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Thermodynamically Consistent Models for Two-Component Vesicles

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Abstract: We develop thermodynamically consistent continuum models for twocomponent vesicles. The models are derived using energy dissipation and mass conservation and account for volume constraints, global area constraints or local inextensibility constraints and can be coupled to fluid flow in- and outside of the membrane. The resulting systems of equations are higher order geometric evolution problems of Willmore flow type, or in the case of coupling with fluid flow, involving higher order generalized Laplace-Young jump conditions, which are coupled to higher order convection-diffusion problems for a scalar concentration field of Cahn-Hilliard type on the evolving surface; Constraints require solution of a non-local system which can be obtained explicitly for global constraints and requires solving a non-local elliptic partial differential equation on the evolving surface for the local constraints. Numerical examples for selected problems are provided.

1. Introduction

Biological membranes are a mixture of many different types of lipids, cholesterol and protein components. Their relative amounts and compositions may differ between functionally distinct domains. Irregularities in lipid packing at domain interfaces may result in increased membrane permeability [12, 44, 35] which has important consequences for drug delivery. The increasing interest in lipid membranes results from the hypothesized coupling of lipid phase segregation in the membrane to fundamental cell biological processes, such as membrane signaling and trafficking [52] and drug delivery. Sub-domains of distinct curvature may have precise biological properties [41], thus an understanding how lipid components can dynamically influence to membrane morphology is of utmost importance. Changes in lipid composition are assumed to assist or antagonize the membrane curvature on one hand, but also may respond to the curvature by concentrating in domains of a preferred curvature. Strong curvature variations have recently been observed experimentally in giant liposomes, where different lipids segregate according to their chemical properties and lead to the formation of buds (e.g., [6, 5, 51]).

In this paper we derive thermodynamically consistent continuum models to describe the dynamics of vesicles. Such models provide a good modeling alternative to reach larger length and time scales that can be accessed by discrete methods. The derived model is an extension of the classical Helfrich model [31] for an elastic membrane. It results in coupled systems of higher order geometric evolution equations for the membrane or higher order boundary conditions for a fluid flow problem inside and outside of the membrane and convection-diffusion equations on the evolving membrane which are coupled to non-local problems to enforce constraints on the evolution.

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Models and investigation of equilibrium configurations as the minima of a suitably defined surface free energy for such a setting have been considered in various contributions, see e.g. [2, 36, 56, 49, 28, 33, 27, 29, 30, 5, 51, 54, 14, 13]. Recently, investigations on equilibrium equations and stability analysis for multicomponent biological membranes have been made in [26]. Dynamical simulations until now have been limited to small deformations or special shapes and simplified models, see e.g., [55, 32, 42, 40, 25]. Phase field models have also been used to simulate the equilibrium [57] and the dynamics [11,39] of multicomponent vesicles. Very recently, a thermodynamically consistent model for the dynamics of two-dimensional multicomponent membranes in Stokes flow was presented and solved using a boundary integral and parametric method [53, 8]. Here, we present general models valid in two and three dimensions. A similar derivation for some problems which are included in our general approach have been given in [21], see also [43] for a related approach and further analytic results.

The outline of the paper is as follows: In Section 2 we specify notations and shortly introduce some differential geometry needed to define derivatives on evolving surfaces. In Section 3 we define the membrane energy, consisting of elastic bending, surface tension and line energies. In Section 4 we derive thermodynamically consistent dynamics models, which include volume conservation, area conservation, local inextensibility and coupling of the vesicle dynamics to viscous fluid flow. In Section 5 we briefly discuss different numerical approaches and show numerical results. In Section 6 we draw conclusions and in the Appendix we give a motivation for approximations for the Gaussian bending energy and the line energy and compute the variational derivatives of the energies.

2. NOTATION

We introduce some differential geometric notations and recall some basic identities. A more detailed account is given in Appendix A, see also [19, 16, 58].

We consider a time intervall $[0, T] \subset \mathbb{R}$, $\underline{T} > 0$. $\Gamma(t)$ be a compact smooth connected and oriented hypersurface in $\mathbb{R}^3$ without boundary. Furthermore, we assume the hypersurfaces $\Gamma(t)$ are given as $\Gamma(t) = X(\cdot, t)(M)$, where M is a suitable reference manifold, e.g., $M = S^2$ the unit sphere and $\mathbf{X} : M \times [0, T] \to \mathbb{R}^3$ with $(z, t) \mapsto \mathbf{X}(z, t) = \mathbf{X}(z_1, z_2, t)$ and $z = (z_1, z_2) \in M$ and $t \in [0, T]$. We define the velocity $\mathbf{v}(\cdot, t) : \Gamma(t) \times [0, T] \to \mathbb{R}^3$ of a point $X(z, t) \in \Gamma(t)$ by

$$\mathbf{v}(\mathbf{X}(z, t), t) := \frac{d}{dt} \mathbf{X}(z, t).$$

Denoting with $\mathbf{n}(\cdot, t) : \Gamma(t) \times [0, T] \to \mathbb{R}^3$ the (inner) normal to $\Gamma(t)$, the velocity $\mathbf{v}$ may be decomposed into normal and tangential components through

$$\mathbf{v} = V\mathbf{n} + \mathbf{T}$$

with $V = \mathbf{v} \cdot \mathbf{n}$ the (scalar) normal velocity and $\mathbf{T} := \mathbf{v} - V\mathbf{n}$ the tangential velocity.

The material derivative $\dot{f}$ of a function $f = f(\mathbf{X}(z, t), t)$ defined on $\Gamma(t) \times [0, T]$ is given by

$$\dot{f}(\mathbf{X}(z, t), t) := \frac{d}{dt} f(\mathbf{X}(z, t), t).$$

If $f(\cdot, t)$ is defined on a neighborhood of $\Gamma(t)$, defined as an open subset $N(t) \in \mathbb{R}^3$ containing $\Gamma(t)$, the material derivative may be expressed as

$$\dot{f} = \partial_t f + \mathbf{v} \cdot \nabla f, \tag{1}$$

where $\cdot$ denotes the Euclidean scalar product in $\mathbb{R}^3$ and ∇ denotes the usual gradient on $\mathbb{R}^3$, acting on the spatial variables. We point out, that here and in the following, we use the same symbol f for the function $f = f(\cdot, t)$ on $\Gamma(t) \times [0, T]$ and an extension to a neighborhood on $N(t) \times [0, T]$.

The tangential gradient of a function $f = f(\cdot, t) : \Gamma(t) \times [0, T] \to \mathbb{R}$ is given by

$$\nabla_\Gamma f(\mathbf{X}(z,t),t) := \sum_{i,j=1}^{2} g^{ij}(\mathbf{X}(z,t),t)\,\partial_i f(\mathbf{X}(z,t),t)\,\partial_j \mathbf{X}(z,t),$$

where (g^{ij}) denotes the inverse of the (induced Riemannian) metric tensor given by $g_{ij} = \partial_i \mathbf{X} \cdot \partial_j \mathbf{X}$ (see Appendix A for more details). The tangential derivative of a (not necessarily tangential) vector field $\mathbf{f} = \mathbf{f}(\cdot, t) : \Gamma(t) \times [0, T] \to \mathbb{R}^3$ is given by

$$\nabla_\Gamma \cdot \mathbf{f}(\mathbf{X}(z,t),t) := \sum_{i,j=1}^{2} g^{ij}(\mathbf{X}(z,t),t)\,\partial_i \mathbf{f} \cdot \partial_j \mathbf{X}.$$

Moreover, the mean curvature H of $\Gamma(t)$ is given by $H = \kappa_1 + \kappa_2$, with κ_1 and κ_2 the principle curvatures of $\Gamma(t)$, and H may be expressed in terms of the normal vector field $\mathbf{n}$ as $H = -\nabla_\Gamma \cdot \mathbf{n}$, which leads to the following identity

$$\nabla_\Gamma \cdot \mathbf{v} = \nabla_\Gamma (V\mathbf{n} + \mathbf{T}) = -VH + \nabla_\Gamma \cdot \mathbf{T}. \tag{2}$$

3. ENERGY

We now define the surface energy for a vesicle and discuss the various terms corresponding to elastic bending, surface tension and phase separation. Vesicles are closed biomembranes consisting of different types of lipid and cholesterol and serve as important, but simplified models of more complex cell-membranes.

3.1 Single-Component Vesicles

The spontaneous-curvature model [31] is based on the assumption that the surface energy associated with bending of the membrane can be expanded in the mean curvature $H = \kappa_1 + \kappa_2$ and the Gaussian curvature $K = \kappa_1 \kappa_2$. The energy E consists of the following parts:

- the normal bending energy

$$E_B = \frac{1}{2} \int_\Gamma b_N (H - H_0)^2 \, dA$$

- the Gaussian bending energy

$$E_G = \int_\Gamma b_G K \, dA$$

- the excess energy associated with the presence of the membrane

$$E_S = \int_\Gamma \gamma \, dA$$

with H_0 the spontaneous curvature, which reflects a possible asymmetry of the membrane, justified by a different chemical environment on both sides of the membrane. H_0 is usually assumed to be spatially homogeneous. b_N is the normal bending stiffness, b_G is the Gaussian bending stiffness and γ is the surface tension. For constant b_G the Gaussian bending energy is proportional to the Euler characteristic of the membrane (Gauss-Bonnet theorem) and so changes in shape, which preserve the topology do not contribute to the energy. Hence E_G can be dropped for such cases. For a review of models based on this energy we refer to [50].

Summarizing, we obtain the following membrane energy E of a single component vesicle without topological changes.

$$E[\Gamma] = E_B[\Gamma] + E_S[\Gamma] = \frac{1}{2}\int_\Gamma b_N (H - H_0)^2 \, dA + \int_\Gamma \gamma \, dA. \tag{3}$$

3.2 Two-Component Vesicles

For a two-component vesicle the specified energies depend on the component and in addition a line energy has to be defined along the phase boundary separating the different components. Such an energy reads $E_T = \int_C \tau \, ds$, with C being the separating curve along the surface and τ being the line tension. Equilibrium shapes of a two-component lipid bilayer membrane were first obtained using such an extended model via constrained energy minimization in [33]. With different values for the Gaussian bending stiffness for the different phases the Gaussian bending energy can no longer be neglected. However, for different constant values of b_G in the different phases the Gaussian bending energy contributes an energy proportional to the geodesic curvature κ_g of the curve C. Thus, by the Gauss-Bonnet theorem, the Gaussian bending energy becomes $E_G = \int_C [b_G] \kappa_g \, ds$ and is even present without topological changes where $[b_G] \in \mathbb{R}$ denotes the jump of b_G accross C. Through a comparison of experimental vesicle geometries and numerical results the importance of the Gaussian bending energy in multicomponent vesicles has recently been verified in [5].

In [55] an order parameter u was introduced to characterize the different components. Since u is defined as the non-dimensional difference of the concentrations of the two types of lipid molecules, one has $u \in [-1, 1]$, where the two components are characterized as the pure phases with $u = 1$ and $u = -1$, respectively. The line energy E_T is now approximated within a phase-field representation as follows:

$$E_T = \int_\Gamma \tau \left(\frac{\xi}{2} \|\nabla_\Gamma u\|^2 + \frac{1}{\xi} W(u) \right) dA$$

with ξ a small parameter and $W(u)$ a double-well potential with minima for $u = -1$ and $u = 1$. Furthermore now the parameters in E_B, E_G and E_S do depend on the composition u. We have $b_N = b_N(u)$, $H_0 = H_0(u)$, $b_G = b_G(u)$ and $\gamma = \gamma(u)$, with an appropriate interpolation of the parameters within the diffuse interface region.

Various models also introduce an ad-hoc additional coupling term of the form $E_{\text{coupling}} = \int_\Gamma uH \, dA$, see [55, 32, 42] or $E_{\text{coupling}} = \int_\Gamma uH^2 dA$, see [3]. Such coupling is of limited applicability. The more general case involves concentrationdependent membrane properties which may induce morphological transitions of the membrane. Note that the ad-hoc coupling above can be viewed as a special case of this more general case.

