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SHORT COMMUNICATION

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Asymmetric lipid bilayers from the perspective of three-dimensional liquid crystal theory

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Abstract The classical theory for asymmetric lipid bilayer surfaces is revisited from the vantage point of three-dimensional liquid crystal theory. Independent tangential motions of the leaflets comprising the bilayer are accommodated in a framework that allows for distinct leaflet properties.

Keywords Lipid bilayers · Asymmetry · Spontaneous curvature

1 Introduction

Our purpose in this brief exposition is to present a modern account of the classical theory of asymmetric lipid bilayers in which asymmetry, i.e., the absence of reflection symmetry with respect to the bilayer surface normal, is conferred by a property called the *spontaneous curvature* [1,2]. Following the seminal work of Helfrich [1], we interpret bilayers as liquid crystal films, but here we derive the associated surface theory via asymptotic expansion of three-dimensional liquid crystal theory, with film thickness—on the order of molecular dimensions—playing the role of the small parameter. In accordance with the observed phenomenology, we allow for the possibility that the two monolayer leaflets constituting the bilayer undergo relative motion in the tangent plane to the surface to which they remain congruent. Though attention is confined here to the purely mechanical theory, our formulation provides a framework in which a number of physical effects can be modeled systematically.

Our motivation derives from renewed interest in asymmetric bilayers on the part of the biophysics community. For example, it has recently been demonstrated that inner (cytoplasmic) leaflets are significantly less saturated than their outer (exoplasmic) counterparts [3]. Atomistic studies indicate that this asymmetry is correlated with higher packing of lipids and inhibited diffusivity in the exoplasmic leaflet [4]. Negatively charged lipids are also present in higher concentrations in the inner leaflet. Asymmetry is thought to affect the interactions between lipids and embedded transmembrane proteins, and is known to play a key role in regulating cellular signaling, cell death and cell-to-cell interactions [5].

In Sect. 2, we present an asymptotic derivation of the two-dimensional energy of a thin film from three-dimensional energies modeling the two leaflets of the bilayer as nematic liquid crystals having distinct properties. This is made explicit, in Sect. 3, for polar nematics described by energies of the Frank type [6,7]. Following a brief survey of the relevant differential geometry of surfaces in Sect. 4, in Sect. 5 we derive the differential

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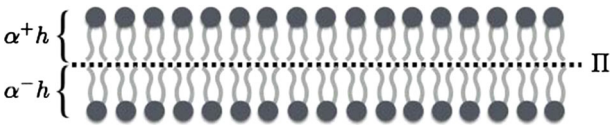

Fig. 1 Bilayer patch in reference configuration

equations of mechanical equilibrium as consequences of a virtual power postulate. The same postulate delivers formulae, derived in Sect. 6, for the edge interactions of a bilayer patch with its surroundings.

2 Leading-order asymptotic energy for small thickness

Consider a local patch of the bilayer in the shape of a prismatic cylinder generated by the parallel translation of a plane region Π forming the interface between the two leaflets of the bilayer. We adopt this patch as a local reference configuration in preparation for a variational treatment based on the notion of patchwise virtual-power introduced by Eugster and dell'Isola [8–10] and Eugster and Glocker [11]. The lipids of the bilayer are presumed to be straight, parallel and of uniform length in this configuration. The upper and lower leaflets have thicknesses $\alpha^\pm h$, where h is the thickness of the cylinder and

$$\alpha^+ + \alpha^- = 1. \tag{1}$$

The energy of the cylinder is

$$\mathcal{E} = \int_\Pi \mathcal{U}\,\mathrm{d}A, \tag{2}$$

where

$$\mathcal{U} = \int_0^{\alpha^+ h} \mathcal{U}^+\,\mathrm{d}\varsigma + \int_{-\alpha^- h}^0 \mathcal{U}^-\,\mathrm{d}\varsigma, \tag{3}$$

in which $\mathcal{U}^\pm$ are the volumetric energy densities of the upper and lower leaflets and ς is a through-thickness coordinate (Fig. 1).

We suppose the thickness h to be much smaller than the next smallest length scale, l say, in the system. If the latter is used as the unit of length ($l = 1$), then the dimensionless thickness $h \ll 1$. Regarding $\mathcal{U}$ as a function of h, we use Leibniz' Rule together with a Taylor expansion to derive

$$\mathcal{U} = hU + o(h), \quad \text{with} \quad U = \alpha^+ U^+ + \alpha^- U^-, \tag{4}$$

in which $U^\pm$, respectively, are the values of $\mathcal{U}^\pm$ at $\varsigma = 0$, i.e., at the interface Π. Accordingly,

$$\mathcal{E}/h = E + o(h)/h, \quad \text{where} \quad E = \int_\Pi U\,\mathrm{d}A \tag{5}$$

is the leading-order energy for small h.

Following [1], we model the leaflets of the bilayer as nematic liquid crystals with energy densities

$$\mathcal{U}^\pm = \mathcal{W}^\pm(\tilde{\mathbf{n}}^\pm,\, \tilde{\mathbf{D}}^\pm), \tag{6}$$

where $\tilde{\mathbf{n}}^\pm$ are fields of unit vectors specifying the local molecular orientation and $\tilde{\mathbf{D}}^\pm = \operatorname{grad}\tilde{\mathbf{n}}^\pm$ are their (spatial) gradients. It is customary [7] to specify a constitutive function for the energy per unit current volume and to regard the liquid crystal as an incompressible medium. Then, $\mathcal{U}^\pm$ are also the energies per unit reference volume, as assumed in the foregoing, and

$$U^\pm = \mathcal{W}^\pm(\mathbf{n}^\pm, \mathbf{D}^\pm), \tag{7}$$

where $\mathbf{n}^\pm$ and $\mathbf{D}^\pm$ are the restrictions to the interface of $\tilde{\mathbf{n}}^\pm$ and $\tilde{\mathbf{D}}^\pm$, respectively.

