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Mini-Workshop: Mathematics of Biological Membranes

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Abstract. The focus of this workshop was the modeling, analysis and numerical simulation of biological membranes. The fundamental models which characterize equilibria are based on bending energies such as the Helfrich energy and suitable generalizations. Talks in the workshop focused on equilibrium shapes of membranes and vesicles, the corresponding relaxation dynamics and the coupling with outer or inner flows.

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Introduction by the Organisers

From the early 1970's on, the understanding of the variety of equilibrium shapes of cell membranes has been a very active field in biophysics. Relaxation dynamics, phase separation on membranes, the coupling to inner/outer flows, and the contribution of domains on membranes to the biological function of cells are still a major focus of research.

The mathematical analysis of the shape and evolution of cell membranes is challenging. Over the last few years we have seen an increasing number of contributions from modelling, analysis and numerics. This workshop reports on recent progress made by the different communities – biophysics, numerics, analysis– and aims at a more complete picture of the relevant questions and adequate techniques.

Variational approaches for the description of equilibrium shapes of membranes are based on phenomenological bending energies, such as proposed by Canham [4] and Helfrich [7]. The Willmore functional is the most important reduction of the Helfrich energy, and understanding its properties is key in the analysis. Recent progress on the Willmore functional and its L^2-gradient flow by Kuwert-Schätzle

[10, 9, 11] and Rivière [12] [Rivière], such as a new formulation of the Euler-Lagrange equation, provide promising techniques to investigate (constrained) minimization problems for different bending energies. (Here and below, names between square brackets refer to workshop presentations).

In many minimization or evolution problems approximations by phase-field models are convenient, since they can deal with topological changes of membranes and phases on the membrane respectively [2, 16, 8]. The connection between the Willmore energy and its phase field approximations are meanwhile better understood [13]. Emphasis in talks has been on thermodynamically consistent phase-field models [Misbah] as well as on their capability to recover singularities in the membrane shapes [Stinner,Rätz].

To find equilibrium shapes a L^2 gradient flow of an appropriate bending energy is the most practical approach. A discussion of more physical models for the relaxation towards an equilibrium has started. One choice is to take the flow of the lipid molecules on the membranes into account [Arroyo]. Other effects have to be considered as well, such as the orientation of molecules in ordered phases [Dolzmann].

Much progress in the numerical simulation of the Willmore flow, of partial differential equations on surfaces, and the coupling of reaction-diffusion processes or inner flows on evovling surfaces with their motion laws has been made [6, 5, 1]. For example, new weak formulations of the gradient flow for the Willmore functional avoid the evaluation of higher derivatives [Dziuk], and the inclusion of tangential motion in the numerical scheme leads to a convenient redistribution of the mesh [Garcke]. It has become feasible to compare equilibrium shapes and phase transition diagrams that have been determined either experimentally or by minimization within some restricted classes of shapes (for instance rotational symmetry) [14, 3] [Svetina].

Cell membranes consist of many different lipid molecules (and other components, such as rafts) and phase separation processes and evolution of phase boundaries are important for the function of a biological cell [Ben Amar]. Variational models account for different physical properties of the distinct phases (for instance different bending or spontaneous curvature constants) and a line tension energy at the boundary between the phases. First simulations of equilibrium configurations and relaxations have been obtained and are becoming more and more efficient [16, 15] [Stinner, Rätz].

The participants of this workshop came from 8 different countries and their expertise was evenly spread over the areas biophysics, analysis, numerics and modeling. On the first day there were three introductory talks on modeling, analysis and numerics respecvtively. On the following days there were more specialized talks, two in the morning and one in the afternoon. The schedule was kept flexible and allowed to have room for extensive and lively discussions which arose after virtually every talk. This was very much appreciated by all participants and was repeatedly reported as a significant advantage of the concept of a miniworkshop in comparison to the regular Oberwolfach meetings.

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Mini-Workshop: Mathematics of Biological Membranes

Table of Contents

Abstracts

Phase-field model for vesicles

Chaouqi Misbah
(joint work with Thierry Biben and Didier Jamet)

A vesicle is a closed membrane made of a phospholipid 2D liquid bilayer. It is viewed as a simple model capable of capturing basic elastic and viscoelastic properties of some real cells, such as red blood cells. Its dynamics drastically differ, for example, from a drop, owing to the membrane inextensibility. A suspension of vesicles can be viewed as a simple model in order to capture essential features of blood flows. The free boundary character (the shape is not fixed) and the vesicle interaction with the flow, together with interactions among vesicles, confer to this problem highly non trivial dynamics, which is a class of complex fluids, for which finding a universal constitutive law continues to pose a formidable challenge. There is a need for development of efficient numerical techniques for solving this multi-scale problem and hoping to capture some elementary processes that would dictate the overall rheology of the suspension. Phase-field approaches may serve as interesting tools to tackle these questions. The models presented here can be used to other situations, like vesicle fusion, fission, membrane instabilities, coupling between membrane and macromolecules on the surface, an so on. The aim of this contribution is to present a first phase-field model and the main quantitative results obtained within this model. A phase field model that is consistent with the second law of thermodynamics is also discussed. This may open some interesting perspectives with regard to numerical schemes, their robustness and efficiency.

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Numerical methods for Willmore flow

Gerhard Dziuk

A new algorithm for the computation of Willmore flow is proposed. The discretization is based on piecewise linear approximations in the context of finite elements. It is formulated with the help of a new formula for the first variation of the Willmore functional

$$W = \frac{1}{2}\int_\Gamma H^2,$$

which does not use the second fundamental form.

Willmore flow is a model problem for higher order geometric flows. It appears in applications such as in material science, imaging, elasticity and as major part of the Helfrich energy in the modelling of cell membranes.

For a history of the numerical treatment of Willmore flow we refer to the publication [3]. A survey concerning the discretization of geometric PDEs and geometric flows can be found in [2]. Error estimates for curves are contained in [1].

1. Notation

For a smooth n-dimensional hypersurface Γ with normal ν we use the notation of the tangential or surface gradient of a function $f : \Gamma \to \mathbb{R}$,

$$\nabla_\Gamma f = \nabla f - \nabla f \cdot \nu\, \nu = \left((\nabla_\Gamma)_1 f, \dots, (\nabla_\Gamma)_{n+1} f \right).$$

Here ∇ denotes the $n+1$-dimensional gradient. The Laplace-Beltrami-Operator on Γ is the tangential divergence of the tangential gradient:

$$\Delta_\Gamma f = \nabla_\Gamma \cdot \nabla_\Gamma f = \sum_{i=1}^{n+1} (\nabla_\Gamma)_i \, (\nabla_\Gamma)_i \, f.$$

If we denote by H the mean curvature, the sum of the principal curvatures, then it is well known that

$$-\Delta_\Gamma \mathrm{id}_\Gamma = H\nu,$$

where $\mathrm{id}_\Gamma(x) = x$ for $x \in \Gamma$. This equation is used to define a weak mean curvature vector in the algorithm, see formula (1) in Lemma 1.

2. First variation and Willmore flow

In [3] the following new formula for the first variation of the Willmore functional was derived. It holds for surfaces Γ for which the appearing quantities exist. In particular we see that the first variation (2) only contains expressions which make sense for piecewise linear (polygonal) surfaces.

Lemma 1. *Let v be the weak mean curvature vector of Γ according to*

$$\int_\Gamma v \cdot \psi + \int_\Gamma \nabla_\Gamma u : \nabla_\Gamma \psi = 0 \qquad \forall \psi \in H^1(\Gamma)^{n+1}. \tag{1}$$

Then the first variation of the Willmore functional at $u = id_\Gamma$ in the direction of $\varphi : \Gamma \to \mathbb{R}^{n+1}$ is given by

$$\begin{aligned} \langle W'(u), \varphi \rangle = -\frac{1}{2} \int_\Gamma |v|^2 \nabla_\Gamma \cdot \varphi - \int_\Gamma \nabla_\Gamma v : \nabla_\Gamma \varphi \\ - \int_\Gamma \nabla_\Gamma \cdot v \nabla_\Gamma \cdot \varphi + \int_\Gamma D(\varphi) \nabla_\Gamma u : \nabla_\Gamma v, \end{aligned} \tag{2}$$

where D is the symmetric tensor $D(\varphi)_{ij} = (\nabla_\Gamma)_i \, \varphi^j + (\nabla_\Gamma)_j \, \varphi^i$, $(i, j = 1, \dots, n+1)$.

Willmore flow is the $L^2(\Gamma)$ gradient flow for the Willmore functional. Lemma 1 allows a weak formulation of this problem. As above we denote by u the identity on Γ. Starting from an initial surface Γ_0 we are looking for a family $\Gamma(t)$, $t \in [0,T)$, with $\Gamma(0) = \Gamma_0$ which moves according to the law

$$\int_\Gamma \dot{u} \cdot \varphi = -\langle W'(u), \varphi \rangle \qquad \forall \varphi.$$

Here $u = \mathrm{id}_\Gamma$ and the dot denotes the material derivative on the moving surface Γ.

3. Algorithm

We formulate the spatially discrete algorithm for Willmore flow.

The smooth surface Γ is approximated by a polyhedral surface Γ_h. It consists of nondegenerate n-simplices T_h in space, (triangles for $n = 2$)

$$\Gamma_h = \bigcup_{T_h \in \mathcal{T}_h} T_h,$$

which form an admissible triangulation $\mathcal{T}_h$. The finite element space is:

$$S_h(t) = \{\eta \in C^0(\Gamma_h(t))^{n+1} |\, \eta|_{T_h} \in \mathbb{P}_1(T_h)^{n+1}, T_h \in \mathcal{T}_h\}.$$

The spatially discrete Willmore flow problem now can be written as follows:

Algorithm 1. *For given initial value $u_{h0} \in S_h(0)$ determine $u_h(\cdot,t)$, $v_h(\cdot,t) \in S_h(t)$ such that $u_h(\cdot,t) = id_{\Gamma_h(t)}$ and*

$$\begin{aligned}\int_{\Gamma_h} \dot{u}_h \cdot \varphi_h - \int_{\Gamma_h} \nabla_{\Gamma_h} v_h : \nabla_{\Gamma_h} \varphi_h + \int_{\Gamma_h} \nabla_{\Gamma_h} v_h : D_h(\varphi_h) \nabla_{\Gamma_h} u_h \\ - \int_{\Gamma_h} \nabla_{\Gamma_h} \cdot v_h \nabla_{\Gamma_h} \cdot \varphi_h - \frac{1}{2} \int_{\Gamma_h} |v_h|^2 \nabla_{\Gamma_h} \cdot \varphi_h = 0 \\ \int_{\Gamma_h} v_h \cdot \psi_h + \int_{\Gamma_h} \nabla_{\Gamma_h} u_h : \nabla_{\Gamma_h} \psi_h = 0\end{aligned}$$

for all $\varphi_h, \psi_h \in S_h(t)$ and for $t \in (0,T]$.