Finally, assuming the Gaussian bending stiffness b_G to be constant in each phase, a phase-field representation of the Gaussian bending energy E_G (without the constant term describing the Euler characteristic) can be introduced as

$$E_{G,\xi} = \frac{1}{\xi}\int_\Gamma [b_G] \left(-\xi \Delta_\Gamma u + \frac{1}{\xi} W'(u) \right) \sqrt{2W(u)} \, dA,$$

with $[b_G] = b_G(1) - b_G(-1)$ denoting the difference of the Gaussian bending stiffness in the two phases. The energy is derived in analogy to a phase field approximation for Willmore flow [15, 38, 47, 17]. A heuristic derivation for the phase-field approximation of the line energy and the Gaussian bending energy is given in Appendix B.

Summarizing, we obtain the following membrane energy E of a two component vesicle, which will be used in the following.

$$\begin{aligned} E[\Gamma, u] &= E_B[\Gamma, u] + E_{G,\xi}[\Gamma, u] + E_S[\Gamma, u] + E_T[\Gamma, u] \\ &= \frac{1}{2}\int_\Gamma b_N(u)(H - H_0))^2 dA \\ &\quad + \frac{1}{\xi}\int_\Gamma [b_G]\left(-\xi\Delta_\Gamma u + \frac{1}{\xi}W'(u)\right)\sqrt{2W(u)}\, dA \\ &\quad \int_\Gamma \gamma(u)\, dA + \tau\int_\Gamma \frac{\xi}{2}\|\nabla_\Gamma u\|^2 + \frac{1}{\xi}W(u)\, dA. \end{aligned} \tag{4}$$

4. DYNAMIC MODEL

Based on the membrane energy given in (4) we will derive thermodynamically consistent dynamic models. The basic ingredients thereby are energy dissipation and mass conservation. We first recall the dynamics for a single-component vesicle. For more complicated problems where the local properties of the membrane depend on the lipid and cholesterol concentrations (i.e., surface phase) and there may be geometric constraints, it is less straightforward to formulate dissipative dynamics laws. We present a class of model equations for multicomponent vesicles using a variational approach together with mass conservation of the surface phase.

4.1 Classical Helfrich Model for Single-Component Vesicle

To begin, we review how a dynamic law for a membrane may be obtained from Newton's law in the case of the classical Helfrich model for a homogeneous membrane. Assuming that the normal bending stiffness coefficient b_N is constant, the elastic bending energy E of the membrane is proportional to the integral of the square of the mean curvature H of the membrane surface Γ, namely

$$E_B[\Gamma] = \frac{1}{2} b_N \int_\Gamma H^2 dA.$$

The corresponding elastic force is obtained as the variational derivative $\delta E_B/\delta\Gamma$ of the elastic energy with respect to variations of the interface. Assuming, that the inertia force of the membrane may be neglected (i.e., the membrane is assumed to be massless), the following two cases may be distinguished:

(i) Local dynamics: the fluid inside and outside of the membrane is highly viscous and the dynamics of the fluid may be neglected. In this case, the fluid establishes a local friction force F_v in opposite direction of the local velocity $\mathbf{v}$ of the membrane, which is usually assumed to be of the form $F_v = -k\mathbf{v}$, with a positive coefficient $k > 0$. Thus, Newton's law yields the local evolution equation

$$k\mathbf{v} = -\frac{\delta E_B}{\delta\Gamma}. \tag{5}$$

This is a geometric evolution equation, which is known as the Willmore flow (e.g., [37]).

(ii) If the dynamics of the fluid is taken into account, a kinematic force balance at the membrane Γ is posed between the membrane and the hydrodynamic forces

$$[\sigma \cdot \mathbf{v}]_\Gamma = \frac{\delta E_B}{\delta\Gamma}, \tag{6}$$

where σ is the fluid stress tensor. In addition, equation (6) has to be supplemented by an equation for the viscous fluid, e.g., the Navier-Stokes or Stokes equation.

In both cases, it can be seen that the total free energy is decreasing, i.e., the dynamics is dissipative. This is consistent with the second law of thermodynamics since we implicitly assume that the temperature is constant. In case (i) the time derivative of the total free energy $E_B[\Gamma]$ is

$$\frac{d}{dt} E_B = \int_\Gamma \frac{\delta E_B}{\delta \Gamma} \mathbf{v} dA = -\frac{1}{k} \int_\Gamma \mathbf{v} \cdot \mathbf{v} dA \leq 0 .$$

In case (ii), the energy decreases due solely to viscous dissipation. That is, in the case of the Navier-Stokes system, the total energy $E = E_K + E_B$ where $E_K = \frac{1}{2}\int \rho |\mathbf{v}|^2 d\Omega$ is the kinetic energy with ρ the fluid density. In the Stokes system, the total energy $E = E_B$. In both cases,

$$\frac{d}{dt} E = -\int \nu \mathbf{D} : \mathbf{D} \, d\Omega ,$$

where ν is the viscosity, $\mathbf{D} = \nabla \mathbf{v} + \nabla \mathbf{v}^T$ is the deformation tensor and $\mathbf{D} : \mathbf{D} = \sum_{ij} D_{ij} D_{ij}$ is the tensor product.

4.2 Energy Dissipation and Mass Conservation for Two-Component Vesicles

As mentioned above, the two basic requirements for a consistent dynamic model are mass conservation and energy dissipation. Mass conservation may be expressed as a global conservation law for the extensive quantity u, i.e.,

$$\frac{d}{dt} \int_\Gamma u dA = 0 , \tag{7}$$

whereas energy dissipation reads

$$\frac{d}{dt} E[\Gamma, u] \leq 0 , \tag{8}$$

with $E = E[\Gamma, u]$ is given in (4). Assuming the phase field u to be extended as a constant in the normal direction off the surface Γ, the time derivative of E is given by

$$\frac{d}{dt} E = \int_\Gamma \partial_t u \frac{\delta E}{\delta u} dA + \int_\Gamma \mathbf{v} \cdot \frac{\delta E}{\delta \Gamma} dA, \tag{9}$$

with $\frac{\delta E}{\delta u}$ the variational derivative of E with respect to variations in u and $\frac{\delta E}{\delta \Gamma}$ the variational derivative of E with respect to variations in Γ. A careful derivation of these derivatives is given in Appendix C. We note, that the partial time derivative $\partial_t u$ is only well defined, if u is extended off the surface, see (1). Moreover, also for the definition and calculation of the variational derivative $\frac{\delta E}{\delta \Gamma}$, an extension of u is needed.

Starting with (9), a dynamic model has to give equations for the unknowns $\partial_t u$ and $\mathbf{v}$ such that (7) and (8) are satisfied. To achieve this, we will express $\partial_t u$ in terms of the (also unknown) surface flux $\mathbf{q}$. Then, we will choose the velocity $\mathbf{v}$ and the flux $\mathbf{q}$ such, that the time derivative of the energy is a negative definite quadratic form in $\mathbf{v}$ and $\mathbf{q}$ thus ensuring maximal dissipation. This approach is analogous to the well-known gradient flow formulations.

For a given tangential surface flux $\mathbf{q}$, we assume the local continuity equation (see [19])

$$\dot{u} + u \nabla_\Gamma \cdot \mathbf{v} = -\nabla_\Gamma \cdot \mathbf{q} , \tag{10}$$

which guarantees the global conservation law (7). Furthermore, using (2) and the assumption that u is extended off the surface as a constant in the normal direction, equation (10) may as well be written as

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH = -\nabla_\Gamma \cdot \mathbf{q} . \tag{11}$$

We now use Eq. (11) as a definition for $\partial_t u$ in Eq. (9) and obtain

$$\frac{d}{dt}E = -\int_\Gamma (\nabla_\Gamma \cdot (u\mathbf{T}) - uVH + \nabla_\Gamma \cdot \mathbf{q}) \frac{\delta E}{\delta u}\, dA + \int_\Gamma \mathbf{v} \cdot \frac{\delta E}{\delta \Gamma}\, dA$$

$$= \int_\Gamma \left[\mathbf{q} \cdot \nabla_\Gamma \frac{\delta E}{\delta u} + V\left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} + uH \frac{\delta E}{\delta u} \right) + \mathbf{T} \cdot \left(\frac{\delta E}{\delta \Gamma} + u\nabla_\Gamma \frac{\delta E}{\delta u} \right) \right] dA \tag{12}$$

$$= \int_\Gamma \left[(\mathbf{q} + u\mathbf{T}) \cdot \nabla_\Gamma \frac{\delta E}{\delta u} + V\left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} + uH \frac{\delta E}{\delta u} \right) + \mathbf{T} \cdot \frac{\delta E}{\delta \Gamma} \right] dA. \tag{13}$$

Here we have used the integration by parts. Note, that in Eq. (13) we have grouped together the diffusion flux $\mathbf{q}$ and the convective flux $u\mathbf{T}$, whereas in (12), we assume the dissipative diffusion flux $\mathbf{q}$ and the convective flux $u\mathbf{T}$ to be independent.

Following the splitting in (12), we may take

$$\mathbf{q} = -\beta_u \nabla_\Gamma \frac{\delta E}{\delta u}$$

$$V = -\beta_V \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} + uH \frac{\delta E}{\delta u} \right)$$

$$\mathbf{T} = -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u\nabla_\Gamma \frac{\delta E}{\delta u} \right),$$

for some positive kinetic coefficients β_u, β_V and β_T, which in general can be arbitrary positive functions depending on the local composition u. Here $\mathbf{I}$ denotes the identity matrix. With these definitions of the unknowns $\mathbf{q}$, V, $\mathbf{T}$, the energy dissipation is indeed a negative definite quadratic form, being diagonal in $\mathbf{q}$, V, $\mathbf{T}$:

$$\frac{d}{dt}E = -\int_\Gamma \frac{1}{\beta_u} \mathbf{q}^2 dA - \int_\Gamma \frac{1}{\beta_V} V^2 dA - \int_\Gamma \frac{1}{\beta_T} \mathbf{T}^2 dA \le 0,$$

and thus energy dissipation, and with it consistency with the 2nd law of thermodynamics is fulfilled. Together with Eq. (11) we obtain the following evolution laws:

Problem 1: (unconstrained dynamics)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \tag{14}$$

$$V = -\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} + uH \frac{\delta E}{\delta u} \right) \tag{15}$$

$$\mathbf{T} = -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u\nabla_\Gamma \frac{\delta E}{\delta u} \right). \tag{16}$$

Eq. (14) is a convective Cahn-Hilliard type equation for u on an evolving surface. Resulting from the way the equation is derived, u is a conserved quantity, which may also be directly verified since

$$\frac{d}{dt}\int_\Gamma u dA = \int_\Gamma \partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH dA = \int_\Gamma \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u}\right) dA = 0.$$

Eq. (15) generalizes the evolution law for the membrane (5). The latter is driven by purely geometric forces whereas in (15) the second term yields a driving force being associated with the presence of different lipid components. Eq. (16) determines the tangential velocity, which is not arbitrary, as in classical interface problems.

Remark 1: An alternative way to derive evolution laws would be to use the splitting (13) and define $\mathbf{q} + u\mathbf{T} = -\gamma_u \nabla_\Gamma \frac{\delta E}{\delta u}$ leading to

$$\partial_t u - uVH = \nabla_\Gamma \cdot \left(\gamma_u \nabla_\Gamma \frac{\delta E}{\delta u}\right)$$

$$V = -\gamma_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} + uH \frac{\delta E}{\delta u}\right)$$

$$\mathbf{T} = -\gamma_T (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma},$$

with positive coefficients γ_u, γ_V and γ_T. The evolution for u in this case is independent of $\mathbf{T}$. As for Problem 1, one immediately verifies, that the energy is dissipative, and that u is a conserved quantity. For the special case that $\frac{\delta E}{\delta \Gamma}$ is in normal direction, i.e., $(\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} = 0$, these Eqs. coincide with Problem 1, if one choses $\gamma_u = \beta_u + \gamma_T u^2$ and $\gamma_V = \beta_V$.

4.3 Constraints

The discussion so far has been for unconstrained evolution, which corresponds to a fully permeable vesicle and flexible bonds between lipids, which allow for spatial variations. We now introduce various constraints on volume and area. We will use Lagrange multipliers to enforce the constraints in the dynamical laws.