Here, as in [1], we suppress lipid *tilt* and thus take $\mathbf{n}^\pm$ to be the unit-normal fields to the images $\pi^\pm$ of the interface Π in the current configurations of the leaves of the bilayer. Because these are assumed to remain

congruent, they are subsets of a single surface ω and accordingly share a common unit-normal field $\mathbf{n}$. Thus, $\mathbf{n}^{\pm} = \mathbf{n}$ and [12]

$$\mathbf{D}^{\pm} = \nabla_s \mathbf{n} + \boldsymbol{\eta}^{\pm} \otimes \mathbf{n}, \tag{8}$$

where $\nabla_s(\cdot)$ is the surficial gradient on ω and $\boldsymbol{\eta}^{\pm}$, respectively, are the restrictions to ω of the derivatives of $\tilde{\mathbf{n}}^{\pm}$ in the directions of $\tilde{\mathbf{n}}^{\pm}$. These represent the curvatures of the trajectories aligned locally with the directions $\tilde{\mathbf{n}}^{\pm}$ of the lipid molecules. Because the latter are fields of unit vectors, we require $\mathbf{n} \cdot \boldsymbol{\eta}^{\pm} = 0$ and conclude that $\boldsymbol{\eta}^{\pm}$ are tangential vector fields on ω.

The Gauss and Weingarten equations of differential geometry furnish

$$\nabla_s \mathbf{n} = -\mathbf{b}, \tag{9}$$

where $\mathbf{b}$ is the symmetric curvature 2-tensor on the local tangent planes of ω. The energy density of the bilayer is thus given by the function

$$U(\mathbf{b}, \mathbf{n}, \boldsymbol{\eta}^{\pm}) = \alpha^{+} U^{+}(\mathbf{b}, \mathbf{n}, \boldsymbol{\eta}^{+}) + \alpha^{-} U^{-}(\mathbf{b}, \mathbf{n}, \boldsymbol{\eta}^{-}), \tag{10}$$

where

$$U^{\pm}(\mathbf{b}, \mathbf{n}, \boldsymbol{\eta}^{\pm}) = \mathcal{W}^{\pm}(\mathbf{n}, -\mathbf{b} + \boldsymbol{\eta}^{\pm} \otimes \mathbf{n}). \tag{11}$$

3 Liquid crystal energies

3.1 The Frank energy for nematics

We model both leaflets of the bilayer as nematic liquid crystals. Unlike the molecules of conventional nematics, lipid molecules are polar. Accordingly, the orientation of the director field $\tilde{\mathbf{n}}$ is physically significant, i.e., the energy is *not* invariant under $\tilde{\mathbf{n}} \to -\tilde{\mathbf{n}}$. The most general quadratic energy that takes this into account is [7, Eq. (3.36)]

$$\begin{aligned}\mathcal{W}(\tilde{\mathbf{n}},\ \tilde{D}) = {} & k_1 (tr\tilde{\mathbf{D}})^2 + k_2 (\mathbf{W}(\tilde{\mathbf{n}}) \cdot \tilde{\mathbf{D}})^2 + k_3 \left|\tilde{\mathbf{D}}\tilde{\mathbf{n}}\right|^2 + (k_2 + k_4)[\mathrm{tr}(\tilde{\mathbf{D}}^2) - (tr\tilde{\mathbf{D}})^2] \\ & + a_0 + (a_1 + a_2 \mathbf{W}(\tilde{\mathbf{n}}) \cdot \tilde{\mathbf{D}}) tr\tilde{\mathbf{D}} + a_3 \mathbf{W}(\tilde{\mathbf{n}}) \cdot \tilde{\mathbf{D}}.\end{aligned} \tag{12}$$

where k_{1-4} are constants satisfying Ericksen's inequalities

$$2k_1 \geq k_2 + k_4, \quad k_2 \geq |k_4| \quad \text{and} \quad k_3 \geq 0, \tag{13}$$

in accordance with the assumed convexity of $\mathcal{W}(\tilde{\mathbf{n}}, \cdot)$, and $\mathbf{W}(\tilde{\mathbf{n}})$ is the skew tensor with axial vector $\tilde{\mathbf{n}}$, i.e., $\mathbf{W}(\tilde{\mathbf{n}})\mathbf{v} = \tilde{\mathbf{n}} \times \mathbf{v}$ for all $\mathbf{v}$.

Frank's energy [7, Eq. (3.63)], obtained by suppressing $a_{0,1,2,3}$, pertains to conventional nonpolar nematics.

3.2 Restriction to the interface

A central aspect of the present model is that Π convects as a material surface with the two leaflets of the bilayer in such a way as to maintain congruency; that is, the (possibly distinct) images $\pi^{\pm}$ of Π under the individual leaflet deformations are subsets of a single surface ω. This assumption is justified by the hydrophobicity of the tail groups of the lipids, which acts to shield them from the surrounding aqueous solution and thereby promotes congruency. Here, we assume that ω can be covered completely by the images of such patches, each of which is assumed, for the sake of notational convenience, to be parametrized by a single coordinate chart.