4. Consistency and stability

In [3], Theorem 4, we prove consistency for piecewise linear approximations of the Willmore functional under certain assumptions on the computation of the weak mean curvature vector.

Theorem 5 in [3] contains a stability result for Algorithm 1. It is based on the following energy relation:

Theorem 1. *Assume that u_h, v_h is a solution of Algorithm 1 with initial value $u_h(\cdot,0) = u_{h0}$ and set $\Gamma_{h0} = \Gamma_h(0)$. Then the energy relation*

$$\int_{\Gamma_h} |\dot{u}_h|^2 + \frac{1}{2} \frac{d}{dt} \int_{\Gamma_h} |v_h|^2 = 0$$

holds for all times in $(0,T]$.

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Compactness and lower-semicontinuity of surfaces with bounded curvature energies

Matthias Röger

The equilibrium shapes of many biological cells have been succesfully described by a bending energy introduced by Canham [1] and Helfrich [3]. For bending constants $k_b, k_G > 0$ and a 'sponteous curvature' $H_0 \in \mathbb{R}$ this energy is given by

$$\mathcal{E}_{He}(\Gamma) \;=\; k_b \int_\Gamma (H(x) - H_0)^2 \, d\mathcal{H}^2(x) + k_G \int_\Gamma K(x) \, d\mathcal{H}^2(x)$$

for a closed embedded orientable surface $\Gamma \subset \mathbb{R}^3$ with principle curvatures κ_1, κ_2, mean curvature $H = \kappa_1 + \kappa_2$, and Gaussian curvature $K = \kappa_1 \kappa_2$. The most important reduction of $\mathcal{E}_{He}$ is the Willmore functional

$$\mathcal{W}(\Gamma) \;=\; \int_\Gamma |\vec{H}|^2 \, d\mathcal{H}^2.$$

We are interested in constrained minimization problems and related compactness and lower-semicontinuity questions. Our preference is on techniques that may also allow to treat the convergence of phase field type approximations. We address some basic questions that might be worth to be discussed during the workshop.

Willmore energy with constraints on area and enclosed volume. To obtain the convergence of energy-bounded sequence we will allow generalized surfaces, here *integral varifolds*, and weak topologies.

Lemma 1. *Fix two positive constants $A, V > 0$ and consider a sequence of surfaces $(\Gamma_j)_{j\in\mathbb{N}}$, $\Gamma_j = \partial E_j$ with $E_j \subset \Omega$ an open set of finite perimeter and*

$$\text{area}(\Gamma_j) \;=\; A, \qquad |E_j| \;=\; V \quad \text{for all } j \in \mathbb{N}, \qquad \sup_{j\in\mathbb{N}} \mathcal{W}(\Gamma_j) \;<\; \infty.$$

Then there exists a subsequence $j \to \infty$, a set of finite perimeter E, and an integral varifold μ with weak mean curvature $\vec{H} \in L^2(\mu)$, such that

$$\mathcal{X}_{E_j} \;\to\; \mathcal{X}_E \quad \text{in } L^1(\Omega), \qquad \Gamma_j \;\to\; \mu \quad \text{as varifolds}, \quad |\mathcal{X}_E| \;\le\; \mu,$$

$$\int_\Omega |\vec{H}|^2 \, d\mu \;\le\; \liminf_{j\to\infty} \int_{\Gamma_j} |\vec{H}_j|^2 \, d\mathcal{H}^2.$$

Furthermore $|E| = V$ and $\mu(\Omega) = A$.

This Lemma is a direct consequence of Allards compactness theorem for integral varifolds and the compactness of sets with uniformly bounded perimeter. The

lower-semicontinuity property follows easily from the weak formulation of the mean curvature vector as the first variation of the area functional:

$$\int_\Omega \vec{H}\cdot\eta\,d\mu \;=\; -\int_\Omega \mathrm{div}_{T_x\mu}\,\eta\,d\mu \;=\; -\lim_{j\to\infty}\int_{\Gamma_j}\mathrm{div}_{tan}\,\eta\,d\mathcal{H}^2 \;=\; \lim_{j\to\infty}\int_{\Gamma_j}\vec{H}_j\cdot\eta\,d\mathcal{H}^2.$$

Applying Hölders inequality, using that $\int_{\Gamma_j}\eta^2\,d\mathcal{H}^2 \to \int_\Omega \eta^2\,d\mu$, and taking the supremum over all η with $\int_\Omega \eta^2\,d\mu = 1$ we obtain the lower-semicontinuity estimate above.

This result, however gives no satisfactory solution to the constrained minimization problem, in particular we have in general $\mathrm{area}(\partial^* E) < \mu(\Omega) = A$. Therefore, Lemma 1 has to be complemented by a regularity result for minimizers, for instance by adapting Simon's proof [6] of the existence minimizers of the Willmore energy in the class of surfaces with prescribed genus. An alternative approach using both the Euler–Lagrange equation and the minimizing property was proposed by Rivière [5], see also his contribution to the miniworkshop.

Spontaneous-curvature-type energy. For a fixed constant H_0 consider

$$\mathcal{E}_{sc}(\Gamma) \;=\; \int_\Gamma (H-H_0)^2\,d\mathcal{H}^2,$$

where H is the scalar curvature of Γ, i.e. $H = \vec{H}\cdot\nu$ for a continuous unit normal field ν on Γ. Given a sequence $(\Gamma_j)_{j\in\mathbb{N}}$ of smooth boundaries with

$$\sup_{j\in\mathbb{N}}\Big(\mathcal{E}_{sc}(\Gamma_j)+\mathcal{A}(\Gamma_j)\Big) \;\le\; \Lambda$$

we obtain for all $j\in\mathbb{N}$ that

$$\int_\Gamma |\vec{H}|^2\,d\mathcal{H}^2 \;=\; \int_\Gamma 2(H-H_0)^2-(H-2H_0)^2+2H_0^2\,d\mathcal{H}^2 \;\le\; 2\Lambda+2H_0^2\Lambda.$$

Therefore the compactness and lower-semicontinuity properties of Lemma 1 hold. However, in constrast to the mean curvature vector the scalar mean curvature does not have a variational characterization and there is no definition of scalar mean curvature for an arbitrary integral varifold μ. In general the lower-semicontinuity of $\mathcal{E}_{sc}$ is wrong. Grosse-Brauckmann [2] gives an example of a family of surfaces Σ_k (with unbounded diamter) with constant scalar mean curvature equal to one that converges to a double plane Σ. Thus $H=0$ in the limit, for any reasonable definition of scalar mean curvature and

$$0 \;=\; \int_{\Sigma_k}(H_k-1)^2\eta\,d\mathcal{H}^2 \;<\; 2\int_\Sigma (H-1)^2\eta\,d\mathcal{H}^2$$

for any nonnegative cutoff function $\eta\in C_c^0(\Omega)$. It is an open question under which conditions one obtains lower-semicontinuity of the functional $\mathcal{E}_{sc}$.

Phase separation type energies. Consider a boundary $\Gamma\subset\mathbb{R}^3$ with

$$\Gamma \;=\; \Gamma_1\cup\Gamma_2\cup\partial\Gamma_1, \qquad \Gamma_1,\Gamma_2\subset\Gamma \text{ open and } C^2-\text{regular}.$$

Fix $0 < k_1 < k_2$ and define

$$\mathcal{E}_{ps}(\Gamma, \Gamma_1) := \int_{\Gamma_1} k_1 |\vec{H}|^2 \, d\mathcal{H}^2 + \int_{\Gamma_2} k_2 |\vec{H}|^2 \, d\mathcal{H}^2 + \mathcal{H}^1(\partial\Gamma_1).$$

Energies of this type arise in the modeling a phase separation on membranes. In the biophysics literature it is often not clearly stated but implicitely assumed that Γ has bounded first variation with mean curvature in $L^2(\mathcal{H}^2 \lfloor \Gamma)$.

A common approach to approximate $\mathcal{E}_{ps}$ is to consider a smooth phase function $\phi : \Gamma \to [-1, 1]$

and to describe different phases on Γ as the regions where $\phi \approx 1$ and $\phi \approx -1$ respectively. Depending on the value of ϕ a bending coefficient is fixed as a function $k : [-1, 1] \to [k_1, k_2]$ that interpolates between $k(-1) = k_1$ and $k(1) = k_2$, and $\mathcal{E}_{ps}$ is approximated by

$$\mathcal{E}^{\varepsilon}_{ps}(\Gamma, \phi) = \int_{\Gamma} k(\phi) |\vec{H}|^2 \, d\mathcal{H}^2 + \int_{\Gamma} \Big(\frac{\varepsilon}{2} |\nabla_{tan} \phi|^2 + \frac{1}{\varepsilon} W(\phi) \Big) \, d\mathcal{H}^2.$$

The second term describes a line tension energy between the two phases, W is a standard double well potential and $\varepsilon > 0$ a small parameter. By Lemma 1 for any family $(\Gamma_\varepsilon, \phi_\varepsilon)_{\varepsilon > 0}$ with uniformly bounded energy and surface area, i.e.

$$\sup_{\varepsilon > 0} \Big(\mathcal{E}^{\varepsilon}_{ps}(\Gamma_\varepsilon, \phi_\varepsilon) + \operatorname{area}(\Gamma_\varepsilon) \Big) < \infty$$

there exists a subsequence $\varepsilon \to 0$ such that Γ_ε converge to an integral varifold μ with bounded variation and weak mean curvature $\vec{H} \in L^2(\mu)$. Therefore $\mathcal{E}^{\varepsilon}_{ps}$ approximates $\mathcal{E}_{ps}$ together with the constraint of having bounded first variation.

The Helfrich bending energy. Let us assume that $k_G < 0$ and $k_b > 4k_G$ and let Γ be a smooth orientable closed surface. Then we obtain a bound on the full second fundamental form S of Γ. In fact, some explicit calculations show that

$$k_b (H - H_0)^2 + k_G K \geq \frac{1}{C_1} (\kappa_1^2 + \kappa_2)^2 - C_2$$

with C_1, C_2 only depending on k_b, k_G, H_0. Therefore

$$\int_{\Gamma} \big(\kappa_1^2 + \kappa_2^2 \big) \, d\mathcal{H}^2 \leq C_1 \Big(\mathcal{E}_{He}(\Gamma) + C_2 \operatorname{area}(\Gamma) \Big).$$

Using Hutchinsons theory of curvature varifold and weak second fundamental form [4] we obtain a compactness and lower-semicontinuity result analogous to Lemma 1. For any family $(\Gamma_j)_{j \in \mathbb{N}}$ of surfaces with uniformly bounded surface area and Helfrich energy there exists a subsequence $j \to \infty$ and an integral varifold μ with weak second fundamental form $S \in L^2(\mu)$ such that

$$\int_{\Omega} |S|^2 \, d\mu \leq \liminf_{j \to \infty} \int_{\Gamma_j} |S_j|^2 \, d\mathcal{H}^2,$$

where S_j denotes the second fundamental form of Γ_j. This result open the possibility of treating minimization problems for the Helfrich energy. Again, the key point is to prove the regularity of minimizers.