4.3.1 *Volume Constraint*

To ensure a constant volume

$$\mathrm{Vol}(t) := \int_{\Omega_{\mathrm{int}}(t)} dx,$$

of the interior domain $\Omega_{\mathrm{int}}(t)$ inside $\Gamma(t)$, we introduce a Lagrange multiplier $\lambda_{\mathrm{Vol}} = \lambda_{\mathrm{Vol}}(t)$ and add the volume constraint to the free energy to get the Lagrangian

$$L[u, \Gamma, \lambda_{\mathrm{Vol}}] = E[u, \Gamma] - \lambda_{\mathrm{Vol}}(t)\,(\mathrm{Vol}(t) - \mathrm{Vol}(0))$$

This leads to

$$\frac{d}{dt} L = \frac{d}{dt} E + \lambda_{\mathrm{Vol}} \int_\Gamma V dA + \partial_t \lambda_{\mathrm{Vol}}(t)\,(\mathrm{Vol}(t) - \mathrm{Vol}(0)).$$

Comparing with (12), dissipative dynamics are obtained along the same lines as above by defining the normal velocity V as

$$V = V^u + \beta_v \lambda_{\mathrm{Vol}},$$

where V^u denotes the unconstrained normal velocity as given by the rhs of (15). Moreover, the equations for the tangential velocity and the conservation law for u are not affected, in particular we have $\mathbf{T} = \mathbf{T}^u$. The Lagrange multiplier λ_{Vol} is uniquely determined by the constraint $\int_\Gamma V\,dA = 0$ as

$$\lambda_{\text{Vol}} = \frac{\int_\Gamma V^u\,dA}{\int_\Gamma \beta_V\,dA}.$$

We thus obtain the following evolution equations:

Problem 2: (dynamics with volume constraint)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \tag{17}$$

$$V = -\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} \right) + \beta_v \lambda_{\text{Vol}} \tag{18}$$

$$\mathbf{T} = -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} \right). \tag{19}$$

$$\lambda_{\text{Vol}} = \frac{\int_\Gamma \beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} \right) dA}{\int_\Gamma \beta_V\,dA} \tag{20}$$

Note that the Lagrange multiplier equation (20) makes the system of equations nonlocal.

Remark 2: A different approach to enforce volume conservations is to modify the evolution equation for the normal velocity V and instead of Eq. (18) define

$$V = -\nabla_\Gamma \mathbf{j} \tag{21}$$

$$\mathbf{j} = -\beta_V \nabla_\Gamma \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} - uH \frac{\delta E}{\delta u} \right). \tag{22}$$

This naturally ensures volume conservation, as

$$\int_\Gamma V dA = \int_\Gamma \nabla_\Gamma \cdot \left(\eta_V \nabla_\Gamma \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} - uH \frac{\delta E}{\delta u} \right) \right) dA = 0. \tag{23}$$

Eq. (21) is related to a conserved Willmore flow and will thus turn out to be a 6th order equation. Besides this additional complication the dynamics will be different than the previously discussed approach and a derivation from elastic theories seems not possible. However, the approach has the advantage to remain local and has been used in a similar way in [10] in a diffuse interface context.

4.3.2 *Area Constraint*

To ensure a constant global area

$$\text{Area}\,(t) := \int_{\Gamma(t)} dA,$$

we need

$$\frac{d}{dt}\,\mathrm{Area}\,(t) = \int_\Gamma \nabla_\Gamma \cdot \mathbf{v}\,dA = \int_\Gamma -HV + \nabla_\Gamma \cdot \mathbf{T}\,dA = -\int_\Gamma HV\,dA = 0\,.$$

One may proceed along the same lines as with the global volume constraint by introducing a Lagrange multiplier $\lambda_{\mathrm{Area}}(t)$ and adding the area constraint to the free energy to obtain the Lagrangian

$$L\,[u,\,\Gamma,\,\lambda_{\mathrm{Area}}] = E\,[u,\,\lambda\Gamma] - \lambda_{\mathrm{Area}}(t)\,(\mathrm{Area}\,(t) - \mathrm{Area}\,(0)).$$

We then have

$$\frac{d}{dt}\,L = \frac{d}{dt}\,E - \lambda_{\mathrm{Area}}\,(t)\int_\Gamma HV\,dA - \partial_t \lambda_{\mathrm{Area}}\,(t)\,(\mathrm{Area}\,(t) - \mathrm{Area}\,(0))$$

Thus instead of Eq. (15) we define

$$V = V^u - \beta_v \lambda_{\mathrm{Area}} H,$$

in order to get maximal energy dissipation (provided the constraint is satisfied). Here, as above, V^u denotes the unconstrained normal velocity as given by the rhs of (15). Moreover, the equations for the tangential velocity and the conservation law for u are not affected, in particular we have $\mathbf{T} = \mathbf{T}^u$.

The equation for the Lagrange multiplier now follows from $\int_\Gamma HV\,dA = 0$, which gives

$$\lambda_{\mathrm{Area}} = \frac{\int_\Gamma HV^u\,dA}{\int_\Gamma \beta_V H\,dA}\,.$$

We thus obtain the following evolution equations:

Problem 3: (dynamics with area constraint)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH \;=\; \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u}\right) \tag{24}$$

$$V = \; -\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH\,\frac{\delta E}{\delta u} - \lambda_{\mathrm{Area}} H\right) \tag{25}$$

$$\mathbf{T} = \; -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n})\,\frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u}\right). \tag{26}$$

$$\lambda_{\mathrm{Area}} = \frac{\int_\Gamma \beta_V H \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH\,\frac{\delta E}{\delta u}\right) dA}{\int_\Gamma \beta_V H\,dA} \tag{27}$$

As in Problem 2, the Lagrange multiplier equation (27) makes the system of equations nonlocal.

4.3.3 *Local Inextensibility*

A stronger constraint than area conservation is local inextensibility. Here we need to ensure for an arbitrary portion Σ of Γ

$$\frac{d}{dt}\int_\Sigma dA = \int_\Sigma \nabla_\Gamma \cdot \mathbf{v} dA = \int_\Sigma -VH + \nabla_\Gamma \cdot \mathbf{T} dA = 0\,.$$

We thus find that the velocity has to be divergence free

$$\nabla_\Gamma \cdot \mathbf{v} = -VH + \nabla_\Gamma \mathbf{T} = 0. \tag{28}$$

To incorporate this local constraint, we introduce a local Lagrange multiplier $\lambda_{\text{Inex}} = \lambda_{\text{Inex}}(\mathbf{X}, t)$, which is a function on $\Gamma(t)$ and add the corresponding constraint to the free energy to get the Lagrangian

$$L[u, \Gamma, \lambda_{\text{Inex}}] = E[u, \Gamma] - \int_\Gamma \lambda_{\text{Inex}} (\sqrt{g(t)} - \sqrt{g(0)})\, dA\,.$$

with $g = (g_{ij})$ the induced metric, see Appendix A for a description. This leads to

$$\frac{d}{dt} L = \frac{d}{dt} E + \int_\Gamma \lambda_{\text{Inex}} HV\, dA - \int_\Gamma \lambda_{\text{Inex}} \nabla_\Gamma \cdot \mathbf{T} dA - \int_\Gamma \partial_t \lambda_{\text{Inex}}\, (\sqrt{g(t)} - \sqrt{g(0)})\, dA$$

Thus instead of Eqs. (15) and (16) we define

$$V = V^u - \beta_V \lambda_{\text{Inex}} H \tag{29}$$

$$\mathbf{T} = \mathbf{T}^u - \beta_T \nabla_\Gamma \lambda_{\text{Inex}} \tag{30}$$

in order to get maximal energy dissipation (provided the constraint is satisfied). Here, as above, V^u and $\mathbf{T}^u$ denote the unconstrained normal velocity and the unconstraint tangential velocity as given by the rhs of (15) and (16), respectively. The equation for the Lagrange multiplier λ_{Inex} is obtained by plugging Eq. (29) and Eq. (30) into the constraint equation (28) as

$$\nabla_\Gamma \cdot (\beta_T \nabla_\Gamma \lambda_{\text{Inex}}) - \beta_V \lambda_{\text{Inex}} H^2 = -V^u H + \nabla_\Gamma \mathbf{T}^u.$$

We thus obtain the following evolution equations:

Problem 4: (dynamics with local inextensibility constraint)

$$\partial_t u + \mathbf{T} \cdot \nabla_\Gamma u \;=\; \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \tag{31}$$

$$V = -\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} + \lambda_{\text{Inex}} H \right) \tag{32}$$

$$\mathbf{T} = -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} + \nabla_\Gamma \lambda_{\text{Inex}} \right). \tag{33}$$

$$\nabla_\Gamma \cdot (\beta_T \nabla_\Gamma \lambda_{\text{Inex}}) - \beta_V \lambda_{\text{Inex}} H^2 = -\nabla_\Gamma \cdot \left(\beta_T (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} \right) + \beta_V \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} - uH \frac{\delta E}{\delta u} \right) H \tag{34}$$

In Eq. (31) we have used, that the velocity is divergence free. Note that the local Lagrange multiplier λ_{Inex} fullfills an elliptic partial differential equation on an evolving surface.

4.3.4 *Volume and Area Constraint*

The dynamics in the case of a global area and volume constraint is now simply obtained by using both Lagrange multipliers λ_{Area} and λ_{Vol} of Problem 2 and Problem 3 and adding both constraints to the energy to obtain the Lagrangian

$$L[u, \Gamma, \lambda_{\text{Area}}] = E[u, \Gamma] - \lambda_{\text{Area}}(t)\, (\text{Area}(t) - \text{Area}(0)) - \lambda_{\text{Vol}}(t)\, (\text{Vol}(t) - \text{Vol}(0)).$$

leading to

$$V = V^u + \beta_V(\lambda_{\text{Vol}} + \lambda_{\text{Area}} H)$$

$$\mathbf{T} = \mathbf{T}^u$$

Using $\int_\Gamma V\,dA = 0$ and $\int_\Gamma HV\,dA = 0$, the multipliers have to be determined from the linear system

$$\lambda_{\text{Vol}} \int_\Gamma \beta_V\,dA + \lambda_{\text{Area}} \int_\Gamma \beta_V\,dA = \int_\Gamma \beta_V V^u\,dA$$

$$\lambda_{\text{Vol}} \int_\Gamma \beta_V H\,dA + \lambda_{\text{Area}} \int_\Gamma \beta_V H^2\,dA = \int_\Gamma \beta_V V^u H\,dA.$$

We note, that in the case of constant β_V, the first of the two above equations may be used to eliminate λ_{Vol} by expressing λ_{Vol} in terms of λ_{Area}.

We thus obtain the following evolution equations:

Problem 5: (dynamics with volume and area constraint)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) - uVH = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \tag{35}$$

$$V = -\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} - \lambda_{\text{Vol}} - \lambda_{\text{Area}} H \right) \tag{36}$$

$$\mathbf{T} = -\beta_T \left((\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \tag{37}$$

$$\lambda_{\text{Vol}} \int_\Gamma \beta_V\,dA + \lambda_{\text{Area}} \int_\Gamma \beta_V H\,dA = \int_\Gamma \beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} \right) dA \tag{38}$$

$$\lambda_{\text{Vol}} \int_\Gamma \beta_V H\,dA + \lambda_{\text{Area}} \int_\Gamma \beta_V H^2\,dA = \int_\Gamma H\beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} \right) dA \tag{39}$$

The Lagrange multiplier equations make the system of equations again nonlocal.