The interfacial energy is the restriction to ω of (12). To derive it, we use (8) and (9) to obtain

$$\mathbf{W}(\mathbf{n}) \cdot \mathbf{D} = \boldsymbol{\eta} \cdot \mathbf{W}(\mathbf{n})\mathbf{n} - \mathbf{W}(\mathbf{n}) \cdot \mathbf{b} = 0, \tag{14}$$

which follows from the symmetry of $\mathbf{b}$, together with

$$\mathrm{tr}\mathbf{D} = -2H, \quad \text{where} \quad H = \tfrac{1}{2} tr\mathbf{b} \tag{15}$$

is the mean curvature of ω. Combining

$$\mathbf{D}^2 = \mathbf{b}^2 - \mathbf{b}\boldsymbol{\eta} \otimes \mathbf{n} \tag{16}$$

with the Cayley–Hamilton formula

$$\mathbf{b}^2 = 2H\mathbf{b} - K\mathbf{1}, \quad \text{where} \quad K = \det \mathbf{b} \tag{17}$$

is the Gaussian curvature of ω and $\mathbf{1} = \mathbf{I} - \mathbf{n} \otimes \mathbf{n}$ is the (two-dimensional) identity on its local tangent plane, we arrive at

$$\operatorname{tr}(\mathbf{D}^2) = \operatorname{tr}(\mathbf{b}^2) = 4H^2 - 2K. \tag{18}$$

Using $\mathbf{Dn} = \boldsymbol{\eta}$, the restriction of the energy to the interface is found to be

$$U(\mathbf{n}, \mathbf{b}, \boldsymbol{\eta}) = \gamma + \beta H + kH^2 + \bar{k}K + k_3 |\boldsymbol{\eta}|^2, \tag{19}$$

where

$$\gamma = a_0, \quad \beta = -2a_1, \quad k = 4k_1 \quad \text{and} \quad \bar{k} = -2(k_2 + k_4). \tag{20}$$

With reference to (5), (7) and (10), the net leading-order composite energy is

$$E = \int_\Pi W \, \mathrm{d}A, \tag{21}$$

where

$$W(H, K, \boldsymbol{\eta}^\pm) = \alpha^+ W^+(H, K, \boldsymbol{\eta}^+) + \alpha^- W^-(H, K, \boldsymbol{\eta}^-), \tag{22}$$

with $W^\pm(H, K, \boldsymbol{\eta}^\pm) = U^\pm(\mathbf{n}, \mathbf{b}, \boldsymbol{\eta}^\pm)$, i.e.,

$$W^\pm(H, K, \boldsymbol{\eta}^\pm) = \gamma^\pm + \beta^\pm H + k^\pm H^2 + \bar{k}^\pm K + k_3^\pm \left|\boldsymbol{\eta}^\pm\right|^2. \tag{23}$$

Accordingly,

$$W(H, K, \boldsymbol{\eta}^\pm) = \gamma + \beta H + kH^2 + \bar{k}K + \alpha^+ k_3^+ \left|\boldsymbol{\eta}^+\right|^2 + \alpha^- k_3^- \left|\boldsymbol{\eta}^-\right|^2, \tag{24}$$

where

$$\gamma = \alpha^+\gamma^+ + \alpha^-\gamma^-, \quad \beta = \alpha^+\beta^+ + \alpha^-\beta^-, \quad k = \alpha^+ k^+ + \alpha^- k^- \quad \text{and} \quad \bar{k} = \alpha^+\bar{k}^+ + \alpha^-\bar{k}^-. \tag{25}$$

We adopt the conventional assumption that deformations of the bilayer conserve interfacial area. This is assumed for each leaflet of the bilayer. It is justified by bulk incompressibility in the parent theory of liquid crystals and by the suppression of lipid tilt [12]; inextensibility of the lipids then implies areal incompressibility. The referential areal energy density W is then also the areal density in the current configuration of the system in the sense that

$$E = \alpha^+ E^+ + \alpha^- E^-, \quad \text{where} \quad E^\pm = \int_{\pi^\pm} W^\pm \, \mathrm{d}a \tag{26}$$

and $\pi^\pm \subset \omega$ are the images of Π under the deformations of the upper and lower leaflets of the bilayer, respectively.

4 Differential geometry

4.1 Elementary surface geometry

A typical configuration of the leaflet interface occupies a surface ω with position field $\mathbf{r}(\theta^\alpha)$ in which θ^α; $\alpha = 1, 2$, are surface coordinates. This surface parametrization induces the tangent basis $\{\mathbf{a}_\alpha\}$, where $\mathbf{a}_\alpha = \mathbf{r}_{,\alpha}$; the (invertible) surface metric $a_{\alpha\beta} = \mathbf{a}_\alpha \cdot \mathbf{a}_\beta$; the dual metric $a^{\alpha\beta}$, where $(a^{\alpha\beta}) = (a_{\alpha\beta})^{-1}$; and the dual tangent basis $\{\mathbf{a}^\alpha\}$, with $\mathbf{a}^\alpha = a^{\alpha\beta}\mathbf{a}_\beta$. The orientation of ω is identified with the unit-normal field $\mathbf{n}$ defined by $\varepsilon_{\alpha\beta}\mathbf{n} = \mathbf{a}_\alpha \times \mathbf{a}_\beta$, where $\varepsilon_{\alpha\beta} = \sqrt{a}e_{\alpha\beta}$, with $a = \det(a_{\alpha\beta})$, is the Levi–Civita alternating tensor and $e_{\alpha\beta}$ is the permutation symbol ($e_{12} = -e_{21} = 1$, $e_{11} = e_{22} = 0$).