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Error analysis for the Willmore-Helfrich Functional

Tristan Rivière

I. The Willmore Equation in Divergence Form.

The Willmore energy of an oriented surface Σ immersed in $\mathbb{R}^3$ reads

$$W(\vec{\Phi}) = \int_\Sigma |H|^2 \ dvol_g \quad , \tag{I.1}$$

where $\vec{\Phi}$ is the immersion, $\vec{H}$ the mean curvature of the surface and g is the induced metric on the surface from the flat metric of $\mathbb{R}^3$. The complete Helfrich energy introduced by Wolfgang Helfrich in the early seventies for the modelization of cell membranes, see [Hef], involves the substraction to H of a spontaneous curvature H_0 and the addition of further terms proportional to the area A of the surface and the enclosed volume V of the immersion in $\mathbb{R}^3$:

$$Hef(\vec{\Phi}) = \int_\Sigma |H - H_0|^2 \ dvol_g + (\mu - H_0^2) \ A + \lambda \ V \quad , \tag{I.2}$$

where λ and μ are constants. These additional terms are sub-critical in comparison to the L^2 norm of the mean curvature and will be ignored in our presentation since they have no essential influence on the nature of the error estimates we present below.

The Euler Lagrange Equation of the Willmore Functional (I.1) has been written, maybe for the first time, by the student of Wilhelm Blaschke, Gerhardt Thomsen, in his dissertation defended in 1923 : $\vec{\Phi}$ is a critical smooth immersion for W if and only if it satisfies

$$(\mathbf{W}) \qquad \Delta_g H + 2H \ (H^2 - K) = 0 \quad ,$$

where Δ_g is the negative Laplace Beltrami operator on the surface Σ for the induced metric g and K is the Gauss curvature of g.

Trying to develop analysis (compactness, regularity properties, error estimates...) with equation (**W**) is made very delicate in particular by the fact that the non-linearity is cubic in the principal curvatures of the immersed surface whereas,

a-priori, the control given by the Lagrangian (I.1) from which the equation is deduced is only quadratic in the principal curvatures.

We first present the following new formulation of Willmore equation in 3 dimension which solves the functional analysis we are raising: $\vec{\Phi}$ is a critical immersion to (I.1), i.e. satisfies (**W**), if and only if, in conformal parametrization ($\vec{\Phi}_x \cdot \vec{\Phi}_y = 0$ and $|\vec{\Phi}_x|^2 = |\vec{\Phi}_y|^2$),

$$(\mathbf{WI}) \qquad div\left(-2\nabla\vec{H} + 3H\,\nabla\vec{n} + \vec{H}\times\nabla^\perp\vec{n}\right) = 0$$

where div and ∇ are the classical divergence and gradient operators with respect to the flat metric on the $x, y-$plane, $\vec{n}$ is the unit normal vector to the immersion, $\vec{H} = H\,\vec{n}$ and $\nabla^\perp$ is the rotation by $\pi/2$ of ∇ : $\nabla^\perp = (-\partial_y\ , \partial_x\ )$. Observe that this formulation (**WI**) of Willmore equation is solving the previous mentioned functional analysis paradox : the new dependance of the principal curvatures in the non-linearity $3H\,\nabla\vec{n} + \vec{H}\times\nabla^\perp\vec{n}$ is now quadratic and compatible with the control given by the lagrangian W.

II. Conservation laws for Willmore equation - the Conformal Willmore Equation.

From the new formulation (**WI**) we deduce the following conservation laws : if $\vec{\Phi}$ is a smooth local conformal parametrization of a Willmore surface then

$$(\mathbf{WII}) \qquad \begin{cases} \text{There exists a vector field locally on } \Sigma,\ \vec{L}\in\mathbb{R}^3, \text{ such that} \\ \\ \nabla\vec{\Phi}\cdot\nabla^\perp\vec{L} = \partial_y\vec{\Phi}\cdot\partial_x\vec{L} - \partial_x\vec{\Phi}\cdot\partial_y\vec{L} = 0 \quad \text{and} \\ \\ \nabla\vec{\Phi}\times\nabla^\perp\vec{L} - 2\nabla^\perp H\,\nabla\Phi = \\ \\ \partial_y\vec{\Phi}\times\partial_x\vec{L} - \partial_x\vec{\Phi}\times\partial_y\vec{L} - 2\left[\partial_y H\,\partial_x\vec{\Phi} - \partial_x H\,\partial_y\vec{\Phi}\right] = 0 \end{cases}$$

When $\vec{\Phi}$ is Willmore - i.e. solves (**WI**) - one takes

$$\text{(II.3)} \qquad \nabla^\perp\vec{L} = -2\nabla\vec{H} + 3H\,\nabla\vec{n} + \vec{H}\times\nabla^\perp\vec{n} \quad ,$$

but more generally the system (**WII**) can be considered as it is stated, independently of the choice (II.3). The system (**WII**) is made of jacobians and can therefore be written in divergence form again. (**WII**) is stable in the sense that solutions to (**WII**) of uniformly bounded Willmore energy converge weakly, modulo extraction of a subsequence, to a solution of (**WII**). It also passes to the limit for Palais-Smale sequences to Willmore. This leads to new proofs of existence results for minimizers of the Willmore functional under various constraints (for a fixed Σ, for a fixed Σ and a fixed conformal class for g, for a fixed Σ and fixed area of g...etc).

The system (**WII**) is equivalent to the conformal Willmore equation - critical points to (I.1) with prescribed conformal structure - : in local conformal coordinates there exists an holomorphic function $f(z)$ such that

$$(\mathbf{CW}) \qquad \Delta_g H + 2H\ (H^2 - K) = e^{2\lambda}\ < h^0, f(z) > \quad ,$$

where $h^0 = h^0_{11} + i h^0_{12}$ is the Weingarten operator in the conformal coordinates $\vec{\Phi}$ - $(h^0_{ij})_{ij}$ is the trace free second fundamental form of Σ - and e^λ is the conformal factor $e^\lambda = |\vec{\Phi}_x| = |\vec{\Phi}_y|$. In fact f is not an arbitrary holomorphic function , it is the local expression of a global holomorphic section of $(T^*_{0,1}\Sigma)^{-1} \otimes (T^*_{0,1}\Sigma)^{-1}$ where $T^*_{0,1}\Sigma$ is the canonical bundle of Σ viewed as a riemann surface with the conformal structure induced by g. Hence f belongs to a complex finite dimensional space. In other words our conservation law system (**WII**) is equivalent to Willmore equation (**W**) modulo a Lagrange multiplier belonging to a finite dimensional complex space - its dimension is 1 for instance when Σ is a torus.

III. Error Estimates for Willmore Equation.

We address in this section the following question : Let $\vec{\Phi}_k$ be a sequence of immersion satisfying "more and more" the Willmore equation, does $\vec{\Phi}_k$ converge to a solution to Willmore equation and "how fast" does this convergence happen ? We illustrate how the system (**WII**) can be helpful to treat such a question by looking at the simplest possible setting :

Let $\vec{\Phi}_k$ be an embedding of $\mathbb{C}$ into $\mathbb{R}^3$ such that $\int_{\mathbb{C}} |\nabla \vec{n}_k|^2\ dvol_{g_k} < \varepsilon_0$ for some $\varepsilon_0 > 0$ that will be chosed small enough later. By a result of S.Müller and V.Sverak and by F.Hélein we can (see [Hel]), modulo a change of parametrization, choose $\vec{\Phi}_k$ to be a sequence of conformal bilipschitz $W^{2,2}$ embedding such that $\|\nabla^2 \vec{\Phi}_k\|_{L^2(\mathbb{C})} + \|\nabla \vec{\Phi}_k\|_{L^\infty(\mathbb{C})}$ is uniformly bounded. Assume that the Willmore equation (**WI**) is satisfied modulo an error e_k which goes to zero strongly in H^{-2} :

$$div\left(-2\nabla \vec{H}_k + 3H_k\, \nabla \vec{n}_k + \vec{H}_k \times \nabla^\perp \vec{n}_k\right) = e_k \longrightarrow 0 \text{ in } H^{-2} \quad .$$

We proceed to the following Hodge decompositions. First, in one hand, there exist a sequence $\vec{L}_k$ uniformly bounded in the weak L^2 space, $L^{2,\infty}$, and a sequence $\vec{E}_k$ converging strongly to zero in L^2 such that $\|\vec{E}_k\|_{L^2} \leq C\ \|e_k\|_{H^{-1}}$ and

$$(\text{III.4}) \qquad -2\nabla \vec{H}_k + 3H_k\, \nabla \vec{n}_k + \vec{H}_k \times \nabla^\perp \vec{n}_k = \nabla^\perp \vec{L}_k + \nabla \vec{E}_k \quad ,$$

in the other hand, we have the existence of S_k, T_k, $\vec{R}_k$ and $\vec{Q}_k$ such that

$$(\text{III.5}) \qquad \begin{cases} \nabla \vec{\Phi}_k \cdot \vec{L}_k = \nabla S_k + \nabla^\perp T_k \quad , \\ \\ \nabla \vec{\Phi}_k \times \vec{L}_k - 2H_k\, \nabla \vec{\Phi}_k = \nabla \vec{R}_k + \nabla^\perp \vec{Q}_k \quad . \end{cases}$$

Some computation - the same as the one which proves (**WI**) $\Longrightarrow$ (**WII**) - leads to the identities $\nabla^\perp \vec{L}_k \cdot \nabla \vec{\Phi}_k = -\nabla \vec{\Phi}_k \cdot \nabla \vec{E}_k = -\Delta T_k$ and $\nabla \vec{\Phi}_k \times \nabla^\perp \vec{L}_k - 2\nabla^\perp H_k \cdot$

$\nabla\vec{\Phi}_k = -\nabla\vec{\Phi}_k \times \nabla\vec{E}_k = \Delta\vec{Q}_k$ We deduce from classical elliptic theory the following estimates

$$\text{(III.6)} \qquad \begin{cases} \|\nabla T_k\|_{L^{2,\infty}} \leq C \left[\|\nabla\vec{\Phi}_k\|_{L^\infty} + \|\Delta\vec{\Phi}\|_{L^2} \right] \|e_k\|_{H^{-1}} \quad , \\ \\ \|\nabla\vec{Q}_k\|_{L^{2,\infty}} \leq C \left[\|\nabla\vec{\Phi}_k\|_{L^\infty} + \|\Delta\vec{\Phi}\|_{L^2} \right] \|e_k\|_{H^{-1}} \quad . \end{cases}$$