4.3.5 *Volume and Local Inextensibility Constraint*

Following the same lines as in the derivation of Problem 5, combining the two constraints of volume and local inextensibility leads to

$$V = V^u + \beta_V(\lambda_{\text{Vol}} - \lambda_{\text{Ines}} H)$$

$$\mathbf{T} = \mathbf{T}^u - \beta_V \nabla_\Gamma \lambda_{\text{Ines}}$$

The Lagrange multipliers are then obtained by plugging these equations into the constraint equations $\int_\Gamma V\,dA = 0$ and $-VH + \nabla_\Gamma \cdot \mathbf{T} = 0$. This leads to

Problem 6: (dynamics with volume and local inextensibility constraint)

$$\partial_t u + \mathbf{T}\cdot\nabla_\Gamma u = \nabla_\Gamma\cdot\left(\beta_u\nabla_\Gamma\frac{\delta E}{\delta u}\right) \tag{40}$$

$$V = -\beta_V\left(\mathbf{n}\cdot\frac{\delta E}{\delta\Gamma} - uH\,\frac{\delta E}{\delta u} - \lambda_{\text{Vol}} + \lambda_{\text{Inex}}H\right) \tag{41}$$

$$\mathbf{T} = -\beta_T\left((\mathbf{I}-\mathbf{n}\otimes\mathbf{n})\frac{\delta E}{\delta\Gamma} + u\nabla_\Gamma\frac{\delta E}{\delta u} + \nabla_\Gamma\lambda_{\text{Inex}}\right). \tag{42}$$

$$\lambda_{\text{Vol}} = \frac{\int_\Gamma\beta_V\left(\frac{\delta E}{\delta\Gamma}\cdot\mathbf{n} - uH\,\frac{\delta E}{\delta u} + \lambda_{\text{Inex}}H\right)dA}{\int_\Gamma\beta_V\,dA} \tag{43}$$

$$\nabla_\Gamma\cdot(\beta_T\nabla_\Gamma\lambda_{\text{Inex}}) - \beta_V\lambda_{\text{Inex}}H^2 - \beta_V\lambda_{\text{Vol}} = \nabla_\Gamma\cdot\left(-\beta_T(\mathbf{I}-\mathbf{n}\otimes\mathbf{n})\frac{\delta E}{\delta\Gamma} + u\nabla_\Gamma\frac{\delta E}{\delta u}\right) - \beta_V\left(\mathbf{n}\cdot\frac{\delta E}{\delta\Gamma} - uH\,\frac{\delta E}{\delta u}\right)H \tag{44}$$

We thus have to deal with a nonlocal elliptic partial differential equation on an evolving surface in order to determine the Lagrange multipliers.

4.3.6 *Further Formulations*

All constraints can be incorporated along the same lines also within the alternative formulation based on the splitting (13) introduced in Remark 1. In a similar way combinations of area and volume constraints can also be formulated based on the model introduced in Remark 2.

4.4 Coupling with Fluid Flow

The interaction of the vesicle with a viscous fluid in- and outside of the vesicle is of interest. It is experimentally known that e.g., red blood cells may align under shear flow at moderate shear rates, however if the blood is diluted with plasma the same cells undergo a tumbling process. A similar influence is observed also for vesicles [34]. We therefore incorporate a viscous fluid flow in the dynamical description of two-component vesicles. Instead of the evolution law (15) and (16) or its constraint counterparts we have to solve a Navier-Stokes or Stokes problem in the time-dependent domain inside and outside of the vesicle with a jump condition for the stress tensor $\sigma = -p\mathbf{I} + \nu\mathbf{D}$, with pressure p, deformation tensor $\mathbf{D} = (\nabla\mathbf{v} + \nabla\mathbf{v}^T)$, fluid velocity v and viscosity ν, and a continuity condition for the velocity. The jump condition is a generalized Laplace-Young condition of the form

$$[\sigma\cdot\mathbf{n}]_\Gamma = -\mathbf{F},$$

where the force $\mathbf{F}$ is obtained by energy variation and thermodynamic consistency. The fluid flow inside and outside of the vesicle

$$\rho\,(\partial_t\mathbf{v} + (\mathbf{v}\cdot\nabla)\,\mathbf{v}) - \nabla\cdot\sigma = \mathbf{b} \tag{45}$$

$$\nabla\cdot\mathbf{v} = 0. \tag{46}$$

with a density ρ and a body force $\mathbf{b}$. Eqs. (45), (46) are supplemented by a farfield boundary condition $\mathbf{v} = \mathbf{v}_\infty$. The volume is now conserved as a result of the incompressibility condition of the fluid.

We thus obtain the following conditions on Γ.

Problem 7: (unconstrained evolution with fluid flow)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) + uVH = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right)$$

$$[\sigma \cdot \mathbf{n}]_\Gamma = \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} \right) \mathbf{n} + (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u}$$

$$[\mathbf{v}]_\Gamma = 0.$$

If we in addition incorporate area conservation we obtain

Problem 8: (area constrained evolution with fluid flow)

$$\partial_t u + \nabla_\Gamma \cdot (u\mathbf{T}) + uVH = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right)$$

$$[\sigma \cdot \mathbf{n}]_\Gamma = \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} + \lambda_{\text{Area}} H \right) \mathbf{n} + (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u}$$

$$[\mathbf{v}]_\Gamma = 0.$$

The Lagrange multiplier λ_{Area} is now a functional of the fluid velocity $\mathbf{v}$ and is obtained by requiring $\int_\Gamma H\mathbf{v} \cdot \mathbf{n}\, dA = 0$ where $\mathbf{v}$ is the full solution of the Navier-Stokes equation.

If we consider the local inextensibility constraint the problem reads

Problem 9: (local inextensibility constraint evolution with fluid flow)

$$\partial_t u + \mathbf{T} \cdot \nabla_\Gamma u = \nabla_\Gamma \cdot \left(\beta_u \nabla_\Gamma \frac{\delta E}{\delta u} \right)$$

$$[\sigma \cdot \mathbf{n}]_\Gamma = \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} - uH \frac{\delta E}{\delta u} + \lambda_{\text{Inex}} H \right) \mathbf{n} + (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} + \nabla_\Gamma \lambda_{\text{Inex}}$$

$$[\mathbf{v}]_\Gamma = 0.$$

The Lagrange multiplier λ_{Inex} is again a functional of the fluid velocity $\mathbf{v}$ and is obtained by requiring $-\mathbf{v} \cdot \mathbf{n}H + \nabla_\Gamma((\mathbf{I} - \mathbf{n} \otimes \mathbf{n})\mathbf{v}) = 0$.

5. EXAMPLES

5.1 Single-Component Vesicle with Volume and Local Inextensibility Constraint

As a first example we consider the case of a one component vesicle (i.e., $u = 1$), with volume and local inextensibility constraint, as in Problem 6. Moreover, we restrict to the normal bending energy, i.e.

$$E[\Gamma] = \frac{1}{2} b_N \int_\Gamma (H - H_0)^2 \, dA.$$

In this case, the functional derivative of E is given by (see Appendix C, (64))

$$\frac{\delta E}{\delta \Gamma} = b_N(\Delta_\Gamma((H - H_0))\mathbf{n} + (H - H_0)\|S\|^2\mathbf{n} - \frac{1}{2}(H - H_0)^2 H\mathbf{n}).$$

In particular $\frac{\delta E}{\delta \Gamma}$ is in normal direction. Assuming also, that β_V and β_T are constant, Problem 6 simplifies to

$$V = -\beta_V\left(\mathbf{n}\cdot\frac{\delta E}{\delta \Gamma} - \lambda_{\text{Vol}} + \lambda_{\text{Inex}} H\right)$$

$$\mathbf{T} = -\beta_T \nabla_\Gamma \lambda_{\text{Inex}}$$

$$\lambda_{\text{Vol}} = \frac{\int_\Gamma \left(\frac{\delta E}{\delta \Gamma}\cdot\mathbf{n} + \lambda_{\text{Inex}} H\right) dA}{\int_\Gamma dA}$$

$$\beta_T \Delta_\Gamma \lambda_{\text{Inex}} - \beta_V \lambda_{\text{Inex}} H^2 - \beta_V \beta_{\text{Vol}} = -\beta_V H\left(\frac{\delta E}{\delta \Gamma}\cdot\mathbf{n}\right),$$

which is a highly nonlinear geometric evolution equation of 4th order for the normal velocity (related to Willmore flow), which is coupled to a non-local elliptic partial differential equation of 2nd order for the Lagrange multiplier λ_{Inex} on the evolving surface and a 1st order equation for the tangential velocity $\mathbf{T}$.

A parametric finite element front tracking approach is used to solve the above equations. The discretization is obtained from the numerical approach for Willmore flow in [48], which is extended to deal with the spontaneous curvature and the non-local elliptic PDE on the evolving surface to compute the Lagrange multiplier. Briefely the numerical approach consists of (1) solve geometric evolution equation for V^u, (2) solve elliptic equation on the surface for λ_{Inex} using V^u, (3) calculate λ_{Vol} using V^u and λ_{Inex}, (4) solve geometric evolution equation for V using λ_{Vol} and λ_{Inex}, (5) solve for $\mathbf{T}$ using λ_{Inex} and (6) update the interface. The tangential velocity allows to maintain a regular mesh without further artificial mesh modifications. Fig. 1 shows the evolution to a discocyte shape for $H_0 = 0$, $b_N = 1$, $\beta_V = 1$ and $\beta_T = 1$.

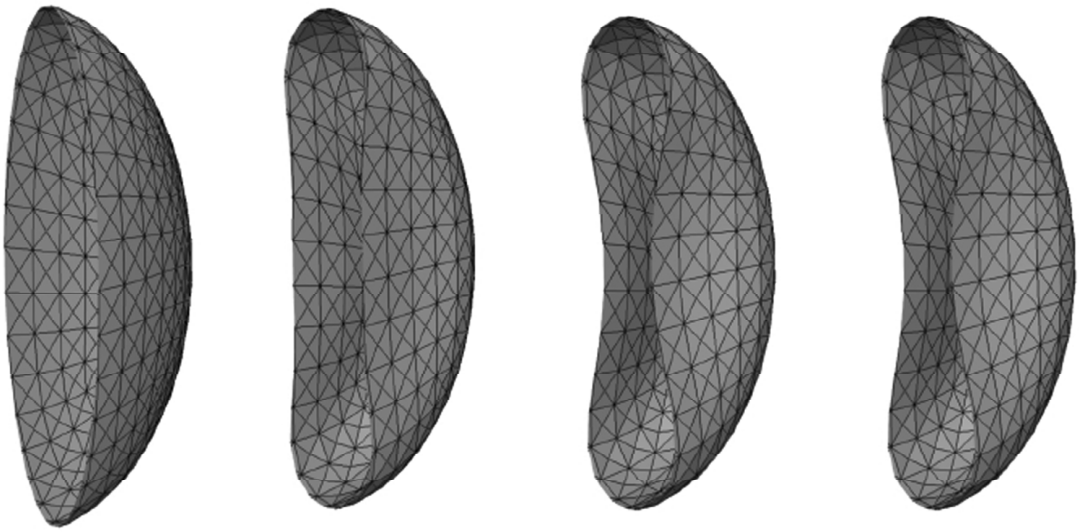

Figure 1: Evolution of a Vesicle with Constant Lipid Concentration Under Volume and Local Inextensibility Constraint

5.2 Single-Component Vesicle with Volume and Global Area Constraint

With the same assumptions as before Problem 5 simplifies to

$$V = -\beta_V \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} - \lambda_{\text{Vol}} - \lambda_{\text{Area}} H \right)$$

$$\lambda_{\text{Vol}} \int_\Gamma \eta_V \, dA + \lambda_{\text{Area}} \int_\Gamma \beta_V H \, dA = \int_\Gamma \beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} \right) dA$$

$$\lambda_{\text{Vol}} \int_\Gamma \beta_V H \, dA + \lambda_{\text{Area}} \int_\Gamma \beta_V H^2 dA = \int_\Gamma H \beta_V \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} \right) dA$$

which is again a highly nonlinear geometric evolution equation of 4th order for the normal velocity (related to Willmore flow), which is coupled to a non-local algebraic system for the Lagrange multipliers. We e.g., refer the reader to [4] for a parametric approach for this problem and [57] for a phase field approximation using a penalty approach instead of the Lagrange multipliers. We also consider a phase-field approximation but with the Lagrange multipliers. The system is solved iteratively with a semi-implicit time stepping scheme, treating all non-local components explicitly. Fig. 2 shows the evolution to a discocyte shape for $H_0 = 0$, $b_N = 1$ and $\beta_V = 1$.