A primary role is played by the Gauss and Weingarten equations [13,14]

$$\mathbf{r}_{;\alpha\beta} = b_{\alpha\beta}\mathbf{n} \quad \text{and} \quad \mathbf{n}_{,\alpha} = -b_{\alpha\beta}\mathbf{a}^\beta, \tag{27}$$

respectively, where

$$\mathbf{r}_{;\alpha\beta} = \mathbf{r}_{,\alpha\beta} - \Gamma^\lambda_{\alpha\beta}\mathbf{r}_{,\lambda} \tag{28}$$

is the second covariant derivative of the surface position field. Here, $\Gamma^\lambda_{\alpha\beta}$ are the Levi–Civita connection coefficients and $b_{\alpha\beta}$ are the coefficients of the second fundamental form on ω; these are symmetric with respect to interchange of the subscripts, and the latter induce the curvature tensor

$$\mathbf{b} = b_{\alpha\beta}\mathbf{a}^\alpha \otimes \mathbf{a}^\beta. \tag{29}$$

The surficial gradient of the field $\mathbf{n}$ is $\nabla_s\mathbf{n} = \mathbf{n}_{,\alpha} \otimes \mathbf{a}^\alpha$, in accordance with (9) and $(27)_2$. Here, the connection coefficients are simply the Christoffel symbols and the connection is therefore metric compatible, i.e., the covariant derivatives of the metric components vanish.

The mean and Gaussian curvatures of ω are [see $(15)_2$ and $(17)_2$]

$$H = \frac{1}{2}a^{\alpha\beta}b_{\alpha\beta}, \quad K = \frac{1}{2}\varepsilon^{\alpha\beta}\varepsilon^{\lambda\mu}b_{\alpha\lambda}b_{\beta\mu}, \tag{30}$$

respectively, where $\varepsilon^{\alpha\beta} = e^{\alpha\beta}/\sqrt{a}$, with $e^{\alpha\beta} = e_{\alpha\beta}$, is the contravariant alternator, and we note the relation

$$b^\beta_\mu \tilde{b}^{\mu\alpha} = K a^{\beta\alpha}, \tag{31}$$

where $b^\beta_\mu = a^{\beta\alpha}b_{\alpha\mu}$ and

$$\tilde{b}^{\alpha\beta} = \varepsilon^{\alpha\lambda}\varepsilon^{\beta\mu}b_{\lambda\mu} \tag{32}$$

is the cofactor of the curvature, expressible as

$$\tilde{b}^{\alpha\beta} = 2Ha^{\alpha\beta} - b^{\alpha\beta} \tag{33}$$

via the identity

$$\varepsilon^{\alpha\lambda}\varepsilon^{\beta\mu} = a^{\alpha\beta}a^{\lambda\mu} - a^{\alpha\mu}a^{\beta\lambda}. \tag{34}$$

The Mainardi–Codazzi equations of surface theory are $b_{\lambda\mu;\beta} = b_{\lambda\beta;\mu}$ [14], or, more concisely, $\varepsilon^{\beta\mu}b_{\lambda\mu;\beta} = 0$. The metric compatibility of the connection implies that the $\varepsilon^{\alpha\lambda}$ are covariant constants; the Mainardi–Codazzi equations are thus equivalent to

$$\tilde{b}^{\alpha\beta}_{;\beta} = 0. \tag{35}$$

4.2 Virtual velocity

The virtual velocity of a leaflet of the bilayer is of the form [12]

$$\dot{\mathbf{r}} = \mathbf{u} = u^\alpha \mathbf{a}_\alpha + w\mathbf{n}, \tag{36}$$

where u^α and w, respectively, are the tangential and normal virtual velocities. Here, we take the coordinates θ^α to be convected with the lipids. The superposed dot stands for $\frac{\partial}{\partial \epsilon}\mathbf{r}(\theta^\alpha;\epsilon)$, evaluated at $\epsilon = 0$, say, which we identify with an equilibrium state. The induced variation of the surface metric is

$$\dot{a}_{\lambda\mu} = \mathbf{u}_{,\lambda}\cdot\mathbf{a}_\mu + \mathbf{a}_\lambda\cdot\mathbf{u}_{,\mu}, \tag{37}$$

in which

$$\mathbf{u}_{,\lambda} = (u_{\alpha;\lambda} - wb_{\alpha\lambda})\mathbf{a}^\alpha + (u^\alpha b_{\alpha\lambda} + w_{,\lambda})\mathbf{n}, \tag{38}$$

by the Gauss and Weingarten equations, where $\mathbf{a}^\alpha = a^{\alpha\beta}\mathbf{a}_\beta$ and $u_{\alpha;\lambda}$ is the covariant derivative defined by

$$u_{\alpha;\lambda} = u_{\alpha,\lambda} - u_\beta \Gamma^\beta_{\alpha\lambda}. \tag{39}$$

Thus,

$$\dot{a}_{\lambda\mu} = u_{\mu;\lambda} + u_{\lambda;\mu} - 2wb_{\lambda\mu}. \tag{40}$$

If $A_{\alpha\beta}$ is the (fixed) metric on a reference surface Ω, then the areal stretch induced by the deformation is $J = \sqrt{a/A}$, where $A = \det(A_{\alpha\beta})$. The fact that the cofactor of $a_{\alpha\beta}$ is $(a)a^{\alpha\beta}$ then yields

$$\dot{J}/J = \frac{1}{2}a^{\alpha\beta}\dot{a}_{\alpha\beta}, \tag{41}$$

and with (37) this may be reduced to

$$\dot{J}/J = \mathbf{a}^\alpha\cdot\mathbf{u}_{,\alpha}. \tag{42}$$

The virtual velocities of the two leaflets of the bilayer at the point with coordinates θ^α on ω are given simply by

$$\dot{\mathbf{r}}^\pm = \mathbf{u}^\pm = u^\alpha_\pm \mathbf{a}_\alpha + w\mathbf{n}, \tag{43}$$

where $u^\alpha_\pm$ are the distinct tangential velocities of the leaflets and w, the normal velocity, is common to both leaflets. This ensures that congruency of the leaflets is maintained as the bilayer deforms.