Moreover the pair $(\vec{R}_k, S_k)$ satisfy the system on $\mathbb{C}$

$$\text{(III.7)} \qquad \begin{cases} \Delta\vec{R}_k = \nabla^\perp\vec{R}_k \times \nabla\vec{n}_k + \nabla S_k \cdot \nabla^\perp\vec{n}_k + div(\nabla T_k \ \vec{n}_k) \quad , \\ \\ \Delta S_k = \nabla^\perp\vec{R}_k \cdot \nabla\vec{n}_k - div(\nabla\vec{Q}_k \cdot \vec{n}_k) \quad . \end{cases}$$

Observe that beside the *error terms* $div(\nabla T_k \ \vec{n}_k)$ and $div(\nabla\vec{Q}_k \cdot \vec{n}_k)$, there are only jacobians in the right-hand-sides of (III.7). We deduce from this last crucial fact the following estimates, for ε_0 chosen small enough, using a Wente type inequality due to F.Bethuel (theorem 3.4.5 in [Hel]) and standard elliptic theory,

$$\text{(III.8)} \qquad \|\nabla\vec{R}_k\|_{L^{2,\infty}} + \|\nabla S_k\|_{L^{2,\infty}} \leq C \left[\|\nabla\vec{\Phi}_k\|_{L^\infty} + \|\Delta\vec{\Phi}\|_{L^2} \right] \|e_k\|_{H^{-1}} \quad .$$

A further independent computation gives

$$\text{(III.9)} \qquad 2\Delta\vec{\Phi} = \left[\nabla^\perp S - \nabla T \right] \cdot \nabla\vec{\Phi} - \left[\nabla\vec{R} + \nabla^\perp\vec{Q} \right] \times \nabla^\perp\vec{\Phi} \quad .$$

Combining (III.6), (III.8) and (III.9) we obtain

$$\text{(III.10)} \qquad \|\Delta\vec{\Phi}\|_{L^{2,\infty}} \leq C \left[\|\nabla\vec{\Phi}_k\|^2_{L^\infty} + \|\Delta\vec{\Phi}\|^2_{L^2} \right] \|e_k\|_{H^{-1}} \quad .$$

We can normalize the sequence $\nabla\vec{\Phi}_k$ in such a way that $\|\nabla\vec{\Phi}_k\|_\infty = \|\nabla id_{\mathbb{C}}\|_\infty$. Thus we conclude for every $p < 2$, that

$$\text{(III.11)} \quad \|\nabla(\vec{\Phi}_k - id_{\mathbb{C}})\|_{W^{1,p}_{loc}} \leq C \left\| div \left(2\nabla\vec{H}_k - 3H_k \nabla\vec{n}_k - \vec{H}_k \times \nabla^\perp\vec{n}_k \right) \right\|_{H^{-2}}$$

We were here considering the simplest framework of the embedding of a plane with little Willmore energy. In the general situation, even for the flow, such an estimate can be established except that the limiting immersion is only a-priori Conformal Willmore (satisfy (**CW**)). Then, the possible cancelation of the holomorphic Lagrange multiplier f , that would make the equation satisfied by the limiting map being exactly Willmore, has to be further understood.

Such an error control estimate of the form (III.11) has been established when the error was converging to zero in the space L^2 by E.Kuwert and R.Schätzle (see [KS]). Here we have gained 2 derivatives by requiring the equation to be solved modulo an error controled only in the space H^{-2} which is critical for Willmore Euler Lagrange equation (WI) - one cannot afford less.

The results presented in this talk have been established in the following two works [Ri] *and* [BR]*, the last one being a collaboration in preparation with Yann Bernard.*

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Dynamics of fluid membranes and budding of vesicles

Marino Arroyo

(joint work with Antonio DeSimone)

We derive the evolution equations for a multi-phase fluid membrane surrounded by a viscous fluid. We discuss some implications for the dynamics of lipid bilayer membranes and for physically based Willmore flows.

1. Introduction

We study the mechanics of multi-phase fluid membranes surrounded by a viscous fluid as a model system for lipid bilayer membranes found in biological and synthetic systems [1]. The partial order of the lipid membrane (the system is ordered in the direction perpendicular to the membrane and disordered in the tangential directions) endows the system with some features of a fluid (in-plane fluidity) and some of a solid (curvature elasticity). A seminal work in the mechanics of Newtonian fluids in the interfacial state is [2]. Here, we consider a fluid surface, surrounded by a viscous fluid, whose area preserving evolution is driven by curvature elasticity and line tension.

We view the fluid membrane as a surface Γ in motion with a velocity field $\boldsymbol{V} : \Gamma \to \mathbb{R}^3$. Throughout the paper we omit the explicit dependence on time. We denote the boundary of the surface by γ, which possibly represents a phase boundary in a multicomponent vesicle. We decompose the velocity field into its in-plane or tangential component $\boldsymbol{v}$ and its normal component v_n so that $\boldsymbol{V} = \boldsymbol{v} + v_n \boldsymbol{n}$ where $\boldsymbol{n}$ denotes the unit normal to the surface. At any given time, we denote by $\boldsymbol{g}$ the metric tensor of the surface, by $\boldsymbol{k} = -\nabla \boldsymbol{n}$ its second fundamental form, and by $H = \operatorname{tr} \boldsymbol{k}$ and $K = \det \boldsymbol{k}$ its mean and Gaussian curvature respectively. Throughout the paper, ∇ denotes the surface covariant derivative.

The energy of the membrane is the sum of the classical Helfrich-Canham curvature energy E_{HC} and the interfacial energy E_I:

$$E_{HC} = \int_\Gamma \frac{\kappa}{2}(H - C_0)^2 \, dS + \int_\Gamma \kappa_G K \, dS, \qquad E_I = \int_\gamma \sigma \, d\ell. \tag{1}$$

Here, C_0 denotes the spontaneous curvature, κ and κ_G are elastic moduli, and σ is the line tension.

For a surface, the rate-of-deformation tensor is $\boldsymbol{d} = 1/2\left[\nabla \boldsymbol{v} + (\nabla \boldsymbol{v})^T\right] - v_n \boldsymbol{k} = (\nabla \boldsymbol{v})^{\text{symm}} - v_n \boldsymbol{k}$. The Lagrangian for a Newtonian area-preserving fluid membrane is

$$\mathcal{L}[\boldsymbol{v}, v_n, p] = \mu \int_\Gamma \boldsymbol{d} : \boldsymbol{d}\ dS - \int_\Gamma (\text{div}\ \boldsymbol{v} - v_n H) p\ dS, \tag{2}$$

where μ is the surface viscosity of the membrane and p is the surface tension (a Lagrange multiplier for the area constraint).

The surrounding fluid is described by the Lagrangian

$$\mathcal{L}^b[\boldsymbol{V}^b, p^b] = \mu^b \int_{\mathbb{R}^3} \boldsymbol{D}^b : \boldsymbol{D}^b\ dV - \int_{\mathbb{R}^3} (\nabla^b \cdot \boldsymbol{V}^b) p^b\ dV - \int_{\mathbb{R}^3} \boldsymbol{b}^b \cdot \boldsymbol{V}^b\ dV. \tag{3}$$

The bulk rate-of-deformation is $\boldsymbol{D}^b = \frac{1}{2}[\nabla^b \boldsymbol{V}^b + (\nabla^b \boldsymbol{V}^b)^T]$, μ^b is the bulk viscosity, p^b is the bulk pressure, and $\boldsymbol{b}^b$ denotes the bulk body force on the surrounding fluid. Throughout the paper, ∇^b denotes the standard nabla operator in $\mathbb{R}^3$.

2. Governing equations for a fluid membrane

The equations governing the evolution of a vesicle with boundary (or a vesicle with an interface) embedded in a surrounding fluid follow from the principle of virtual power which balances dissipation with energy release rate

$$\delta\left(\mathcal{L}[\boldsymbol{v}, v_n, p] + \mathcal{L}^b[\boldsymbol{V}^b, p^b] + \dot{E}_{HC}[\boldsymbol{v}, v_n] + \dot{E}_I[\boldsymbol{v}, v_n]\right) = 0, \tag{4}$$

subject to (i) the no-slip condition $\boldsymbol{V}^b|_\Gamma = \boldsymbol{V}$ and (ii) $d\boldsymbol{x}/dt = \boldsymbol{V}(\boldsymbol{x})$ for $\boldsymbol{x} \in \Gamma$.

The Euler-Lagrange equations are

(5)

$$\delta_{\boldsymbol{V}^b}: \quad -\nabla^b p^b - \mu^b\left[\nabla^b \times \nabla^b \times \boldsymbol{V}^b\right] + \boldsymbol{b}^b = \boldsymbol{0} \quad \text{in} \quad \mathbb{R}^3 \backslash \Gamma$$

$$\delta_{p^b}: \quad \nabla^b \cdot \boldsymbol{V}^b = 0 \quad \text{in} \quad \mathbb{R}^3 \backslash \Gamma$$

$$\delta_{\boldsymbol{v}}: \quad -\nabla p - \mu\left[(\boldsymbol{\delta} \mathbf{d} \boldsymbol{v}^\flat)^\sharp + 2(\boldsymbol{k} - H\boldsymbol{g}) \cdot \nabla v_n - 2K\boldsymbol{v}\right] + \left(\boldsymbol{t}^b_+ + \boldsymbol{t}^b_-\right) = \boldsymbol{0} \quad \text{in} \quad \Gamma$$

$$2\mu\left[(\nabla \boldsymbol{v})^{\text{symm}} - v_n \boldsymbol{k}\right] \cdot \boldsymbol{\nu} + \left[-p + \tfrac{\kappa}{2}(H - C_0)^2 + \kappa_G K - \sigma k_g\right] \boldsymbol{\nu} = \boldsymbol{0} \quad \text{in} \quad \partial\Gamma$$

$$\delta_p: \quad -\text{div}\ \boldsymbol{v} + v_n H = 0 \quad \text{in} \quad \Gamma$$

$$\delta_{v_n}: \quad -2\mu\left[\nabla \boldsymbol{v} : \boldsymbol{k} - (H^2 - 2K) v_n\right] + pH - (t^b_{n+} - t^b_{n-}) + \kappa\left[\Delta H + \tfrac{H - C_0}{2}(H^2 - 4K + HC_0)\right] = 0 \quad \text{in} \quad \Gamma$$

$$-\kappa(\nabla H \cdot \boldsymbol{\nu}) + \kappa_G \nabla(\boldsymbol{t} \cdot \boldsymbol{k} \cdot \boldsymbol{\nu}) \cdot \boldsymbol{t} - \sigma k_n = 0 \quad \text{in} \quad \partial\Gamma$$

$$\kappa(H - C_0) + \kappa_G(H - \boldsymbol{\nu} \cdot \boldsymbol{k} \cdot \boldsymbol{\nu}) = 0 \quad \text{in} \quad \partial\Gamma$$

Here, we denote by $\boldsymbol{t}^b_\pm$ the tangential component of the traction exerted by the bulk fluid on each side of the orientable membrane Γ, by $\boldsymbol{t}$ the unit tangent vector to γ, by $t^b_{n\pm}$ its normal component, by $\boldsymbol{\nu}$ the unit vector orthogonal to both $\boldsymbol{n}$ and

$\boldsymbol{t}$ on γ, and by k_g and k_n the geodesic and normal curvatures of γ respectively. The term $(\boldsymbol{\delta}\mathbf{d}\boldsymbol{v}^\flat)^\sharp$ generalizes the curl-curl of the velocity on a manifold with the language of exterior calculus and differential forms.

