\perp}$ as well as $\nabla_{\perp} \mathbf{n} = l^a K_a^b \mathbf{e}_b$. Therefore the boundary contribution of Eq. (22) takes the form

$$\delta_{\perp} M_{\text{free}} = - \int_C ds \{ (\mathbf{n} \cdot \tilde{\mathbf{z}}) \nabla_{\perp} \Phi_0 + (\mathbf{l} \cdot \tilde{\mathbf{z}}) [K_{\perp} + (\mathbf{l} \cdot \tilde{\mathbf{z}}) \tilde{K}_{\perp}] \Phi_0 \}. \quad (26)$$

For the boundary contribution M_C , we have

$$\delta_X M_C = \int_C ds [\Theta \tilde{\kappa} \Phi_0 + \delta_X \Theta]. \quad (27)$$

We emphasize that this term contributes *only* to the strong bonding limit. The first term comes from the variation of arclength: $\delta_X ds = \tilde{\kappa} \Phi_0$. We now exploit the fact that $\cos \Theta$

$= -\mathbf{l} \cdot \tilde{\mathbf{z}}$ to express $\delta_X \Theta$ in terms of $\delta_X(\mathbf{l} \cdot \tilde{\mathbf{z}})$; to evaluate the latter we note that $\delta_X \Theta = (\sin \Theta)^{-1} \delta_X(\mathbf{l} \cdot \tilde{\mathbf{z}})$, and that

$$\delta_X(\mathbf{l} \cdot \tilde{\mathbf{z}}) = (\delta_X \mathbf{l}) \cdot \tilde{\mathbf{z}} = \mathbf{n} \cdot \tilde{\mathbf{z}} (\mathbf{n} \cdot \delta_X \mathbf{l}). \quad (28)$$

In general, we have for the tangent vectors to the free surface,

$$\mathbf{n} \cdot \delta_X \mathbf{e}_a = \nabla_a \Phi - K_{ab} \Phi^b, \quad (29)$$

so that

$$(\delta_X \mathbf{l}) \cdot \tilde{\mathbf{z}} = (\nabla_{\perp} \Phi - (\mathbf{l} \cdot \tilde{\mathbf{z}}) K_{\perp} \Phi_0) \mathbf{n} \cdot \tilde{\mathbf{z}}. \quad (30)$$

Note that $\delta_X M_C$ need not vanish even when M_C itself does.

Finally, the induced change in M on the contact region due to the displacement of C is just

$$\delta_X M_{\text{contact}} = \int_C ds \tilde{K} \Phi_0. \quad (31)$$

It is now straightforward to read off the boundary condition by equating the coefficient of Φ_0 for the corresponding expression for F to zero:

$$(\mathbf{l} \cdot \tilde{\mathbf{z}})(\mu + \beta K_{\parallel}) + (\mu - w) + \beta \tilde{K} + \beta \Theta \tilde{\kappa} = 0. \quad (32)$$

We have used the fact that K can be expressed as $K = K_{\parallel} + K_{\perp}$, where $K_{\parallel} = K_{ab} t^a t^b$ is the projection of K_{ab} onto the unit tangent to C , t^a . In general, some simplification is possible by using the identity

$$K_{\parallel} = \mathbf{n} \cdot \dot{\mathbf{t}} = \cos \Theta \tilde{K}_{\parallel} + \sin \Theta \tilde{\kappa}. \quad (33)$$

In particular, for axially symmetric geometries, we note that $K_{\parallel} = K_R$ is consistent with $\tilde{K}_{\parallel} = \sin \Psi / R$, and $\tilde{\kappa} = \cos \Psi / R$, with the identification $\theta = \Psi + \Theta$.

Note that Eq. (32) is consistent with Ref. [16] where an axially symmetric (indeed, spherical) vesicle adhering to a flat substrate ($\tilde{K} = 0$) is described.

IV. NO APPROXIMATIONS

We now examine the general case, as given by the energy (12), including the bending energy F_b . As discussed in Sec. III A, in order to avoid discontinuities at the boundary we impose $\Theta = 0$ or $\mathbf{l} \cdot \tilde{\mathbf{z}} = -1$ as a constraint.

For the tangential deformation of F_b , from Eq. (20), and using $\tilde{\mathbf{z}} \cdot \mathbf{l} = -1$, we have immediately

$$\delta_{\parallel} F_b = -\alpha \int_C ds K^2 \Phi_0. \quad (34)$$

The novel nontrivial boundary term associated with the normal deformation of the free surface originates in the term

$$2\alpha \int_{\text{free}} dA K \gamma^{ab} \delta_{\perp} K_{ab} \quad (35)$$

contributing from the variation of F_b free. Modulo the free bulk shape equation (described in Ref. [22]), there remains

$$\delta_{\perp} F_b \text{ free} = 2\alpha \int_C ds (\Phi \nabla_{\perp} K - K \nabla_{\perp} \Phi). \quad (36)$$