5 Energy, virtual power and equilibrium

To obtain the equilibrium equations, we invoke the virtual-power principle for the simply connected patch Π. Areal incompressibility, i.e., $J^\pm = 1$, is accommodated by extending the energy to unconstrained states and introducing appropriate Lagrange-multiplier fields [15]. The extension of the energy (26) of the patch is

$$E = \alpha^+E^+ + \alpha^-E^-, \quad \text{where} \quad E^\pm = \int_\Pi [J^\pm W^\pm + \lambda^\pm(J^\pm - 1)]\,\mathrm{d}A + \int_{\partial\Pi}\tilde{\mu}^\pm(J^\pm - 1)\,\mathrm{d}S, \tag{44}$$

and $\lambda^\pm$ and $\tilde{\mu}^\pm$ are Lagrange multiplier fields. Multipliers on the boundary are included because the tangential and normal derivatives of the virtual bilayer velocities $\mathbf{u}^\pm$, which figure in the expression for the variation of the energy to be derived, are constrained by areal incompressibility.

Equilibria are defined to be those states that satisfy the virtual-power statement

$$\dot{E} = P, \tag{45}$$

where

$$P = \alpha^+P^+ + \alpha^-P^- \tag{46}$$

is the virtual power imparted to the patch, in which $P^\pm$ pertain to the individual leaflets, and

$$\dot{E} = \alpha^+ \dot{E}^+ + \alpha^- \dot{E}^-, \quad \text{with} \quad \dot{E}^\pm = \int_{\pi^\pm} [\dot{W}^\pm + (W^\pm + \lambda^\pm) \dot{J}^\pm / J^\pm] \, \mathrm{d}a + \int_{\partial\pi^\pm} \mu^\pm \dot{J}^\pm / J^\pm \, \mathrm{d}s, \quad (47)$$

where $\mu^\pm \, \mathrm{d}s = \tilde{\mu}^\pm J^\pm \, \mathrm{d}S$.

We note that variation of (44) with respect to the multipliers simply returns the constraints and is therefore not made explicit.

5.1 Variation with respect to $\boldsymbol{\eta}^\pm$

Setting $u_\pm^\alpha = 0$ and $w = 0$, we obtain the energy variation

$$\dot{E}/2 = \alpha^+ \int_{\pi^+} k_3^+ \boldsymbol{\eta}^+ \cdot \dot{\boldsymbol{\eta}}^+ da + \alpha^- \int_{\pi^-} k_3^- \boldsymbol{\eta}^- \cdot \dot{\boldsymbol{\eta}}^- da, \quad (48)$$

and conclude, as $\dot{\boldsymbol{\eta}}^\pm$ are arbitrary tangential vector fields, that $\boldsymbol{\eta}^+$ and $\boldsymbol{\eta}^-$ vanish if the virtual powers $P^\pm$ attending $\dot{\boldsymbol{\eta}}^\pm$ also vanish. Here we assume that $k_3^\pm > 0$ in accordance with the strict form of $(13)_3$. We thus base our further considerations on the leaflet energies

$$W^\pm(H, K) = \gamma^\pm + \beta^\pm H + k^\pm H^2 + \bar{k}^\pm K, \quad (49)$$

and bilayer energy

$$W(H, K) = \gamma + \beta H + k H^2 + \bar{k} K. \quad (50)$$

The identifications $\gamma = kC^2$ and $\beta = -2kC$, where C is a constant, reduce the latter to the classical Helfrich form [1,2]

$$W(H, K) = k(H - C)^2 + \bar{k} K \quad (51)$$

in which C is the so-called spontaneous curvature.

Minimum-energy considerations in the setting of conservative problems require that k, and hence γ, be nonnegative [16].

5.2 Variational derivatives of the leaflet energies

In this subsection, we derive formulae valid for arbitrary virtual velocities of a leaflet. We focus attention on a single leaflet and temporarily suppress the superscript $^\pm$.

Because J and W depend on the surface position field through its first and second derivatives with respect to the coordinates, there exist vector fields $\mathbf{N}^\alpha$ and $\mathbf{M}^{\alpha\beta}$ such that

$$\dot{W} + (W + \lambda)\dot{J}/J = \mathbf{N}^\alpha \cdot \mathbf{u}_{,\alpha} + \mathbf{M}^{\alpha\beta} \cdot \mathbf{u}_{;\alpha\beta}, \quad (52)$$

where $\mathbf{u} = \dot{\mathbf{r}}$ is the virtual velocity and $\mathbf{u}_{;\alpha\beta} = \mathbf{u}_{,\alpha\beta} - \Gamma^\lambda_{\alpha\beta} \mathbf{u}_{,\lambda}$ is the second covariant derivative of $\mathbf{u}$. This is symmetric in the subscripts, and thus, no generality is lost by imposing $\mathbf{M}^{\alpha\beta} = \mathbf{M}^{\beta\alpha}$.