3. Discussion

Our work is relevant to the quantitative study of biophysically relevant phenomena such as budding, and it also provides a new system of geometric PDEs.

3.1. **Budding kinetics.** We solve Eqs. 5 in the simplest yet non-trivial geometry relevant for the study of budding, namely a spherical bud protruding off an infinitely large planar fluid membrane made of a different phase [3]. We argue that inner dissipation sets the time-scale of small buds, which are relevant to the cell function, and cannot be neglected for larger synthetic systems such as GUVs [1].

3.2. **A physical flow for the Willmore energy.** We now consider a closed, single phase vesicle with no spontaneous curvature ($C_0 = 0$). For small-sized vesicles, the bulk dissipation can be neglected and Eqs. 5 reduce to

$$\begin{aligned} -\nabla p + \mu\left[-(\boldsymbol{\delta}\mathbf{d}\boldsymbol{v}^\flat)^\sharp - 2(\boldsymbol{k} - H\boldsymbol{g})\cdot\nabla v_n + 2K\boldsymbol{v}\right] &= \mathbf{0} \\ -\operatorname{div}\boldsymbol{v} + v_n H &= 0 \\ -2\mu\left[\nabla\boldsymbol{v} : \boldsymbol{k} - (H^2 - 2K)v_n\right] + pH + \kappa\left[\Delta H + \tfrac{H}{2}(H^2 - 4K)\right] &= 0 \end{aligned} \tag{6}$$

in Γ. These equations provide a physically-based flow for the Willmore energy, to be contrasted with its L_2 gradient flow [4]

$$v_n = -\left[\Delta H + \frac{H}{2}(H^2 - 4K)\right] \quad \text{in} \quad \Gamma. \tag{7}$$

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Computational Surface Partial Differential Equations

Charlie Elliott

1. Introduction

In this talk we described computational methods for solving PDEs on evolving surfaces. In particular we are concerned with diffusion and transport. The motivation in the context of this workshop is to solve reaction diffusion equations on bio-membranes. In particular we have in mind Allen-Cahn and Cahn-Hilliard equations which may be used to model phase separation for multi-component membranes and also to approximate line tension as diffuse interfaces located on the curved surface. In particular the motivation is to study the computational modelling of phase separation phenomena on biomembranes with respect to the lipid composition resulting in intermembrane domains. In addition to the classical bending energy (cf.[5]), according to the model in [7], a line energy describing the excess free energy of the phase boundary may be taken into account. This may be approximated by a diffuse interface model for the line energy. The idea is then to use the methods developed in [4, 5, 6, 7, 8] for partial differential equations on fixed and evolving surfaces and the methods of [4, 1] for Willmore flow or the diffuse interface approach of [14] in order to relax appropriate initial configurations to local minimisers by gradient flow dynamics.

2. The advection diffusion equation

Conservation of a scalar with a diffusive flux on an evolving hypersurface $\Gamma(t)$ leads to the diffusion equation

$$\dot{u} + u\,\nabla_\Gamma \cdot v - \nabla_\Gamma \cdot (\mathcal{D}_0 \nabla_\Gamma u) = 0 \tag{1}$$

on $\Gamma(t)$. Here $\dot{u}$ denotes the advective surface material derivative, v is the velocity of the surface and ∇_Γ is the tangential surface gradient. If $\partial\Gamma(t)$ is empty then the equation does not need a boundary condition. Otherwise we can impose Dirichlet or Neumann boundary conditions on $\partial\Gamma(t)$.

3. Evolving Surface Finite Element Method (ESFEM)

The finite element approximation is based on the variational form

$$\frac{d}{dt}\int_{\Gamma(t)} u\varphi + \int_{\Gamma(t)} \mathcal{D}_0 \nabla_\Gamma u \cdot \nabla_\Gamma \varphi = \int_{\Gamma(t)} u\dot{\varphi} \tag{2}$$

where φ is an arbitrary test function defined on the surface $\Gamma(t)$ for all t. This provides the basis of our evolving surface finite element method (ESFEM) which is applicable to arbitrary evolving n–dimensional hypersurfaces in $\mathbb{R}^{n+1}$ (curves in $\mathbb{R}^2$) with or without boundary. This is the extension of the method of Dziuk [2] for the Laplace-Beltrami equation on a stationary surface. The principal idea is to use a polyhedral approximation of Γ based on a triangulated surface. It follows that a quite natural local piecewise linear parameterisation of the surface is employed rather than a global one. The finite element space is then the space of continuous piecewise linear functions on the triangulated surface whose nodal basis functions enjoy the transport property

$$\dot{\phi}_j = 0.$$

The implementation is thus rather similar to that for solving the diffusion equation on flat stationary domains. For example, the backward Euler time discretization leads to the ESFEM scheme

$$\frac{1}{\tau}\left(\mathcal{M}(t^{m+1})\alpha^{m+1} - \mathcal{M}(t^m)\alpha^m\right) + \mathcal{S}(t^{m+1})\alpha^{m+1} = 0$$

where $\mathcal{M}(t)$ and $\mathcal{S}(t)$ are the time dependent surface mass and stiffness matrices and α^m is the vector of nodal values at time t^m. Here, τ denotes the time step size.

4. Level set or implicit surface approach

We also define an Eulerian level set method for parabolic partial differential equations on an evolving hypersurface $\Gamma(t)$ contained in a domain $\Omega \subset \mathbb{R}^{n+1}$. The method is based on formulating the partial differential equations on all level set surfaces of a prescribed time dependent function Φ whose zero level set is $\Gamma(t)$. Eulerian surface gradients are formulated by using a projection, $\mathcal{P}_\Phi$, of the gradient in $\mathbb{R}^{n+1}$ onto the level surfaces of Φ. These Eulerian surface gradients are used to define weak forms of surface elliptic operators and so generate weak formulations of surface elliptic and parabolic equations. The resulting equation is then solved in one dimension higher but can be solved on a mesh which is unaligned to the level sets of Φ. We consider both second order and fourth order elliptic operators with natural second order splittings. The finite element method is applied to the weak form of the split system of second order equations using piece-wise linear elements on a fixed grid yielding an Eulerian ESFEM. The computation of the mass and element stiffness matrices are simple and straightforward. The method is based on the following variational form

$$\frac{d}{dt}\int_\Omega u\eta|\nabla\Phi| + \int_\Omega \mathcal{D}_0\nabla_\Phi u\cdot\nabla_\Phi\eta|\nabla\Phi| = \int_\Omega u\dot{\eta}|\nabla\Phi|. \tag{3}$$

where $\nabla_\Phi = \mathcal{P}_\Phi u$.

We use fixed in time finite element functions so that now the test functions now will satisfy $\dot{\eta} = v\cdot\nabla\eta$.

We assume that the domain Ω is triangulated by an admissible triangulation $\mathcal{T}_h = \bigcup_{T\in\mathcal{T}_h} T$ which consists of simplices T. The discrete space then is

$$S_h = \{U \in C^0(\overline{\Omega}) |\, U|_T \text{ is a linear polynomial, } T \in \mathcal{T}_h\}.$$

The discrete space is generated by the nodal basis functions χ_i, $i = 1,\dots,N$,

$$S_h = \operatorname{span}\{\chi_1,\dots,\chi_N\}.$$

The resulting discretisation is

$$\frac{d}{dt}\left(\mathcal{M}(t)\alpha\right) + \mathcal{S}(t)\alpha = \mathcal{C}(t)\alpha \tag{4}$$

where $\mathcal{M}(t)$ is the evolving mass matrix

$$\mathcal{M}(t)_{kj} = \int_\Omega \chi_j\chi_k|\nabla\Phi|,$$

$\mathcal{C}$ is a transport matrix

$$\mathcal{C}(t)_{kj} = \int_\Omega \chi_j v \cdot \nabla \chi_k |\nabla \Phi|,$$

and $\mathcal{S}(t)$ is the evolving stiffness matrix

$$\mathcal{S}(t)_{jk} = \int_\Omega \mathcal{A} \nabla_\Phi \chi_j \nabla_\Phi \chi_k |\nabla \Phi|.$$

Since the mass matrix $\mathcal{M}(t)$ is uniformly positive definite on $[0, T]$ and the other matrices are bounded,

we get existence and uniqueness of the semi-discrete finite element solution.

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Shape behavior of vesicular objects

Saša Svetina

Vesicular objects comprise liquid interior separated from the environment by thin envelopes such as membranes or unicellular sheets. Their shapes correspond to the minimum of the membrane elastic energy and can thus be determined by employing variational calculus. The related theoretical work revealed their extraordinary rich shape behavior. It is the purpose here to give an overview of this behavior by focusing on some of its aspects that have been studied by our group. The talk is on the relation between membrane elastic properties and shapes of unconstrained vesicles, on shapes of vesicles strained by an axial force, on vesicle self-reproduction and on coupling between vesicle shape and lateral distribution of mobile membrane inclusions. It consists in commenting and explaining the below listed results and conclusions obtained in referred analyses.