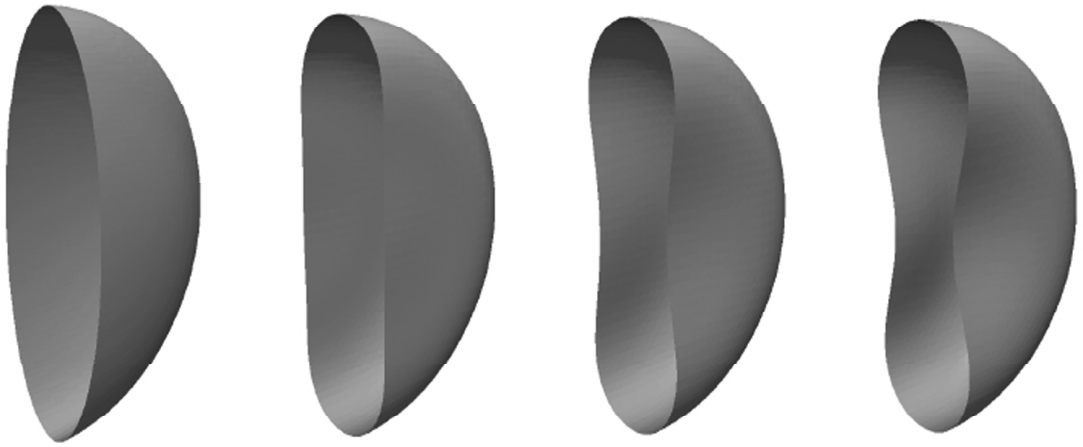

Figure 2: Evolution of a Vesicle with Constant Lipid Concentration Under Volume and Global Area Constraint

5.3 Two-Component Vesicle with Volume and Global Area Constraint

For recent numerical results for Problem 5 we refer to [57] using a phase-field approach and to [21] using front tracking and parametric finite elements. We are not aware of simulation results for Problem 6.

5.4 Single-Component Vesicles with Global Area Constraint and Fluid Flow

Also fluid flow interactions have been considered for single-component vesicles. Under the same assumptions as above Problem 8 reduces to

$$[\sigma \cdot \mathbf{n}]_\Gamma = \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} + \lambda_{\text{Area}} H \right) \mathbf{n}$$

$$[\mathbf{v}]_\Gamma = 0.$$

which serve as boundary conditions for the Navier-Stokes equation. For recent numerical results with flow only in the interior we refer to [8]. Two dimensional simulations have also been considered within a phase field approach, see e.g., [7].

5.5 Two-Component Vesicle with Local Inextensibility Constraint and Fluid Flow

We now consider Problem 9 with a stationary Stokes flow instead of the Navier-Stokes equations. The problem reads in the two fluid phases

$$\nabla \cdot \sigma = 0$$

$$\nabla \cdot \mathbf{v} = 0$$

with a far-field boundary condition $\mathbf{v} = \mathbf{v}_\infty$. We further assume that β_u is constant and use $\nabla_\Gamma \cdot \mathbf{T} - VH = 0$ to regroup terms in (12) such that

$$\frac{d}{dt} E = \int_\Gamma \left[\mathbf{q} \cdot \nabla_\Gamma \frac{\delta E}{\delta u} + V \left(\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} + uH \frac{\delta E}{\delta u} \right) + \mathbf{T} \cdot \left(\frac{\delta E}{\delta \Gamma} + u \nabla_\Gamma \frac{\delta E}{\delta u} \right) \right] dA$$

$$= \int_\Gamma \left[\mathbf{q} \cdot \nabla_\Gamma \frac{\delta E}{\delta u} + V\mathbf{n} \cdot \frac{\delta E}{\delta \Gamma} + \mathbf{T} \cdot \frac{\delta E}{\delta \Gamma} - \mathbf{T} \nabla_\Gamma u \frac{\delta E}{\delta u} - u \frac{\delta E}{\delta u} (\nabla_\Gamma \cdot \mathbf{T} - VH) \right] dA.$$

This allows us to define (by considering in addition the Lagrange multipliers)

$$\partial_t u + \mathbf{T} \cdot \nabla_\Gamma u = \beta_u \nabla_\Gamma \frac{\delta E}{\delta u}$$

$$[\sigma \cdot \mathbf{n}]_\Gamma = \left(\frac{\delta E}{\delta \Gamma} \cdot \mathbf{n} + \lambda_{\text{Inex}} H \right) \mathbf{n} + (\mathbf{I} - \mathbf{n} \otimes \mathbf{n}) \frac{\delta E}{\delta \Gamma} - \nabla_\Gamma u \frac{\delta E}{\delta u} + \nabla_\Gamma \lambda_{\text{Inex}}$$

$$[\mathbf{v}]_\Gamma = 0.$$

which differs from the formulation used in Problem 9. To determine the Lagrange multiplier the constraint $\nabla_\Gamma \cdot \mathbf{T} - VH = 0$ is used with $\mathbf{T}$ and V the tangential and normal components of the Stokes velocity on the membrane. We consider the normal bending and line energy, i.e.

$$E[\Gamma, u] = \frac{1}{2} \int_\Gamma b_N(u) (H - H_0(u))^2 dA + \tau \int_\Gamma \frac{\xi}{2} \|\nabla_\Gamma u\|^2 + \frac{1}{\xi} W(u) dA,$$

for which the variational derivatives are given in Appendix C, (64), (65), (68) and (69).

$$\frac{\delta E}{\delta \Gamma} = \Delta_\Gamma (b(u)(H - H_0(u))) \mathbf{n} + b(u)(H - H_0(u)) \|S\|^2 \mathbf{n}$$

$$- \frac{1}{2} b(u)(H - H_0(u))^2 H \mathbf{n} + \tau\xi \langle \nabla_\Gamma u, (\text{Hess } \mathbf{X}) \nabla_\Gamma u \rangle_\Gamma$$

$$- \tau \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 H \mathbf{n} - \tau \frac{1}{\xi} W(u) H \mathbf{n} \tag{47}$$

$$\frac{\delta E}{\delta u} = b(u)(H - H_0(u))H_0'(u) + \frac{1}{2}b'(u)(H - H_0(u))^2 - \tau\xi\Delta_\Gamma u + \tau\frac{1}{\xi}W'(u). \quad (48)$$

A pseudo-spectral boundary integral method is used to solve the highly nonlinear problem in 2d, see [53] for details.We note that in 2d the variational derivative simplifies and especially the term with Hess **X** vanishes.

Briefely the nonlocal functional dependency of the fluid velocity on λ_{Inex} is solved using an iterative solver. Each iteration thereby requires the solution of the Stokes problem. The preconditioner used is based on a small scale decomposition of the Stokes integral operators.

To compute λ_{Inex} exploit the linearity of Stokes flow and decompose $\mathbf{v} = \mathbf{v}^{\text{Area}} + \mathbf{u}$ with $\mathbf{v}^{\text{Area}} = \mathbf{v}^u + \lambda_{\text{Area}}\mathbf{w}$ the globally area preserving velocity field as in Problem 8 (with Stokes flow), **u** the correction to make this velocity field locally inextensible, $\mathbf{v}^u$ the unconstrained fluid velocity as obtained in Problem 7 (with Stokes flow), **w** the solution of eqs. (45) and (46) with jump conditions $[\sigma \cdot \mathbf{n}]_\Gamma = H\mathbf{n}$ and $[\mathbf{w}]_\Gamma = 0$. As the last problem is independent of u it can be computed first and the obtained velocity **w** can be used to solve Problem 8 (with Stokes flow) with $\mathbf{v}^{\text{Area}} = \mathbf{v}^u + \lambda_{\text{Area}}\mathbf{w}$ in the evolution equation for u, with λ_{Area} obtain form $\int_\Gamma H(\mathbf{v}^u + \lambda_{\text{Area}}\mathbf{w}) \cdot \mathbf{n}\, dA = 0$

$$\lambda_{\text{Area}} = -\frac{\int_\Gamma H\mathbf{v}^u \cdot \mathbf{n} dA}{\int_\Gamma H\mathbf{w} \cdot \mathbf{n} dA}.$$

To obtain the correction u we solve Eqs. (45) and (46) with jump conditions $[\sigma \cdot \mathbf{n}]_\Gamma = \nabla_\Gamma(\lambda_{\text{Inex}} - \lambda_{\text{Area}})$ and $[\mathbf{u}]_\Gamma = 0$. Together with the constraint written as $-\mathbf{u} \cdot \mathbf{n}H + \nabla_\Gamma((\mathbf{I} - \mathbf{n} \otimes \mathbf{n})\mathbf{u}) = \mathbf{v}^{\text{Area}} \cdot \mathbf{n}H - \nabla_\Gamma \cdot ((\mathbf{I} - \mathbf{n} \otimes \mathbf{n})\mathbf{v}^{\text{Area}})$ we obtain a nonlocal system for λ_{Inex}.

Figure 3 Shows the influence of the surface phases on the tumbling of a two-component vesicle with 30-70 mixture under an extensional flow using $b_N = (1 - u) + 0.5u$, $H_0 = 5(1 - u) + 0.1u$, $b_G = 0$, $\gamma = 0$, $\beta_u = 1$, $\nu = 1$ and $\mathbf{v} = (-5x, 5y)$. The initial vesicle is defined by $x(\theta, 0) = 0.1 \cos(\theta)$ and $y(\theta, 0) = \sin(\theta)$, with an initial concentration $u(\theta, 0) = 0.3 + 0.001(\cos(\theta) + \cos(3\theta) + \cos(4\theta))$ for $\theta \in [0, 2\pi]$. We further define $\mathbf{v}_\infty = (25y, 0)$, diffuse interface width $\xi = 0.1$ and line tension $\tau = 100$.

6. CONCLUSIONS

We have derived thermodynamically consistent models for two-component vesicles from a free energy which accounts for bending, surface tension and phase separation. The basic ingredients were mass conservation and energy dissipation. The resulting system of equations couples higher order convection-diffusion equations of Cahn-Hilliard type on an evolving surface to the geometric evolution of the surface, which is related to Willmore flow. The incorporation of constraints on volume and area or local inextensibility couple the system of equations to additional non-local relations. Instead of the geometric evolution the evolution of the vesicle can also be described through an interaction with a viscous flow field inside and outside of the surface. This requires the solution of a Navier-Stokes or Stokes equation with higher order jump conditions for the stress tensor. The model derivation is supplemented with numerical simulations. The derived models can easily be extended to the case of multiple (more than two) components. Further extensions might consider the effect of surface viscosity to account for the fluid like properties of the membrane [22, 9, 45]. The applicability of the approach for cell membranes can only be qualitatively. A quantitative treatment would require to consider additional effects, such as thermal fluctuations, membrane bound protein or interactions with the cytoskeleton. For discussions on modeling differences between vesicles and cell membranes we refer to [23, 24, 20, 59].