We note that $\Phi = \mathbf{n} \cdot \tilde{\mathbf{z}} \Phi_0 = 0$, so that the first term vanishes. For the second term, on C , Eq. (25) gives $\nabla_{\perp} \Phi = (\tilde{K}_{\perp} - K_{\perp}) \Phi_0$, so that the novel contribution is

$$\delta_{\perp} F_b \text{ free} = 2\alpha \int_C ds K (K_{\perp} - \tilde{K}_{\perp}) \Phi_0. \quad (37)$$

It is now straightforward to read off the boundary condition (there is no term proportional to $\nabla_{\perp} \Phi_0$)

$$-\alpha K^2 - \beta K_{\parallel} + \alpha \tilde{K}^2 + \beta K_{\parallel} + 2\alpha (K_{\perp} - \tilde{K}_{\perp}) K = w. \quad (38)$$

If we now use the fact that $K_{\parallel} - \tilde{K}_{\parallel} = 0$ when $\Theta = 0$, Eq. (38) reduces to the remarkably simple expression

$$K_{\perp} - \tilde{K}_{\perp} = \sqrt{w/\alpha}. \quad (39)$$

This expression is independent of β .

The curvature K_{\perp} is completely fixed at the boundary by Eq. (39). We note that the off-diagonal term with respect to the basis l^a and t^a , $K_{\perp\perp} = l^a t^b K_{ab} = \mathbf{n} \cdot \dot{\mathbf{l}}$ will not generally be zero. Just like K_{\parallel} , however, it will be completely determined by its substrate counterpart, $K_{\perp\perp} = \tilde{K}_{\perp\perp}$. Thus, all three components of the curvature are fixed at the boundary.

If the substrate is flat at the boundary, we have $K_{\perp} = \sqrt{w/\alpha}$. For an axially symmetric shape, $K_{\perp} = K_{\ell} = \theta'$ and Eq. (39) therefore reproduces the well known boundary condition [11],

$$\theta' = \sqrt{w/\alpha}. \quad (40)$$

We note that if the substrate is axially symmetric and not flat, Eq. (40) is modified to

$$\theta' - \Psi' = \sqrt{w/\alpha}, \quad (41)$$

where Ψ' is the curvature along a meridian of the substrate. This agrees with the expression given in footnote 14 of [11].

V. STRESSES AT THE BOUNDARY

In equilibrium, the forces directed along the normal from the boundary into the membrane must balance. In Ref. [22], it is shown that the stress tensor for the model (12) can be expressed as

$$\mathbf{f}^a = [\alpha K (K^{ab} - K \gamma^{ab}) + \beta (K^{ab} - K \gamma^{ab}) - \mu \gamma^{ab}] \mathbf{e}_b - 2\alpha \nabla^a K \mathbf{n}. \quad (42)$$

This is the stress tensor on the free surface. It satisfies

$$\nabla_a \mathbf{f}^a = p \mathbf{n} \quad (43)$$

at each point.

Let us for simplicity suppose that the substrate is flat, so that $\tilde{K}_{ab} = 0$. The corresponding stress tensor in that part of the vesicle which is bound to the substrate $\tilde{\mathbf{f}}^a$ is then

$$\tilde{\mathbf{f}}^a = (w - \mu) \tilde{\gamma}^{ab} \tilde{\mathbf{e}}_b, \quad (44)$$

which is isotropic. Note that $\mathbf{f}_{\text{contact}}$ does not satisfy the conservation law Eq. (43). Thus the construction of a Gaussian pillbox of infinitesimal thickness on the boundary does not lead to a useful identity. We note, however, that $\mathbf{l} \cdot \mathbf{f}^a l_a$ is the pressure acting on the boundary due to unbalanced stresses in the free bulk at its boundary. We have

$$\mathbf{l} \cdot \mathbf{f}^a l_a = \alpha K (2K_{\perp} - K) - \beta K_{\parallel} - \mu. \quad (45)$$

Similarly,

$$\tilde{\mathbf{z}} \cdot \tilde{\mathbf{f}}^a \tilde{z}_a = w - \mu. \quad (46)$$

The stresses must balance in equilibrium. When they do, Eq. (39) is reproduced. This derivation is not only more efficient than the variational argument, it also homes in immediately on the physics at the boundary.

VI. CONCLUSIONS

We have shown how a combination of simple geometrical and variational techniques as well as conservation laws can be applied to study the adhesion of vesicles described by a

geometrical Hamiltonian. This provides a useful platform for either a numerical or perturbative approach to adhesion, particularly when one is interested in nonaxially symmetric shapes. Axially symmetric shapes are very special ones.

These techniques also generalize to so-called floppy or egg-carton membranes where a term penalizing curvature gradients also appears in the Hamiltonian [12,25]. Now, not only is the contact angle fixed, but its first derivative vanishes. It is the second derivative that will be proportional to the bond strength. The interesting shapes are also certainly not axially symmetric.

Note added in proof. Recently, Ref. [26] was brought to our attention, where the adhesion of “linear” vesicles in two dimensions is considered.

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