Elastic energy of fluid membranes composed of two or more layers that are in contact but can laterally slide one by the other involves in addition to area expansivity and local bending terms [1] also the **nonlocal bending term**. [2, 3, 4] The relative influence of this term increases as the number of layers is increasing. [5] A prototype of shape behavior of vesicular objects is vesicle with a bilayer membrane. The material constants that affect shapes of flaccid vesicles are membrane spontaneous curvature (C_0) [1] and difference between the equilibrium areas of the two membrane layers (preferred area difference, ΔA_0). [6] Shapes of vesicular objects can be conveniently classified within the **strict bilayer couple model** [7] in which the shapes are predicted by minimizing membrane local bending energy at constant vesicle volume, membrane area, and the integral of the mean curvature over the membrane area (integrated membrane curvature). Integrated membrane curvature is in the case of bilayer membranes proportional to the difference between the areas of the two membrane layers (ΔA). In the strict bilayer couple model shapes depend on two geometrical quantities, the reduced volume (v: vesicle volume divided by the volume of the sphere with the same membrane area, and reduced integrated membrane curvature (Δa: integrated membrane curvature divided by its value for the sphere; in bilayers it is equal to the reduced difference between the areas of the two layers).[7] Shapes belong to different **shape classes** defined as including all shapes of the same symmetry that transform continuously when continuously varying v and Δa. Classes are bounded in the $v/\Delta a$ shape phase diagram by symmetry breaking lines and lines of different limiting shapes.[7] **The limiting shapes** can be obtained by the variational principle: at given Δa they correspond to extreme values of v. They are compositions of sections of spheres and cylinders with only two possible values of their radii.[7] Typical example of a limiting shape is sphere with a certain number of equal buds. In the central part of the $v/\Delta a$ phase diagram (around $\Delta a \sim 1$) the shapes with the lowest bending energy are nonaxisymmetric,[8, 9, 10] at $\Delta a < 1$ they are oblate axisymmetric exhibiting at first also equatorial mirror symmetry,[4, 7] and at $\Delta a > 1$ they are prolate axisymmetric also exhibiting at first also equatorial

mirror symmetry. [11] At reduced volumes close to 1 and $\Delta a > 1$ a typical shape is composed of a nearly spherical main body and a protrusion.[12]

In the **generalized bilayer couple model** [4, 8, 13] the shapes of unconstrained vesicles depend on the effective value of the reduced preferred area difference $\Delta a_{0,eff} = \Delta a_0 + (k_c/k_r)c_0/2$ where k_c and k_r are local and nonlocal bending constants, respectively, and c_0 is the reduced spontaneous curvature (spontaneous curvature times the radius of the sphere with vesicle membrane area). In its two limits ($k_r = 0$, spontaneous curvature model [14] and $k_r = \infty$, strict bilayer couple model [7]) the system differs with respect to the stability of possible vesicle shapes. This difference can be understood on the basis of specific dependence of local membrane bending energy on Δa. The ratio k_r/k_c which divides the spontaneous curvature and strict bilayer couple type behaviors of vesicle shapes is an increasing function of the reduced vesicle volume v. [15] For phospholipid membranes the ratio k_r/k_c obtained experimentally by the tether pulling experiment [16, 17] is close to 3 which is the value for the bilayer composed of layers of homogeneous fluid material. For proper mechanical behavior of closed unicellular sheets the value of this ratio must be much higher. [15]

Solving the shape equation for vesicles strained by axial force is of interest because it helps to understand the formation of thin tubes - **membrane tethers**. [18, 19] In axially strained vesicles the principal curvatures at poles exhibit logarithmic singularity. [20] Tethers form after at increasing axial force originally flaccid vesicle attains a lemon-like limiting shape, because then-after it can increase its height (pole to pole distance) only by taking from the main vesicle body the membrane while using a negligible amount of the vesicle volume.

The phenomena of vesicle budding and consequent vesiculation process indicate a possible basis for **vesicle self-reproduction**. [21, 22] Already the simplest possible spontaneous curvature model of shape behavior of a vesicle with an exponentially growing membrane area shows that vesicles self-reproduce only when a relationship is satisfied between membrane material properties and external conditions. [21] The phenomenon of self-reproduction of vesicles thus involves the principle of selectivity which indicates the vesicular origin of the emergence of cellular life. [23]

Membrane inclusions such as membrane embedded peptides or proteins exhibit a curvature dependent interaction with the surrounding lipid matrix due to the mismatch between their intrinsic curvature and the local membrane curvature. [24] Shapes of vesicles with membrane inclusions can be obtained by minimizing the free energy that includes elastic energy of the membrane and free energy contribution due to the inclusion-membrane interaction. [25] Vesicle shapes adjust to the presence of inclusions by increasing the areas of regions with curvatures favorable to them and decreasing the areas of regions with in this sense unfavorable curvatures in the direction that their lateral distribution deviates from the homogeneous one as little as possible.

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Analysis and numerical simulation of the evolution of patterns in the gel phase of lipid membranes

Georg Dolzmann
(joint work with Sören Bartels, Ricardo H. Nochetto)

In this talk we focus on the analysis of mathematical models for membranes in the gel or $L_{\beta'}$ phase. This phase is characterized by the fact that the thermal fluctuations of the hydrophobic tails of the lipid molecules in the membrane are small. Moreover, it is experimentally observed [6, 7] that the tails form a fixed angle (of 32°) with respect to the layer normal and have locally the same orientation.

Therefore one can define a two-dimensional order parameter n which is the projection of the director onto the tangent plane to the membrane surface. As usual we define the corresponding symmetric and traceless order parameter Q by $Q = n \otimes n - (1/2)I$ and identify Q via $Q = Aq$ after suitable normalizations with the unit-length vector q that corresponds to the first row in Q.

We consider the system in the Monge gauge and assume that the energy of a flat piece of the membrane described by a graph u over a two-dimensional domain Ω is zero while a curved membrane has stored elastic energy. In a linearized setting, the energy of the system consists of three parts, the homogeneous, Frank, and curvature-elastic terms (see, e.g., [4, 10])

$$F = \int_\Omega d\mathbf{r}\big(f_{hom} + f_F + F_{curv}\big)\,,$$

where (using the summation convention)

$$f_{hom} = \frac{A}{2}\,Q_{ij}^2 + \frac{C}{4}\,(Q_{ij}^2)^2\,, \qquad f_F = \frac{M'}{2}\,(\partial_i Q_{jk})^2\,.$$

As a lowest order approximation of the coupling between the elastic deformation and the order parameter we adopt the model

$$f_{curv} = \frac{\kappa}{2}\,(\Delta u)^2 + \delta E_{ij} Q_{jk} \partial_i \partial_k u$$

where E_{ij} is the unit tensor for achiral lipids [4] and the totally antisymmetric tensor for chiral lipids [9]. This model was proposed in [10]; see also [8] and the references therein. In the following we assume that the lipid molecules are achiral. This is for example true for dioleoyl phosphatidylcholine (DOPC) which is frequently used in artificial membranes.

After suitable nondimensionalization, the experimental values for the elastic moduli reported in [10] lead to a constant of order 10^4 in front of the homogeneous energy. We therefore propose to consider a modified energy functional where we replace the Ginzburg Landau term enforcing the constraint on the length of the

order parameter by the rigid constraint $|q| = 1$. This leads (after integration by parts) to

$$E[q,u] = \frac{\kappa}{2}\int_\Omega |\Delta u|^2 \mathrm{d}x + \frac{M}{2}\int_\Omega |\nabla q|^2 \mathrm{d}x - \delta \int_\Omega \nabla u \cdot \operatorname{Div} Aq \mathrm{d}x \tag{1}$$

subject to the holonomic constraint $|q| = 1$ almost everywhere in Ω and with Dirichlet boundary conditions for u and q and $M = 2M'$. The boundary condition $\Delta u = 0$ is obtained as a natural boundary condition. The L^2-gradient flow dynamics is given (in the strong formulation) by

$$\begin{aligned} \partial_t q &= -\gamma_q \frac{\delta L}{\delta q} = -\gamma_q\big(-M\Delta q + \delta A^* D^2 u + \lambda q\big)\,, \\ \partial_t u &= -\gamma_u \frac{\delta L}{\delta u} = -\gamma_u\big(\kappa\Delta^2 u + \delta \operatorname{div}\operatorname{Div} Aq\big), \end{aligned} \tag{2}$$

where λ is the Lagrangian multiplier corresponding to the constraint $|q| = 1$, $(\operatorname{Div} Aq)_i$ is the divergence of the ith row of the matrix Aq and A^* is the adjoint of A. The numerical scheme is based on the corresponding weak formulation (after integration by parts) and includes the energy inequality, see [3] for details.

Notation: In the following, $q_h \in [\mathbb{V}_h]^2$ and $u_h \in \mathbb{V}_h$ are approximations to q and u with Courant elements on a regular and weakly acute triangulation $\mathcal{T}_h$, $\widetilde{\Delta}_h^0 u_h \in \mathbb{V}_h^0$ denotes a discrete analog of the Laplace operator defined by

$$(\widetilde{\Delta}_h^0 u_h, \phi_h)_h = -(\nabla u_h, \nabla \phi_h) \quad \text{for all } \phi_h \in \mathbb{V}_h^0$$

where $(\cdot,\cdot)_h$ is the inner product defined via mass lumping, $\mathbb{V}_h^0$ is the set of all functions in $\mathbb{V}_h$ with zero trace, and $\mathcal{F}_h[q_h]$ is the space of finite element functions that are tangential to $q_h(z)$ at all nodes of the triangulation. For two sequences $\big(\phi^n\big)_{n\geq 0}$ and $\big(\widetilde{\phi}^n\big)_{n\geq 0}$ we define two backward difference quotients by

$$d_\tau^- \phi^{n+1} = \tau^{-1}\big(\phi^{n+1} - \phi^n\big)\,, \quad \widetilde{d}_\tau^- \widetilde{\phi}_n = \tau^{-1}\left(\widetilde{\phi}^n - \phi^{n-1}\right).$$

Algorithm 1. *Choose* $(q_h^0, u_h^0) \in \big[\mathbb{V}_h\big]^2 \times \mathbb{V}_h^0$ *such that* $|q_h^0(z)| = 1$ *for all* $z \in \mathcal{N}_h$, $q_h^0|_\Gamma = q_{\mathrm{D},h}$. *Set* $n = 0$.

(1) Compute $\widetilde{q}_h^{n+1} \in q_h^n + \mathcal{F}_h\big[q_h^n\big]$ *such that*

$$\frac{1}{\gamma_q}(\widetilde{d}_\tau^- \widetilde{q}_h^{n+1}, \psi_h)_h + M(\nabla \widetilde{q}_h^{n+1}, \nabla \psi_h) = \delta(\nabla u_h^n, \operatorname{Div} A\psi_h) \quad \textit{for all } \psi_h \in \mathcal{F}_h\big[q_h^n\big].$$

(2) Define $q_h^{n+1} \in \big[\mathbb{V}_h\big]^2$ *satisfying the constraint* $|q_h^{n+1}| = 1$ *at the nodes by*

$$q_h^{n+1}(z) = \frac{\widetilde{q}_h^{n+1}(z)}{|\widetilde{q}_h^{n+1}(z)|} \quad \textit{for all } z \in \mathcal{N}_h\,.$$

(3) Compute $u_h^{n+1} \in \mathbb{V}_h$ *such that*

$$\frac{1}{\gamma_u}(d_\tau^- u_h^{n+1}, \phi_h)_h + \kappa(\widetilde{\Delta}_h^0 u_h^{n+1}, \widetilde{\Delta}_h^0 \phi_h)_h = \delta(\operatorname{Div} Aq_h^{n+1}, \nabla \phi_h) \quad \textit{for all } \phi_h \in \mathbb{V}_h^0.$$

(4) Stop if $n + 1 \geq T/\tau$; *set* $n = n + 1$ *and go to (1) otherwise.*

It follows from the Lax Milgram Lemma that the discrete solutions exist for all h and $\tau > 0$. Existence of solutions and convergence to a solution of the partial differential equation are guaranteed by the following theorem.