For example [17],

$$\dot{H} = \tfrac{1}{2} a^{\alpha\beta} \mathbf{n} \cdot \mathbf{u}_{;\alpha\beta} - b^{\alpha\beta} \mathbf{a}_\beta \cdot \mathbf{u}_{,\alpha} \quad \text{and} \quad \dot{K} = \tilde{b}^{\alpha\beta} \mathbf{n} \cdot \mathbf{u}_{;\alpha\beta} - 2K \mathbf{a}^\alpha \cdot \mathbf{u}_{,\alpha}, \quad (53)$$

whereas [see (42)]

$$\dot{J}/J = \mathbf{a}^\alpha \cdot \mathbf{u}_{,\alpha}. \quad (54)$$

For either leaflet energy, it follows from (49) that

$$\dot{W} = (\beta + 2kH)\dot{H} + \bar{k}\dot{K}, \quad (55)$$

with the moduli, of course, pertaining to the considered leaflet, and hence that

$$\mathbf{N}^{\mu} = N^{\mu\beta}\mathbf{a}_{\beta}, \quad \mathbf{M}^{\mu\beta} = M^{\mu\beta}\mathbf{n}, \tag{56}$$

with

$$N^{\mu\beta} = (\lambda + \beta H + kH^2 - \bar{k}K)a^{\mu\beta} - (\beta + 2kH)b^{\mu\beta} \quad \text{and} \quad M^{\mu\beta} = \tfrac{1}{2}(\beta + 2kH)a^{\mu\beta} + \bar{k}\tilde{b}^{\mu\beta}, \tag{57}$$

in which the constant γ in W has been absorbed into the multiplier λ [cf. (49)].

We write the right-hand side of (52) as

$$\mathbf{N}^{\alpha}\cdot\mathbf{u}_{,\alpha} + \mathbf{M}^{\alpha\beta}\cdot\mathbf{u}_{;\alpha\beta} = \varphi^{\alpha}_{;\alpha} - \mathbf{u}\cdot\mathbf{T}^{\alpha}_{;\alpha}, \tag{58}$$

where

$$\mathbf{T}^{\alpha} = \mathbf{N}^{\alpha} - \mathbf{M}^{\alpha\beta}_{;\beta}, \tag{59}$$

with

$$\mathbf{M}^{\beta\alpha}_{;\beta} = M^{\beta\alpha}_{;\beta}\mathbf{n} - M^{\beta\alpha}b^{\mu}_{\beta}\mathbf{a}_{\mu}, \tag{60}$$

and

$$\varphi^{\alpha} = \mathbf{T}^{\alpha}\cdot\mathbf{u} + \mathbf{M}^{\alpha\beta}\cdot\mathbf{u}_{,\beta}, \tag{61}$$

in which [cf. $(27)_2$ and (56)]

$$\mathbf{T}^{\alpha} = (N^{\alpha\mu} + M^{\alpha\beta}b^{\mu}_{\beta})\mathbf{a}_{\mu} - M^{\alpha\beta}_{;\beta}\mathbf{n}. \tag{62}$$

Combining (52) and (58) with Stokes' theorem, we derive

$$\int_{\pi}[\dot{W} + (W+\lambda)\dot{J}/J]\,\mathrm{d}a = \int_{\partial\pi}\varphi^{\alpha}\nu_{\alpha}\,\mathrm{d}s - \int_{\pi}\mathbf{u}\cdot\mathbf{T}^{\alpha}_{;\alpha}\,\mathrm{d}a, \tag{63}$$

where $\boldsymbol{\nu} = \nu_{\alpha}\mathbf{a}^{\alpha}$ is the exterior unit normal to $\partial\pi$ and

$$\mathbf{u}\cdot\mathbf{T}^{\alpha}_{;\alpha} = u_{\mu}\mathbf{a}^{\mu}\cdot\mathbf{T}^{\alpha}_{;\alpha} + w\mathbf{n}\cdot\mathbf{T}^{\alpha}_{;\alpha}, \tag{64}$$

with

$$\mathbf{a}^{\mu}\cdot\mathbf{T}^{\alpha}_{;\alpha} = (N^{\alpha\mu} + M^{\alpha\beta}b^{\mu}_{\beta})_{;\alpha} + M^{\alpha\beta}_{;\beta}b^{\mu}_{\alpha} \tag{65}$$

and

$$\mathbf{n}\cdot\mathbf{T}^{\alpha}_{;\alpha} = (N^{\alpha\mu} + M^{\alpha\beta}b^{\mu}_{\beta})b_{\mu\alpha} - M^{\beta\alpha}_{;\beta\alpha}. \tag{66}$$

To reduce the first term on the right-hand side of (63), we use the normal-tangential decomposition [13]

$$\mathbf{u}_{,\beta} = \tau_{\beta}\mathbf{u}' + \nu_{\beta}\mathbf{u}_{\nu}, \tag{67}$$

where $\boldsymbol{\tau} = \mathbf{r}' = \tau_{\alpha}\mathbf{a}^{\alpha} = \mathbf{n}\times\boldsymbol{\nu}$ is the unit tangent to $\partial\pi$, $\mathbf{u}' = \tau^{\alpha}\mathbf{u}_{,\alpha} = \mathrm{d}\mathbf{u}/\mathrm{d}s$, with $\tau^{\alpha} = \mathrm{d}\theta^{\alpha}/\mathrm{d}s$, is the tangential derivative of $\mathbf{u}$, and $\mathbf{u}_{\nu} = \nu^{\alpha}\mathbf{u}_{,\alpha}$ is the normal derivative. The term involving the tangential derivative is integrated by parts. If $\partial\pi$ is piecewise smooth in the sense that its tangent $\boldsymbol{\tau}$ is piecewise continuous, having discontinuities at a finite number of corners, then

$$\int_{\partial\pi}\varphi^{\alpha}\nu_{\alpha}\,\mathrm{d}s = \int_{\partial\pi}(\{\mathbf{T}^{\alpha}\nu_{\alpha} - (\mathbf{M}^{\alpha\beta}\nu_{\alpha}\tau_{\beta})'\}\cdot\mathbf{u} + \mathbf{M}^{\alpha\beta}\nu_{\alpha}\nu_{\beta}\cdot\mathbf{u}_{\nu})\,\mathrm{d}s - \sum\mathbf{M}^{\alpha\beta}[\nu_{\alpha}\tau_{\beta}]_{i}\cdot\mathbf{u}_{i}, \tag{68}$$

in which the square bracket refers to the forward jump as a corner of the boundary is traversed, and the sum ranges over all corners, i.e., $[\cdot] = (\cdot)_{+} - (\cdot)_{-}$, where, in the present context, the subscripts $\pm$ identify limits as a corner located at arclength station s is approached through larger and smaller values of arclength.