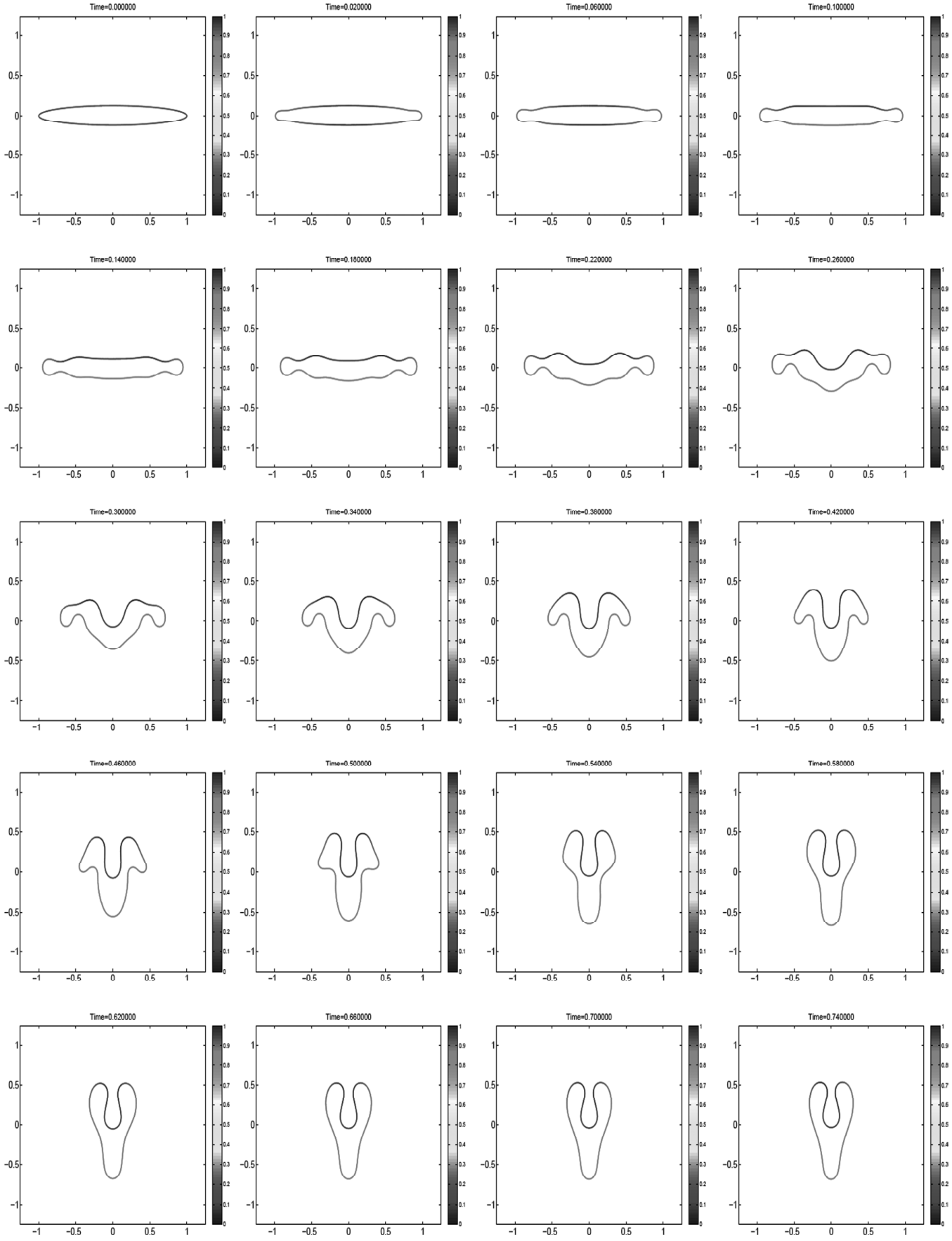

Figure 3: Evolution of a Vesicle with an Initially Mixed Lipid Concentration Under the Influence of an Extensional Flow and Local Inextensibility Constraint

A. Differential Geometry

Although our object of interest is a moving surface $\Gamma = \Gamma(t) \subset \mathbb{R}^3$, we will neglect the time dependence of Γ in the following, where we first introduce some basic differential geometric notations and recall some basic identities, before we compute variational derivatves of the energies introduced in section 3.2, equation (4). Although all notations and results in Appendix A and Appendix C are valid for arbitrary dimensions, we restrict ourselves to the case of twodimensional surfaces.

We assume that Γ is a smooth, closed two-dimensional surface without boundary and the boundary $\Gamma = \partial\Omega_{\text{int}}$ of a bounded, connected, open domain $\Omega_{\text{int}} \subset \mathbb{R}^3$. Furthermore, we assume that Γ is given by a smooth mapping

$$\mathbf{X} : \Omega \subset \mathbb{R}^2 \to \mathbb{R}^3, \qquad \mathbf{X} = \mathbf{X}(z_1, z_2).$$

The Euclidean scalar product on $\mathbb{R}^3$ will be denoted by $x \cdot y = \sum_i x_i y_i$. Derivatives (with respect to the parametrization) are denoted by $\mathbf{X}_i := \frac{\partial \mathbf{X}}{\partial z_i}$. The tangent space $\mathbf{T}_p\Gamma$ of the surface Γ at the point $p = \mathbf{X}(z_1, z_2) \in \Gamma$ is spanned by the tangent vectors $\mathbf{X}_1$, $\mathbf{X}_2$. Moreover, the inner normal of Γ is denoted by $\mathbf{n}$.

Next we recall the definition of the first and the second fundamental form on Γ. The first fundamental form g, also called the metric on Γ, defines a scalar produkt on each tangent space $\mathbf{T}_p\Gamma$ and is taken to be the restriction of the standard scalar produkt on $\mathbb{R}^3$

$$g_p(u, v) = u \cdot v, \qquad u, v \in \mathbf{T}_p\Gamma.$$

Here and in the following, the subscript p will be suppressed and we will use the following notation: for $u = u_i \mathbf{X}_i$, $v = v_i \mathbf{X}_i$, where here and in the following the summation over repeated indices is understood, we write

$$g(u, v) = \langle u, v \rangle_\Gamma = g_{ij} u_i v_j, \qquad \text{where} \quad g_{ij} = g(\mathbf{X}_i, \mathbf{X}_j).$$

Moreover, upper indices denote the inverse $(g_{ij})^{-1} = (g_{ij})$. The norm on Γ is thus defined through the following norm in each tangent space $\mathbf{T}_p\Gamma : \|u\|_\Gamma := \sqrt{\langle u, u \rangle_\Gamma}$. For $X, Y \in (\mathbf{T}_p\Gamma)^3$ we define

$$\langle X, Y \rangle_{\Gamma, \mathbb{R}^3} := \sum_{i=1}^{3} \langle X^i, Y^i \rangle_\Gamma .$$

In a similar way, the second fundamental form is given by $h_{ij} = II(\mathbf{X}_i, \mathbf{X}_j) = -\mathbf{n}_i \cdot \mathbf{X}_j$ with $II(u, v) = h_{ij} u_i v_j$. This may also be expressed in terms of the shape operator $S : \mathbf{T}_p\Gamma \to \mathbf{T}_p\Gamma$ as $II(u, v) = g(Su, v)$, and therefore S is given by $S_{ij} = g^{ik} h_{kj}$. This immidiately implies the Weingarten equations $\mathbf{n}_i = -S_{ij} \mathbf{X}_i$. The norm of S is defined through $\|S\| = \sqrt{tr(SS^T)} = \sqrt{S_{ij} S_{ji}}$.

The mean curvature we define through $H = trS = \Sigma_{i=1}^{2} \kappa_i$, with κ_i the principal curvatures. Note that $\|S\|^2 = H^2 - 2K$, where K is the Gaussian curvature. The Christoffel symbols are given by $\Gamma_{ij}^k = \frac{1}{2} g^{kl}(\partial_i g_{jl} + \partial_j g_{il} - \partial_l g_{ij})$.

We use the surface Laplacian $\Delta_\Gamma = g^{ij}\partial_{ij} - g^{ij}\Gamma_{ij}^k \partial_k$ and the surface gradient $\nabla_\Gamma = g^{ij} \mathbf{X}_i \partial_j$ and the following identities see [58] and [48]

$$\Delta_\Gamma \mathbf{X} = H\mathbf{n}, \tag{49}$$

$$\langle \nabla_\Gamma \mathbf{X}, \nabla_\Gamma u \rangle_\Gamma = \nabla_\Gamma u = g^{ij} \partial_i u \, \mathbf{X}_j \tag{50}$$

and

$$\Delta_\Gamma \mathbf{n} = -\|S\|^2 \mathbf{n} - \nabla_\Gamma H, \tag{51}$$

respectively.

Furthermore, we denote the Riemannian connection by D. The Hessian Hess $f : \mathbf{T}\Gamma \to \mathbf{T}\Gamma$ of a function $f : G \to \mathbb{R}$ is defined as the covariant derivative of the gradient of f

$$(\text{Hess } f)Y := D_Y \nabla_\Gamma f \tag{52}$$

for a vector field $Y \in \mathbf{T}\Gamma$. Then one obtains

$$\langle \nabla_\Gamma \langle \nabla_\Gamma f, \nabla_\Gamma u\rangle_\Gamma, \nabla_\Gamma w\rangle_\Gamma = \langle (\text{Hess } f)\nabla_\Gamma w, \nabla_\Gamma u\rangle_\Gamma + \langle \nabla_\Gamma f, (\text{Hess } u)\nabla_\Gamma w\rangle_\Gamma \tag{53}$$

for functions $f, u, w : \Gamma \to \mathbb{R}$. In addition, the Hessian is symmetric

$$\langle (\text{Hess } f)X, Y\rangle_\Gamma = \langle X, (\text{Hess } f)Y\rangle_\Gamma. \tag{54}$$

B. Motivation for Diffuse Interface Approximations

Here we give a motivation for the used diffuse interface approximations of the line energy and the Gaussian bending energy. We start with

- the line energy

$$E_T = \int_\Gamma \tau \left(\frac{\xi}{2} \|\nabla_\Gamma u\|^2 + \frac{1}{\xi} W(u) \right) dA.$$

The energy can be viewed as a Ginzburg-Landau type energy defined on a surface. Used within a conserved evolution for u on a stationary surface the equation reads

$$\partial_t u = \Delta_\Gamma \mu$$

$$\mu = \tau \left(-\xi \nabla_\Gamma u + \frac{1}{\xi} W'(u) \right)$$

which is a Cahn-Hilliard equation on a stationary surface. Its counterpart in $\mathbb{R}^2$ is known to reduce for $\xi \to 0$ to the Mullins-Sekerka problem, see [46]. If we assume that this limit also holds on a surface, we obtain the surface Mullins-Sekerka problem

$$\text{DG } m = 0 \quad \text{on} \quad \Gamma \setminus C$$

$$\mu = \tau \kappa_g \quad \text{on} \quad C$$

$$v_g = \frac{1}{2} \left[\frac{\partial \mu}{\partial \mathbf{m}} \right] \quad \text{on} \quad C,$$

with κ_g the geodesic curvature of the curve C, v_g the intrinsic normal velocity of the curve C and $\mathbf{m}$ the conormal to the curve C. The equations can also be derived directly from the line energy $E_T = \int_C \tau \, ds$ introduced in [33], which is the motivation for using the line energy above.

The Gaussian bending energy has not been analyzed before using a diffuse interface approximation. The motivation for

- the Gaussian bending energy

$$E_{G,\xi} = \frac{1}{\xi} \int_\Gamma [b_G] \left(-\xi \Delta_\Gamma u + \frac{1}{\xi} W'(u) \right) \sqrt{2W(u)}\, dA$$

results by analogy from a phase-field approximation for theWillmore energy. In [38, 17, 47] it is shown that $E_{\text{Willmore}} = \frac{1}{2} \int_C H^2 dA$ can be approximated by

$$E_{\text{Willmore, diffuse}} = \frac{1}{2}\frac{1}{\xi}\int_{\tilde{\Omega}}\left(-\xi\Delta u + \frac{1}{\xi}W'(u)\right)^2 dx$$

with a phase-field variable u, a double well potential $W(u) \sim (1+u)^2(1-u)^2$ and a domain $\tilde{\Omega} \subset \mathbb{R}^3$ including Γ. This result was extended in [18] to approximate $E_{\text{Helfrich}} = \frac{1}{2}\int_\Gamma (H - H_0)^2 dA$ by

$$E_{\text{Helfrich, diffuse}} = \frac{1}{2}\frac{1}{\xi}\int_{\tilde{\Omega}}\left(-\xi\Delta u + \frac{1}{\xi}W'(u) + \sqrt{2W(u)}\,H_0\right)^2 dx\,.$$

With $H_0 = -1$, the Helfrich-energy contains the term $\int_\Gamma H\,dA$. Using the known diffuse interface approximations from the remaining terms $\frac{1}{2}\int_\Gamma H^2 dA$ and $\frac{1}{2}\int_\Gamma 1\,dA$ the diffuse interface approximation for $\int_\Gamma H\,dA$ must read

$$E_{\text{curvature, diffuse}} = \int_{\tilde{\Omega}}\left(-\xi\Delta u + \frac{1}{\xi}W'(u)\right)\sqrt{2W(u)}\,dx$$

Assuming that this result can be carried over to curves on surfaces, $E_{G,\,\xi}$ gives a diffuse interface approximation for the Gaussian bending energy $E_G = \int_C [b_G]\,\kappa_g\,ds$.

Neither formal nor rigorous results for the convergence of these diffuse interface energies on surface to their sharp interface counterparts for curves on surfaces are known. So the model is based on the assumption that results known in $\mathbb{R}^2$ can be carried over to surfaces by simply replacing the operators by their geometric counterparts.