Theorem 2. *Suppose that $\Omega \subset \mathbb{R}^2$ is a convex and polygonal domain and that the elastic moduli and the coupling constant satisfy $\delta^2 \leq c_0 \kappa M$ where $c_0 > 0$ depends only on Ω and the geometry $\mathcal{T}_h$. Then there exists a constant c_1 which depends only on the initial data such that the functions q_h^n and u_h^n in Algorithm 1 are defined for all $n \in \mathbb{N}$, $0 < \tau \leq c_1$ and $h > 0$. Moreover, there exists a weak solution of the system (2) subject to suitable initial and boundary conditions which can be obtained as a limit of a sequence of solutions calculated with Algorithm 1 for $\tau, h \to 0$.*

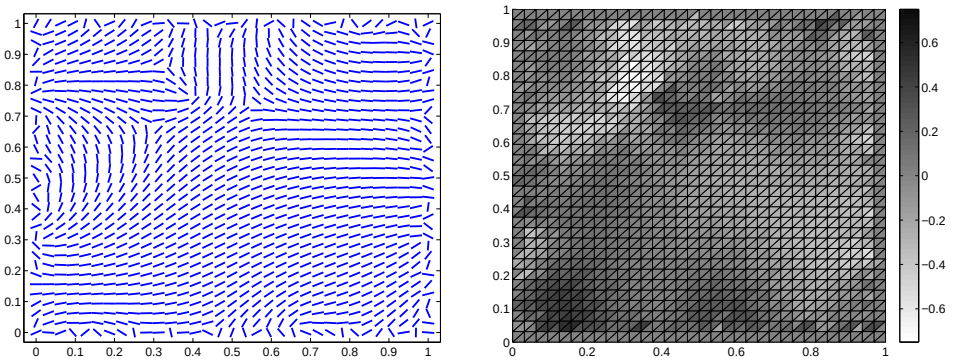

FIGURE 1. Formation of domains in the membrane computed with Algorithm 1. The initial configuration consists of a random field corresponding to the isotropic phase of the membrane [5]. Left panel: orientation n, right panel: curvature Δu. ($T = 2$, $\gamma_q = \gamma_u = 1/10$, $\kappa = M = \delta = 1$.)

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Numerical approximation of curvature driven surface evolution

Harald Garcke
(joint work with John W. Barrett, Robert Nürnberg)

Mathematical models for biological bilayer membranes lead to elastic energies of the form

$$E(\Gamma) := \frac{c_1}{2}\int_\Gamma (\varkappa - \overline{\varkappa})^2 ds + \frac{c_2}{2}\int_\Gamma \mathcal{K} dx + \frac{\varrho}{2}(M - M_0)^2\,. \tag{1}$$

Here Γ is a hypersurface in $\mathbb{R}^3$, $\varkappa$ is its mean curvature, $\overline{\varkappa}$ is a given so called spontaneous curvature, $\mathcal{K}$ is the Gauss curvature of the surface, $M = \int_\Gamma \varkappa ds$ is the integrated mean curvature and $c_1, c_2, \varrho \in \mathbb{R}^+$, $M_0 \in \mathbb{R}$ are given constants. The term $\int_\Gamma \mathcal{K} ds$ is constant if one fixes the topological class and hence we will set $c_2 = 0$ as the Gauss curvature term will only enter the energy as a constant.

The term $\int_\Gamma \varkappa ds$ describes to leading order the area difference between the two layers in the membrane. Typically it is difficult to exchange molecules between the two layers and hence the number of molecules is approximately fixed in each layer. This will lead to leading order to a fixed value of $\int_\Gamma \varkappa ds$. This fact is taking care of energetically through the term $\frac{\varrho}{2}(M - M_0)^2$.

The L^2-gradient flow of (1) taking volume and area constraints into account is given as

$$\mathcal{V} = -c_1\Delta_s\varkappa - c_1(\varkappa - \overline{\varkappa})|\nabla_s \vec{\nu}|^2 + \frac{c_1}{2}(\varkappa - \overline{\varkappa})^2\varkappa - \varrho(M - M_0)(|\nabla_s \nu|^2 - \varkappa^2) + \lambda\varkappa + \mu \tag{2}$$

where $\mathcal{V}$ is the normal velocity and λ, μ are Lagrange multipliers related to area and volume constraints, respectively.

In [1] a novel finite element approximation for (2) which approximates the smooth surface by a polyhedral surface was introduced. The proposed method has very good properties with respect to the distribution of mesh points – a fact which is very important as often mesh distortions appear in other numerical approaches. A property of the method is that the velocity of the discrete surface is not restricted to normal directions. In fact the tangential degree of freedoms are used to minimize a discrete Dirichlet integral and the good mesh behaviour can partly be explained via discrete conformal maps (see [2]).

Another ingredient of the approach in [1] is an approximation of the Weingarten map with the help of the gradient of discrete normals which are defined on the vertices of the triangulation. A good approximation of the Weingarten map is important in order to obtain all the curvature information needed to numerically approximate (2).

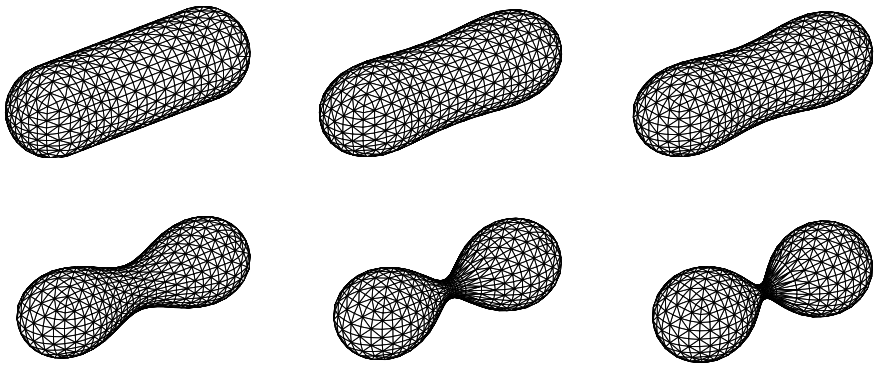

FIGURE 1. Flow with $\overline{\varkappa} = -2$. $\vec{X}(t)$ for $t = 0,\ 0.05,\ 0.1,\ 0.25,\ 0.5,\ 1$.

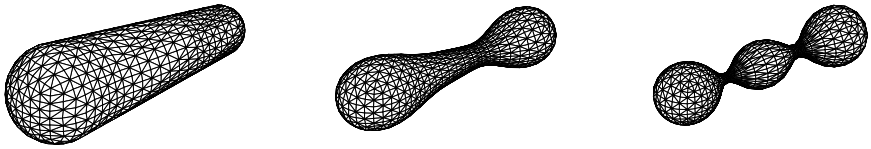

FIGURE 2. Flow with $\overline{\varkappa} = -3$ without volume preservation. $\vec{X}(t)$ for $t = 0,\ 0.1,\ 0.21$.

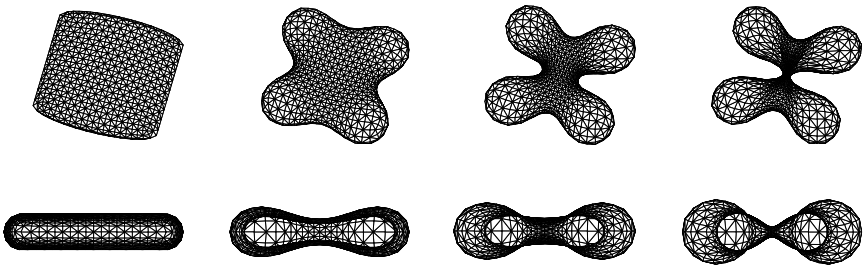

FIGURE 3. Flow with $\overline{\varkappa} = -2$. $\vec{X}(t)$ for $t = 0,\ 0.1,\ 0.15,\ 0.22$. Below the corresponding cross-sections.

With the help of our numerical method we were able to compute a variety of shapes appearing during the shape evolution of biological membranes. Examples of the evolutions are shown in the Figures 1, 2, 3, 4. For further details we refer to [1].

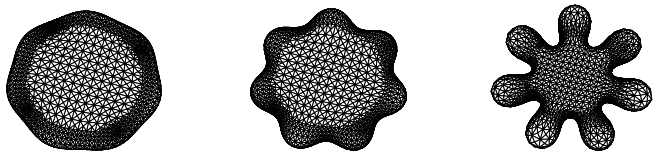

FIGURE 4. Flow with $\overline{\varkappa} = -2$. $\vec{X}(t)$ for $t = 0,\ 0.2,\ 0.42$.

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Phase-field modeling of the dynamics of multicomponent vesicles: Spinodal decomposition, coarsening, budding and fission

ANDREAS RÄTZ

(joint work with John Lowengrub and Axel Voigt)

Motivated by experiments described in [1], we first present recent results [2], where we restrict ourselves to stationary membranes and introduce an approach to deal with the numerical solution of partial differential equations on a $(d-1)$-dimensional surface $\Gamma \subset \mathbb{R}^d$. Thereby, we reformulate the problem on a domain $\Omega \subset \mathbb{R}^d$ containing Γ implicitly given by the 1/2-level set of a phase-field variable $\phi_\epsilon : \Omega \to \mathbb{R}$, where an explicit form of ϕ_ϵ can be given by

$$\phi_\epsilon(x) = \frac{1}{2}\left(1 - \tanh\left(\frac{3r(x)}{\epsilon}\right)\right)$$

with a signed distance function r of Γ and a small parameter $\epsilon > 0$ defining the width of the diffuse interface. Following ideas of [3], by multiplication with $\phi_\epsilon^2(1-\phi_\epsilon)^2$, we restrict all terms in the PDE to the diffuse interface.

Formal matched asymptotics can be applied in order to formally show the convergence of the reformulated problem to the original PDE on the surface, as the diffuse interface width shrinks to zero. The main advantage of the approach is the possibility to formulate the problem on a Cartesian grid. With adaptive grid refinement the additional computational cost resulting from the higher dimension can be significantly reduced. Numerical examples (adaptive linear finite elements) include as a benchmark a linear diffusion equation on a sphere as well as a viscous Cahn-Hilliard equation on a sphere and a torus, in order to study a spinodal decomposition and coarsening scenario on a stationary surface.

In a second part, we follow methods from [4] and develop a thermodynamically consistent phase-field model to simulate the dynamics of multicomponent vesicles [5]. The model accounts for bending stiffness, spontaneous curvature, excess

(surface) energy and a line tension between the coexisting surface phases. Our approach is similar to that recently used by Wang and Du [6] with a key difference. Here, we solve the surface mass conservation equation explicitly; this equation was not considered in [6]. Global volume and area constraints are obtained by a penalty approach. In addition, the resulting system can be viewed as a coupling of a Cahn-Hilliard-like equation (fourth order) for the lipid concentration and a diffuse-interface approximation of a Willmore-flow-like evolution equation (fourth order). This energy dissipation fulfilling system of nonlinear, nonlocal equations is numerically solved using an adaptive finite element method.