5.3 Tangential leaflet equilibrium

Consider variations with $\mathbf{u}$ and $\mathbf{u}_\nu$ vanishing on $\partial\pi$ (and at corners) with $\mathbf{u} = u_\mu \mathbf{a}^\mu$ in the interior of $\pi (= \pi^+$ or $\pi^-)$. For these, we have the variation

$$\dot{E} = \int_\pi [\dot{W} + (W + \lambda)\dot{J}/J]\,\mathrm{d}a = -\int_\pi u_\mu \mathbf{a}^\mu \cdot \mathbf{T}^\alpha_{;\alpha}\,\mathrm{d}a \tag{69}$$

of the energy of a leaflet, in which variation of λ has been suppressed. Canceling the common factor α^+ or α^-, as appropriate, it follows, from (45)–(47), that the corresponding leaflet power is of the form

$$P = \int_\pi g^\mu u_\mu da, \tag{70}$$

where g^μ is a tangential force per unit area acting on the leaflet. With u_μ unrestricted, we thus arrive at

$$(N^{\alpha\mu} + M^{\alpha\beta} b^\mu_\beta)_{;\alpha} + M^{\alpha\beta}_{;\beta} b^\mu_\alpha + g^\mu = 0 \quad \text{in} \quad \pi. \tag{71}$$

To reduce this for the leaflet energy (49), we use (33) and (57), obtaining

$$N^{\alpha\mu} + M^{\alpha\beta} b^\mu_\beta = (\lambda - kH^2) a^{\alpha\mu} + \left(\tfrac{1}{2}\beta + kH\right) \tilde{b}^{\alpha\mu}, \tag{72}$$

with divergence [cf. (35)]

$$(N^{\alpha\mu} + M^{\alpha\beta} b^\mu_\beta)_{;\alpha} = a^{\alpha\mu}\lambda_{,\alpha} - 2kH a^{\alpha\mu} H_{,\alpha} + k\tilde{b}^{\alpha\mu} H_{,\alpha}, \tag{73}$$

and combination with [see $(57)_2$]

$$M^{\alpha\beta}_{;\beta} = k a^{\alpha\beta} H_{,\beta} \tag{74}$$

furnishes

$$(N^{\alpha\mu} + M^{\alpha\beta} b^\mu_\beta)_{;\alpha} + M^{\alpha\beta}_{;\beta} b^\mu_\alpha = a^{\alpha\mu}\lambda_{,\alpha}. \tag{75}$$

Then, reinstating the leaflet labels, we find that (71) reduces simply to

$$a^{\alpha\mu}\lambda^\pm_{,\alpha} + g^\mu_\pm = 0 \quad \text{in} \quad \pi^\pm. \tag{76}$$

The multipliers $\lambda^\pm$ are therefore uniform if the tangential forces vanish, as assumed in conventional expositions of theory [2]. However, a number of biologically relevant physical effects, such as intra-leaflet diffusion [12,18] and viscous flow [12,19], can give rise to non-uniform multiplier fields.

5.4 Normal equilibrium of the bilayer

We consider normal variations involving both leaflets of the bilayer together. Taking variations as in the previous subsection, now with $\mathbf{u}^\pm = w\mathbf{n}$ in the interior of an overlap region $\pi^* = \pi^+ \cap \pi^-$, we obtain the energy variation

$$\dot{E} = -\int_{\pi^*} w\mathbf{n} \cdot \mathbf{T}^\alpha_{;\alpha} da, \tag{77}$$

where [cf. (62)]

$$\mathbf{T}^\alpha = (N^{\alpha\mu} + M^{\alpha\beta} b^\mu_\beta)\mathbf{a}_\mu - M^{\alpha\beta}_{;\beta}\mathbf{n}, \tag{78}$$

with

$$N^{\alpha\mu} = \alpha^+ N^{\alpha\mu}_+ + \alpha^- N^{\alpha\mu}_- \quad \text{and} \quad M^{\alpha\mu} = \alpha^+ M^{\alpha\mu}_+ + \alpha^- M^{\alpha\mu}_- \tag{79}$$

in which $N_{\pm}^{\alpha\mu}$ and $M_{\pm}^{\alpha\mu}$ are given by (57) with moduli and Lagrange multipliers pertaining to $\pi^{\pm}$, respectively. Thus, the associated power is

$$P = \int_{\pi^*} pw \, \mathrm{d}a, \tag{80}$$

where p is the net lateral pressure acting on the surface in the direction of $\mathbf{n}$. With (45) and with w unrestricted, we arrive at

$$(N^{\alpha\mu} + M^{\alpha\beta} b_{\beta}^{\mu}) b_{\mu\alpha} - M^{\beta\alpha}_{;\beta\alpha} + p = 0 \quad \text{in} \quad \pi^*. \tag{81}$$

We note in passing that (71) and (81) are the general equilibrium equations for a pressurized Kirchhoff–Love shell [13,14].