C. Variational Derivative

We provide the variational derivatives of E with respect to Γ and u. The calculations closely follow the approach in [58]. Similar results can be found in [21, 1]. The variation with respect to Γ we denote by $\bar{\mathbf{X}}(z_1, z_2, \varepsilon) := \mathbf{X}(z_1, z_2) + \varepsilon\Phi(z_1, z_2)$ with a vector valued function $\Phi : \Omega \to \mathbb{R}^3$ and $\varepsilon \in I$ for some open interval $I \subset \mathbb{R}$ with $0 \in I$. Furthermore we will use the operator $\delta := \frac{d}{d\varepsilon}|_{\varepsilon=0}$. For variations with respect to u we use $\phi : \Gamma \to \mathbb{R}$ and $\bar{u} = u + \varepsilon\phi$. Accordingly, all quantities depending on one of the previous variations are denoted in the same way.

In order to compute the variation of the energy we need the following variations, where we use the general assumption that u is extended as a constant in the normal direction.

Lemma 1:

$$\delta(d\bar{A}) = \langle\nabla_\Gamma\Phi, \nabla_\Gamma\mathbf{X}\rangle_{\Gamma,\mathbb{R}^3} dA, \tag{55}$$

$$\delta(\bar{g}^{ij}) = -g^{ki}(\partial_k\Phi\cdot\partial_l\mathbf{X} + \partial_l\Phi\cdot\partial_k\mathbf{X})g^{lj}, \tag{56}$$

$$\delta\bar{H} = 2\langle\nabla_\Gamma\Phi, \nabla_\Gamma\mathbf{n}\rangle_{\Gamma,\mathbb{R}^3} + \Delta_\Gamma\Phi\cdot\mathbf{n} = \Delta_\Gamma(\Phi\cdot\mathbf{n}) - \Phi\cdot\Delta_\Gamma\mathbf{n}, \tag{57}$$

$$\delta\bar{u} = \Phi\cdot\langle\nabla_\Gamma u, \nabla_\Gamma\mathbf{X}\rangle_\Gamma = \Phi\cdot\nabla_\Gamma u. \tag{58}$$

Proof: We only sketch the proof and follow the calculations in [58]. We use the summation convention and write

$$\Phi = g^{ij}\Phi\cdot\mathbf{X}_i\mathbf{X}_j + \Phi\cdot\mathbf{n}\mathbf{n}. \tag{59}$$

One essential result that is needed is the variation of the metric

$$\delta\bar{g}^{ij} = \partial_i\Phi\cdot\partial_j\mathbf{X} + \partial_j\Phi\cdot\partial_i\mathbf{X}. \tag{60}$$

For a differentiable matrix $A = A(\varepsilon) \in \mathbb{R}^{d\times d}$ with some dimension $d \in \mathbb{N}$ one has

$$\frac{d}{d\varepsilon} \det A(\varepsilon)\Big|_{\varepsilon=0} = \det A(0)\, tr\left(A(0)^{-1} \frac{d}{d\varepsilon} A(\varepsilon)\Big|_{\varepsilon=0} \right).$$

Because $dA = \sqrt{\det(g_{ij})}\, dz$ we get

$$\begin{aligned} 2\, dA\, \delta(d\bar{A}) &= \delta(\det \bar{g}_{ij})\, dz = \det(g_{ij})\, g^{ij} \delta \bar{g}_{ij}\, dz = g^{ij}(\partial_i \Phi \cdot \partial_j \mathbf{X} + \partial_j \Phi \cdot \partial_i \mathbf{X})\, dA \\ &= 2\langle \nabla_\Gamma \Phi, \nabla_\Gamma \Phi \rangle_{\Gamma, \mathbb{R}^3}\, dA, \end{aligned}$$

which yields (55). The proof of (56) easily follows from (60). In order to obtain

$$\delta(\bar{H}) = \delta(\bar{g}^{ij}\bar{h}_{ij}) = \delta(\bar{g}^{ij})\, h_{ij} + g^{ij}\delta(\bar{h}_{ij})$$

one needs to compute

$$\delta \bar{h}_{ij} = \delta(\partial_{ij}\bar{\mathbf{X}} \cdot \bar{\mathbf{n}}) = \delta(\partial_{ij}\bar{\mathbf{X}}) \cdot \mathbf{n} + \partial_{ij}\mathbf{X} \cdot \delta(\bar{\mathbf{n}}).$$

After some calculations one obtains

$$g^{ij}\delta(\partial_{ij}\bar{\mathbf{X}}) \cdot \mathbf{n} = g^{ij}\partial_{ij}\Phi \cdot \mathbf{n}$$

as well as

$$g^{ij}\partial_{ij}\mathbf{X} \cdot \delta(\bar{\mathbf{n}}) = -g^{ij}\Gamma^l_{ij}\partial_l \Phi \cdot \mathbf{n}.$$

Form this we get

$$g^{ij}\delta\bar{h}_{ij} = \Delta_\Gamma \Phi \cdot \mathbf{n}. \tag{61}$$

From (56) one gets

$$\delta(\bar{g}^{ij})\, h_{ij} = -2 g^{lj} S_{kj} \partial_l \Phi \cdot \partial_k \mathbf{X} = 2\langle \nabla_\Gamma \Phi, \nabla_\Gamma \mathbf{X} \rangle_{\Gamma, \mathbb{R}^3},$$

and finally we arrive at (57). The proof of (58) easily follows from (59).

In the following section we compute the variational derivatives of E separately for each contribution E_B, $E_{G,\xi}$, E_S and E_T. Thereby, we consider variations

$$\delta_\Gamma E(\mathbf{X}, u; \Phi) := \frac{d}{d\varepsilon} E(\mathbf{X} + \varepsilon\Phi, u)\big|_{\varepsilon=0} \tag{62}$$

and

$$\delta_u E(\mathbf{X}, u; \phi) := \frac{d}{d\varepsilon} E(\mathbf{X}, u + \varepsilon\phi)\big|_{\varepsilon=0}. \tag{63}$$

C.1 *Normal Bending Energy*

The functional derivative of E_B with respect to Γ reads:

$$\begin{aligned}
\delta_\Gamma E_B(\mathbf{X}, u; \Phi) &= \int_\Gamma b(u)(H - H_0(u))\,\delta\bar{H}\,dA - \int_\Gamma b(u)(H - H_0(u))\,H_0'(u)\,\delta\bar{u}\,dA \\
&\quad + \int_\Gamma \frac{1}{2} b(u)(H - H_0(u))^2\,\delta(d\bar{A}) + \frac{1}{2}\int_\Gamma b'(u)\,\delta\bar{u}\,(H - H_0(u))^2\,dA \\
&= \int_\Gamma b(u)(H - H_0(u))(\Delta_\Gamma(\Phi\cdot\mathbf{n}) - \Phi\cdot\Delta_\Gamma\mathbf{n})\,dA \\
&\quad - \int_\Gamma b(u)(H - H_0(u))\,H_0'(u)\,\nabla_\Gamma u\cdot\Phi\,dA \\
&\quad + \int_\Gamma \frac{1}{2} b(u)(H - H_0(u))^2\,\langle\nabla_\Gamma\Phi, \nabla_\Gamma\mathbf{X}\rangle_{\Gamma,\mathbb{R}^3}\,dA \\
&\quad + \int_\Gamma \frac{1}{2} b'(u)(H - H_0(u))^2\,\nabla_\Gamma u\cdot\Phi\,dA \\
&= \int_\Gamma \Delta_\Gamma(b(u)(H - H_0(u)))\,\Phi\cdot\mathbf{n}\,dA - \int_\Gamma b(u)(H - H_0(u))\,\Phi\cdot\Delta_\Gamma\mathbf{n}\,dA \\
&\quad - \int_\Gamma b(u)(H - H_0(u))\,H_0'(u)\,\Phi\cdot\nabla_\Gamma u\,dA \\
&\quad - \int_\Gamma \frac{1}{2} b(u)(H - H_0(u))^2\,\Phi\cdot\Delta_\Gamma\mathbf{X}\,dA - \int_\Gamma \frac{1}{2} b'(u)(H - H_0(u))^2\nabla_\Gamma u\cdot\Phi\,dA \\
&\quad - \int_\Gamma b(u)(H - H_0(u))\nabla_\Gamma H\ \cdot\Phi\,dA + \int_\Gamma b(u)(H - H_0(u))\,H_0'(u)\nabla_\Gamma u\cdot\Phi\,dA \\
&\quad + \int_\Gamma \frac{1}{2} b'(u)(H - H_0(u))^2\,\nabla_\Gamma u\cdot\Phi\,dA \\
&= \int_\Gamma \Delta_\Gamma(b(u)(H - H_0(u)))\,\Phi\cdot\mathbf{n}\,dA + \int_\Gamma b(u)(H - H_0(u))\|S\|^2\,\Phi\cdot\mathbf{n}\,dA \\
&\quad - \frac{1}{2}\int_\Gamma b(u)(H - H_0(u))^2 H\,\Phi\cdot\mathbf{n}\,dA\,.
\end{aligned}$$

where integration by parts and the identities in Eq. (49)-(51) have been used. Thus we obtain

$$\frac{\delta E_B}{\delta\Gamma} = \Delta_\Gamma(b(u)(H - H_0(u)))\mathbf{n} + b(u)(H - H_0(u))\|S\|^2\,\mathbf{n} - \frac{1}{2} b(u)(H - H_0(u))^2 H\mathbf{n}\,. \tag{64}$$

For $b(u) = 1$ and $H_0(u) = 0$ we obtain the well known variational derivative for the Willmore functional.

The functional derivative of E_B with respect to u reads:

$$\delta_u E_B(\Gamma, u; \phi) = \int_\Gamma \frac{1}{2} b'(u)(H - H_0(u))\,\phi\,dA - \int_\Gamma b(u)(H - H_0(u))\,H_0'(u)\,\phi\,dA\,.$$

We thus obtain

$$\frac{\delta E_B}{\delta u} = \frac{1}{2} b'(u)(H - H_0(u)) - b(u)(H - H_0(u)) H_0'(u). \tag{65}$$

C.2 *Surface Energy*

The functional derivative of E_S with respect to Γ reads

$$\begin{aligned}
\delta_\Gamma E_S(\mathbf{X}, u; \Phi) &= \int_\Gamma \gamma'(u)\,\delta\bar{u}\,dA + \int_\Gamma \gamma(u)\,\delta(d\bar{A}) \\
&= \int_\Gamma \gamma'(u)\nabla_\Gamma u \cdot \Phi\, dA + \int_\Gamma \gamma(u)\langle \nabla_\Gamma \Phi, \nabla_\Gamma \mathbf{X}\rangle_{\Gamma,\mathbb{R}^3}\, dA \\
&= \int_\Gamma \gamma'(u)\nabla_\Gamma u \cdot \Phi\, dA - \int_\Gamma \gamma(u)\Phi \cdot \nabla_\Gamma \mathbf{X}\, dA - \int_\Gamma \gamma'(u)\nabla_\Gamma u \cdot \Phi\, dA \\
&= -\int_\Gamma \gamma(u) H \Phi \cdot \mathbf{n}\, dA,
\end{aligned}$$

which yields

$$\frac{\delta E_S}{\delta \Gamma} = -\gamma(u) H\mathbf{n}. \tag{66}$$

The functional derivative of E_S with respect to u reads

$$\delta_u E_S(\Gamma, u; \phi) = \int_\Gamma \gamma'(u)\phi\, dA.$$

We thus obtain

$$\frac{\delta E_S}{\delta u} = \gamma'(u). \tag{67}$$

C.3 *Line Energy*

We now compute the functional derivative of E_T with respect to Γ, where we assume $\tau = 1$, for simplicity. The energy can be rewritten as

$$E_T = \frac{1}{\xi}\int_\Gamma \frac{\xi^2}{2} g^{ij}\partial_i u\,\partial_j u + W(u)\, dA$$

and we obtain

$$\begin{aligned}
\delta_\Gamma E_T(\mathbf{X}, u; \Phi) = &\int_\Gamma \frac{\xi}{2}\delta(\bar{g}^{ij})\partial_i u\,\partial_j u\, dA + \int_\Gamma \xi g^{ij}\partial_i(\delta\bar{u})\,\partial_j u\, dA + \int_\Gamma \frac{\xi}{2}\|\nabla_\Gamma u\|_\Gamma^2\,\delta(d\bar{A}) \\
&+ \int_\Gamma \frac{1}{\xi} W'(u)\,\delta\bar{u}\, dA + \int_\Gamma \frac{1}{\xi} W(u)\,\delta(d\bar{A})
\end{aligned}$$