To reduce (81) for the energy (50), we use (57) with $a^{\mu\alpha} b_{\mu\alpha} = 2H$ and $\tilde{b}^{\mu\alpha} b_{\mu\alpha} = 2K$, which follow from $(30)_1$ and (31), respectively, finding that

$$(N^{\alpha\mu} + M^{\alpha\beta} b_{\beta}^{\mu}) b_{\mu\alpha} = 2\lambda H + 2kH(K - H^2) + \beta K. \tag{82}$$

Then, with (74), Eq. (81) reduces to the well-known *shape equation*

$$k[\Delta H + 2H(H^2 - K)] - \beta K - 2\lambda H = p, \tag{83}$$

where

$$\Delta H = a^{\alpha\beta} H_{;\alpha\beta} = \frac{1}{\sqrt{a}} (\sqrt{a} a^{\alpha\beta} H_{,\beta})_{,\alpha} \tag{84}$$

is the surficial Laplacian of H. Here, in contrast to the classical theory [2], λ $(= \alpha^{+}\lambda^{+} + \alpha^{-}\lambda^{-})$ is non-uniform if either leaflet is subjected to a tangential distributed force.

6 Edge conditions

Edge conditions are of secondary interest in this subject because applications are primarily concerned with closed surfaces. However, in the present framework they are readily obtained from the patchwise virtual power postulate and so we derive them here for the sake of completeness. A number of works that encompass edge interactions are available in the literature [17,20,21].

With the equilibrium equations (76) and (83) satisfied, the variation of the energy—of a leaflet or the bilayer—reduces to

$$\dot{E} = \int_{\partial\pi} (\varphi^{\alpha} v_{\alpha} + \mu \dot{J}/J) \, \mathrm{d}s. \tag{85}$$

We use this to extract the relevant expressions for the actions exerted at the boundaries of a patch.

6.1 Tangential actions on the boundaries of leaflet patches

From our development thus far, we see that (85) holds for the individual leaflets, with superscripts $^{\pm}$ appended as appropriate. We continue the convention of suppressing these when discussing a single leaflet. Applying this with tangential leaflet virtual velocities $\mathbf{u} = u^{\beta}\mathbf{a}_{\beta}$, we conclude, from (45) and (68), after division by α, that the relevant contribution to the leaflet power is

$$P = \int_{\partial\pi} \{t_{\beta} u^{\beta} + \mu_{\beta} (v^{\alpha} u^{\beta}_{;\alpha})\} ds - \sum (f_i)_{\beta} (u_i)^{\beta}, \tag{86}$$

where

$$t_{\beta} = M b_{\beta\alpha} v^{\alpha} + \mathbf{a}_{\beta} \cdot \{\mathbf{T}^{\alpha} v_{\alpha} - (T\mathbf{n} + \mu\boldsymbol{\tau})'\}, \quad \mu_{\beta} = \mu v_{\beta} \quad \text{and} \quad (f_i)_{\beta} = [\mu\tau_{\beta}]_i \tag{87}$$

are the tangential force density, double force density [22] and corner force, respectively, with

$$M = M^{\alpha\beta}\nu_\alpha\nu_\beta \quad \text{and} \quad T = M^{\alpha\beta}\nu_\alpha\tau_\beta. \tag{88}$$

Using $\mathbf{n}' = -b_{\alpha\mu}\tau^\alpha\mathbf{a}^\mu$ and

$$\boldsymbol{\tau}' = -\kappa_g\boldsymbol{\nu} + \kappa_\tau\mathbf{n}, \tag{89}$$

where

$$\kappa_\tau = b_{\alpha\beta}\tau^\alpha\tau^\beta \quad \text{and} \quad \kappa_g = -\nu_\lambda(d\tau^\lambda/\mathrm{d}s + \tau^\alpha\tau^\beta\Gamma^\lambda_{\alpha\beta}) \tag{90}$$

are the normal and geodesic curvatures of $\partial\pi$, respectively, the leaflet traction, double forces and corner forces are given finally by

$$t^\pm_\beta = M^\pm b_{\beta\alpha}\nu^\alpha + T^\pm b_{\alpha\beta}\tau^\alpha + \mu^\pm\kappa_g\nu_\beta - (\mu^\pm)'\tau_\beta + \mathbf{a}_\beta\cdot\mathbf{T}^\alpha_\pm\nu_\alpha, \quad \mu^\pm_\beta = \mu^\pm\nu_\beta \quad \text{and} \quad (f^\pm_i)_\beta = [\mu^\pm\tau_\beta]_i. \tag{91}$$

6.2 Normal actions on the boundary of a bilayer patch

Assuming the equilibrium equations to be satisfied in the interior of $\pi^* = \pi^+\cap\pi^-$, the residual variation of the total energy of the bilayer patch π^* is [cf. (85)]

$$\dot{E} = \int_{\partial\pi^*}(\varphi^\alpha\nu_\alpha + \mu\dot{J}/J)\,\mathrm{d}s, \tag{92}$$

which we apply with $\mathbf{u}^\pm = w\mathbf{n}$. Thus, the boundary integral of $\varphi^\alpha\nu_\alpha$ is given by (68), with

$$\mathbf{u}_\nu = \nu^\alpha(w\mathbf{n})_{,\alpha} = w_\nu\mathbf{n} - wb^\beta_\alpha\nu^\alpha\mathbf{a}_\beta. \tag{93}$$

From (45), we derive the associated virtual power

$$P = \int_{\partial\pi^*}(Sw + Cw_\nu)\,\mathrm{d}s - \sum f_i w_i, \tag{94}$$

where

$$S = \mathbf{n}\cdot\mathbf{T}^\alpha\nu_\alpha - T' - \mu\kappa_\tau, \quad C = M \quad \text{and} \quad f_i = [T]_i \tag{95}$$

are the transverse shear force density, bending moment density and transverse corner force, respectively.

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