$$= -\int_\Gamma \frac{\xi}{2} g^{ki}(\partial_k \Phi \cdot \partial_l \mathbf{X} + \partial_l \Phi \cdot \partial_k \mathbf{X}) g^{lj} \partial_i u \, \partial_j u dA$$

$$+ \int_\Gamma \xi g^{ij} \partial_i (\Phi \cdot \langle \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma) \partial_j u dA + \int_\Gamma \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 \langle \nabla_\Gamma \Phi, \nabla_\Gamma \mathbf{X} \rangle_{\Gamma, \mathbb{R}^3} dA$$

$$+ \int_\Gamma \frac{1}{\xi} W'(u) \Phi \cdot \langle \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma dA + \int_\Gamma \frac{1}{\xi} W(u) \langle \nabla_\Gamma \Phi, \nabla_\Gamma \mathbf{X} \rangle_{\Gamma, \mathbb{R}^3} dA$$

$$= -\int_\Gamma \xi \langle \nabla_\Gamma \Phi, \nabla_\Gamma u \rangle_\Gamma \cdot \langle \nabla_\Gamma \mathbf{X}, \nabla_\Gamma u \rangle_\Gamma dA$$

$$+ \int_\Gamma \xi \langle \nabla_\Gamma (\Phi \cdot \langle \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma), \nabla_\Gamma u \rangle_\Gamma dA$$

$$+ \int_\Gamma \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 \langle \nabla_\Gamma \Phi, \nabla_\Gamma \mathbf{X} \rangle_{\Gamma, \mathbb{R}^3} dA - \int_\Gamma \frac{1}{\xi} W(u) \Phi \cdot \Delta_\Gamma \mathbf{X} dA$$

$$= \int_\Gamma \xi \Phi \cdot \langle \nabla_\Gamma \langle \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma, \nabla_\Gamma u \rangle_\Gamma dA$$

$$- \int_\Gamma \frac{\xi}{2} \Phi \cdot \langle \nabla_\Gamma \|\nabla_\Gamma u\|_\Gamma^2, \nabla_\Gamma \mathbf{X} \rangle_\Gamma dA$$

$$- \int_\Gamma \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 \, H \Phi \cdot \mathbf{n} dA - \int_\Gamma \frac{1}{\xi} W(u) H \Phi \cdot \mathbf{n} \, dA.$$

From this one gets by (53)

$$\frac{\delta E_T}{\delta \Gamma} = \xi \langle \nabla_\Gamma \langle \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma, \nabla_\Gamma u \rangle_\Gamma - \frac{\xi}{2} \langle \nabla_\Gamma \|\nabla_\Gamma u\|_\Gamma^2, \nabla_\Gamma \mathbf{X} \rangle_\Gamma - \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - \frac{1}{\xi} W(u) H\mathbf{n}$$

$$= \xi \langle (\mathrm{Hess}\, u) \nabla_\Gamma u, \nabla_\Gamma \mathbf{X} \rangle_\Gamma + \xi \langle \nabla_\Gamma u, (\mathrm{Hess}\, \mathbf{X}) \nabla_\Gamma u \rangle_\Gamma - \xi \langle (\mathrm{Hess}\, u) \nabla_\Gamma \mathbf{X}, \nabla_\Gamma u \rangle_\Gamma$$

$$- \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - \frac{1}{\xi} W(u) H\mathbf{n}.$$

Therefore, by (54), we obtain the result

$$\frac{\delta E_T}{\delta \Gamma} = \xi \langle \nabla_\Gamma u, (Hess\, \mathbf{X}) \nabla_\Gamma u \rangle_\Gamma - \frac{\xi}{2} \|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - \frac{1}{\xi} W(u) H\mathbf{n}. \tag{68}$$

The functional derivative of E_T with respect to u reads

$$\delta_u E_T(\Gamma, u; \phi) = \int_\Gamma \xi \langle \nabla_\Gamma u, \nabla_\Gamma \phi \rangle_\Gamma + \frac{1}{\xi} W'(u) \phi dA.$$

We thus obtain

$$\frac{\delta E_T}{\delta u} = -\xi \Delta_\Gamma u + \frac{1}{\xi} W'(u). \tag{69}$$

C.4 *Gaussian Bending Energy*

The Gaussian bending energy can be rewritten as

$$\begin{aligned} E_{G,\xi}[\Gamma, u] &= \frac{[b_G]}{\xi}\int_\Gamma \left(-\xi\Delta_\Gamma u + \frac{1}{\xi}W'(u)\right)\sqrt{2W(u)}\,dA \\ &= -[b_G]\int_\Gamma \Delta_\Gamma u\sqrt{2W(u)}\,dA + [b_G]\xi^{-2}\int_\Gamma W'(u)\sqrt{2W(u)}\,dA \\ &= [b_G]\int_\Gamma \|\Delta_\Gamma u\|_\Gamma^2 \frac{W'(u)}{\sqrt{2W(u)}}\,dA + [b_G]\xi^{-2}\int_\Gamma W'(u)\sqrt{2W(u)}\,dA. \end{aligned}$$

We define

$$f(u) := [b_G]\frac{W'(u)}{\sqrt{2W(u)}}, \qquad g(u) := [b_G]\xi^{-2}W'(u)\sqrt{2W(u)} \tag{70}$$

and obtain

$$E_{G,\xi}[\Gamma, u] = \int_\Gamma \|\Delta_\Gamma u\|_\Gamma^2 \, f(u)\,dA + \int_\Gamma g(u)\,dA. \tag{71}$$

Analogously to the previous section, the functional derivative of $E_{G,\xi}$ with respect to Γ reads:

$$\begin{aligned} \delta_\Gamma E_{G,\xi}(\mathbf{X}, u; \Phi) &= \int_\Gamma \delta(\|\overline{u}\|_\Gamma^2)\, f(u)\,dA + \int_\Gamma \|u\|_\Gamma^2 \delta(f(\overline{u}))\,dA + \int_\Gamma \|\nabla_\Gamma u\|_\Gamma^2 \, f(u)\,\delta(d\overline{A}) \\ &\quad + \int_\Gamma \delta(g(\overline{u})\,dA + \int_\Gamma g(u)\,\delta(d\overline{A}) \\ &= -2\int_\Gamma \langle \nabla_\Gamma \Phi, \nabla_\Gamma u\rangle_\Gamma \cdot \langle \nabla_\Gamma \mathbf{X}, \nabla_\Gamma u\rangle_\Gamma \, f(u)\,dA + 2\int_\Gamma \langle \nabla_\Gamma(\Phi\cdot\langle\nabla_\Gamma u, \nabla_\Gamma \mathbf{X}\rangle_\Gamma, \nabla_\Gamma u\rangle_\Gamma \, f(u)\,dA \\ &\quad + \int_\Gamma \|\nabla_\Gamma u\|_\Gamma^2 \, \Phi\cdot f'(u)\langle\nabla_\Gamma u, \nabla_\Gamma \mathbf{X}\rangle_\Gamma\,dA + \int_\Gamma \|\nabla_\Gamma u\|_\Gamma^2 \cdot f(u)\langle\nabla_\Gamma\Phi, \nabla_\Gamma \mathbf{X}\rangle_{\Gamma,\mathbb{R}^3}\,dA \\ &\quad + \int_\Gamma g'(u)\Phi\cdot\langle\nabla_\Gamma u, \nabla_\Gamma \mathbf{X}\rangle_\Gamma\,dA + \int_\Gamma g(u)\langle\nabla_\Gamma\Phi, \nabla_\Gamma \mathbf{X}\rangle_{\Gamma,\mathbb{R}^3}\,dA \\ &= 2\int_\Gamma \Phi\cdot\langle\nabla_\Gamma\langle\nabla_\Gamma u, \nabla_\Gamma u\rangle_\Gamma, \nabla_\Gamma u\rangle_\Gamma \, f(u)\,dA - \int_\Gamma \|\nabla_\Gamma u\|_\Gamma^2 \, f(u)\,\Phi\cdot\Delta_\Gamma \mathbf{X}\,dA \\ &\quad - \int_\Gamma f(u)\Phi\cdot\langle\nabla_\Gamma\|\nabla_\Gamma u\|_\Gamma^2, \nabla_\Gamma \mathbf{X}\rangle_\Gamma\,dA - \int_\Gamma g(u)\,\Phi\cdot\Delta_\Gamma\mathbf{X}\,dA \\ &= 2\int_\Gamma \Phi\cdot\langle\nabla_\Gamma\langle\nabla_\Gamma u, \nabla_\Gamma u\rangle_\Gamma, \nabla_\Gamma u\rangle_\Gamma \, f(u)\,dA - \int_\Gamma \|\nabla_\Gamma u\|_\Gamma^2 \, f(u)\,H\Phi\cdot\mathbf{n}\,dA \\ &\quad - \int_\Gamma f(u)\Phi\cdot\langle\nabla_\Gamma\|\nabla_\Gamma u\|_\Gamma^2, \nabla_\Gamma \mathbf{X}\rangle_\Gamma\,dA - \int_\Gamma g(u)\,H\Phi\cdot\mathbf{n}\,dA. \end{aligned}$$

We thus obtain

$$\begin{aligned} \frac{\delta E_{G,\xi}}{\delta\Gamma} &= 2f(u)\langle\nabla_\Gamma\langle\nabla_\Gamma u, \nabla_\Gamma \mathbf{X}\rangle_\Gamma, \nabla_\Gamma u\rangle_\Gamma - f(u)\langle\nabla_\Gamma\|\nabla_\Gamma u\|_\Gamma^2, \nabla_\Gamma \mathbf{X}\rangle_\Gamma \\ &\quad - f(u)\|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - g(u)H\mathbf{n}, \end{aligned}$$

and again, by (53) and (54), one gets

$$\frac{\delta E_{G,\xi}}{\delta \Gamma} = f(u)\langle \nabla_\Gamma u, (\mathrm{Hess}\,\mathbf{X})\nabla_\Gamma u\rangle_\Gamma - f(u)\|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - g(u)H\mathbf{n}. \tag{72}$$

The variation with respect to u reads

$$\delta_u E_{G,\xi}(\Gamma, u; \phi) = \int_\Gamma f(u)\langle \nabla_\Gamma u, \nabla_\Gamma \phi\rangle_\Gamma dA + \int_\Gamma f'(u)\|\nabla_\Gamma u\|_\Gamma^2 \phi dA + \int_\Gamma g'(u)\phi dA.$$

We thus obtain

$$\frac{\delta E_{G,\xi}}{\delta u} = -\nabla_\Gamma \cdot (f(u)\nabla_\Gamma u) + f'(u)\|\nabla_\Gamma u\|_\Gamma^2 + g'(u). \tag{73}$$

C.5 *Summary*

Now, we can collect all results in order to obtain

$$\begin{aligned}
\frac{\delta E}{\delta \Gamma} &= \Delta_\Gamma(b(u)(H - H_0(u)))\mathbf{n} + b(u)(H - H_0(u))\|S\|^2\mathbf{n} \\
&\quad - \frac{1}{2}b(u)(H - H_0(u))^2 H\mathbf{n} - \gamma(u)H\mathbf{n} + \chi\langle \nabla_\Gamma u, (\mathrm{Hess}\,\mathbf{X})\nabla_\Gamma u\rangle_\Gamma \\
&\quad - \frac{\xi}{2}\|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - \frac{1}{\xi}W(u)H\mathbf{n} + f(u)\langle \nabla_\Gamma u, (\mathrm{Hess}\,\mathbf{X})\nabla_\Gamma u\rangle\Delta_\Gamma \\
&\quad - f(u)\|\nabla_\Gamma u\|_\Gamma^2 H\mathbf{n} - g(u)H\mathbf{n} \\
\frac{\delta E}{\delta u} &= b(u)(H - H_0(u))H_0'(u) + \frac{1}{2}b'(u)(H - H_0(u))^2 + \gamma'(u) \\
&\quad - \xi\nabla_\Gamma u + \frac{1}{\xi}W'(u) - \nabla_\Gamma \cdot (f(u)\nabla_\Gamma u) + f'(u)\|\nabla_\Gamma u\|_\Gamma^2 + g'(u).
\end{aligned}$$

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