Differences between the spontaneous curvatures and the bending rigidities of the surface phases are found numerically to lead to the formation of buds, asymmetric vesicle shapes and vesicle fission. In addition, simulations of configurations far-from-equilibrium indicate that phase separation via spinodal decomposition and coarsening not only affect the vesicle shape but also that the vesicle shape affects the phase separation dynamics and may lead to lower energy states than might be achieved by evolving initially phase-separated configurations.

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Inhomogeneous lipidic membranes

Martine Ben Amar

Internal organization is one of the most intriguing aspect of the cell. Living cells have to actively maintain gradients of all sorts. Compartmentalization and trafficking aid it in doing so, and both processes extensively use mambranes. Not only are the various organelles in eukaryotic cells surrounded by membranes, but the basic intermediates in the intracellular transport pathways as well are membrane structures such as tubes and vesicles [1]. The generation and properties of these structures have been extensively studied, and much is already known about their biology, biochemistry [2, 3] and their biophysics [2, 5]. The emerging view is that the shape of the bilayer membrane *in vivo* is controlled not only by embedded and associated proteins [6] but also to a large extent by the mechanical properties of the bilayer itself [7]. For tubular structures in particular, mechanical effects

play a major role: recent biomimetic experiments [5] have shown that kinesin motors attached to microtubules can exert pulling forces on the membrane and prompt the formation of tubular structures that closely resemble similar structures identified in living cells.The existence of small membrane domains with a lipid composition that is markedly different from that of the rest of the membrane (sometimes referred to as "rafts" although considerable debate remains as to their precise interpretation) appears to be another key element of intracellular vesicular traffic [8]. Sphingolipid domains in particular have been shown to be more structured than a classical liquid membrane due to specific interactions between their constituents [1], and under appropriate conditions tend to aggregate into so-called *liquid-ordered* domains. As a consequence, these domains are mechanically different from the rest of the bilayer. The heterogeneity in membrane composition is often attributed to a phase transition leading to a local segregation between the various lipids and proteins constituting the membrane. The domain structure of heterogeneous membranes has been implicated in a multitude of cellular process [9]. Recently, an experimental model system of vesicles including "raft-like domains" has been developed [10]; it provides an elegant and efficient tool to study their properties in a more controlled way than *in vivo*. This procedure allows for systematic studies on the effects of membrane composition [11], temperature changes [12] and elastic properties of the domain[13].

Membrane domains enriched in certain lipids in particular are attracting much attention, and we have investigated the effect of such domains on the shape and fate of vesicules [14],[15],[16] and membrane tubes [17],[18]. Experiments have demonstrated that forced lipid phase separation can trigger domain instabilities [14],[15] but also tube fission [17],[18] , and we have demonstrated how this can be understood purely from the difference in elastic constants between the domains. We give a physical interpretation of the budding of the raft phase. An approach based on the Canham-Helfrich [4] energy of the system including the presence of proteins is used to derive a shape equation and to study possible instabilities. This model [14],[15] shows two different situations strongly dependent on the nature of the proteins: a regime of easy budding when the proteins are strongly coupled to the membrane and a regime of difficult budding. These results give a physical evidence for protein transportation by raft in the cell. We also investigate the viscous properties [20] of membrane domains enriched with specific lipids such as cholesterol. Using inhomogeneous giant unilammelar vesicles with cholesterol enriched raft-like domains we perform a suction experiment by adding a controlled quantity of High Density Lipoproteins, which remove the cholesterol lipids of the vesicle. Focusing on one domain, we observe its size decrease up to complete disappearance. In addition undulations of its boundary appears for a sufficient quantity of lipoproteins. This contour instability is reminiscent of the viscous fingering instability of thin films, occurring during a suction process. A theoretical model based on a two-dimensional Stokes flow [20], relates the number of oscillations to the physical parameters of the experiment and we deduce a reasonable value of the viscosity of the membrane.

The formation of two-phase lipidic tubes of membrane in the framework of the Canham-Helfrich model has been investigated [17],[18]. The two phases have different elastic moduli (bending and Gaussian rigidity), different tensions and a line tension prevents the mixing. For a set of parameters close to experimental values, periodic patterns with arbitrary wavelength can be found numerically. A wavelength selection is detected via the existence of an energy minimum. When the chemical composition induces an important enough size disequilibrium between both phases, a segregation into two half infinite tubes is preferred to a periodic structure.

In conclusion, the Canham-Helfrich [4] model extended to multi-domain membranes [14],[15] is able to explain shapes and shape instabilities of vesicules and tubes. We also show that viscous fingering instabilities can also occur in inhomogeneous membranes, proving the liquid properties of these systems.

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A Continuum Cartoon of Lipid Bilayers

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(joint work with Matthias Röger)

1. Introduction

In this talk I discuss the upscaling of a microscale model of cell membranes. More detailed information, a precise statement of the full result, and a complete proof can be found in [1].

1.1. **Partial localisation and solid-like behaviour.** Lipid bilayers are *thin structures*, in the sense that there is a separation of length scales: the thickness of a lipid bilayer is fixed to approximately two lipid lengths, while the in-plane spatial extent is only limited by the surroundings. Structures that are thin in one or more directions and 'large' in others we call *partially localised*.

In a cell membrane, the lipid molecules behave fluid-like with respect to in-plane rearrangements. However, as planar structures lipid bilayers show a remarkable *solid-like behaviour*: they resist various types of deformation, such as extension, bending, and fracture, much in the way a sheet of rubber does.

2. Descriptions on different scales

Various descriptions of lipid molecules can be found in the literature. Microscopic models describe positions of molecules or, in 'coarse-grained' versions, of groups of molecules (*e.g.* heads and tails). On the macroscale cell membranes are considered as smooth closed hypersurfaces. We will investigate a *mesoscale* model that introduces an energy functional defined on a class of density functions of head and tail particles.

2.1. **Energy on the macroscale: The Helfrich Hamiltonian and the Elastica functional.** Canham, Helfrich, and Evans pioneered the modelling of lipid bilayer vesicles by energy methods [3, 4, 5]. The name of Helfrich is now associated with a surface energy for closed vesicles, represented by a smooth boundaryless surface S, of the form

$$E_{\text{Helfrich}}(S) = \int_S \left[k(H - H_0)^2 + \overline{k}K\right] d\mathcal{H}^2. \tag{1}$$

Here $k > 0$ and $\overline{k}, H_0 \in \mathbb{R}$ are constants, H and K are the (scalar) total and Gaussian curvature, and $\mathcal{H}^2$ is the two-dimensional Hausdorff measure. This energy functional, and many generalisations in the same vein, have been remarkably successful in describing the wide variety of vesicle shapes [2].

A natural two-dimensional reduction of the Helfrich curvature energy is given by the classical bending energy of the curve, the *Elastica functional*

$$\mathcal{W}(\gamma) = \frac{1}{4}\int_\gamma \kappa^2 \, d\mathcal{H}^1. \tag{2}$$

Here γ is a smooth closed curve in $\mathbb{R}^2$ and κ equals the scalar curvature of γ. This functional has a long history going back at least to Jakob Bernoulli; critical points of this energy are known as *Euler Elastica*.

2.2. **Energy on a mesoscale: The functional $\mathcal{F}_\varepsilon$.** Whereas microscale descriptions often are too complex, the macroscale models are only phenomenological and sometimes too simple. We consider here an energy functional on a scale in between. The derivation is inspired by well-known models of block copolymers, and uses a number of sometimes radical simplifications. Nevertheless we demonstrate that the model captures enough of the essence of lipid bilayers to address the issues of partial localisation and solid-like behaviour.

In a rescaled version the mesoscale energy is given by a class of admissible functions

(3)
$$\mathcal{K}_\varepsilon := \left\{ (u,v) \in \mathrm{BV}\big(\mathbb{R}^2; \{0, \frac{1}{\varepsilon}\}\big) \times L^1\big(\mathbb{R}^2; \{0, \frac{1}{\varepsilon}\}\big) : \int u = \int v = M,\ uv = 0 \text{ a.e.} \right\}$$

and functionals $\mathcal{F}_\varepsilon$,

(4)
$$\mathcal{F}_\varepsilon(u,v) := \begin{cases} \varepsilon \displaystyle\int |\nabla u| + \frac{1}{\varepsilon} d_1(u,v) & \text{if } (u,v) \in \mathcal{K}_\varepsilon, \\ \infty & \text{otherwise.} \end{cases}$$

Here $d_1(\cdot,\cdot)$ is the Monge-Kantorovich distance as defined in Definition 5, $\varepsilon > 0$ is a small parameter and $M > 0$ is fixed.

Despite the simplifications in the derivation the physical origin of the various elements of $\mathcal{F}_\varepsilon$ remains identifiable:

- The functions u and v represent densities of tail and head particles;
- The term $\varepsilon \int |\nabla u|$, coupled with the restriction to functions u and v that take only two values, and have disjoint support, represents an interfacial energy;
- The Monge-Kantorovich distance $d_1(u,v)$ between u and v is a weak remnant of the covalent bonding between head and tail particles.

By (3) the small parameter $\varepsilon > 0$ introduces a *large density* scaling. We prove that $\mathcal{F}_\varepsilon$ favours partially localised structures and that the parameter ε in fact corresponds to 'the thickness' of the support of u, v. We will also show that $\mathcal{F}_\varepsilon$ displays solid-like behaviour in the sense of a penalisation of stretching, fracture, and bending.

3. Results

We study the behaviour of the mesoscale energy $\mathcal{F}_\varepsilon$ in the singular limit $\varepsilon \to 0$ and consider the rescaled functionals

$$\mathcal{G}_\varepsilon = \frac{\mathcal{F}_\varepsilon - 2M}{\varepsilon^2}.$$

Our result can be described as follows:

Theorem 3. *Take any sequence $(u_\varepsilon, v_\varepsilon)_{\varepsilon>0} \subset \mathcal{K}_\varepsilon$ such that $\mathcal{G}_\varepsilon(u_\varepsilon, v_\varepsilon)$ remains bounded. Then the sequence $(u_\varepsilon)_{\varepsilon>0}$ converges as measures to a finite collection of closed curves of class $W^{2,2}$. Moreover, each curve in this collections appears an even number of times and the curves do not intersect transversally.*

Theorem 4. *The functionals $\mathcal{G}_\varepsilon$ Gamma-converge to the curve bending energy $\mathcal{W}$, generalised to systems of curves: For a system of curves $\Gamma = (\gamma_1, ..., \gamma_N), N \in \mathbb{N}$, which satisfies the conditions that $\gamma_1, ..., \gamma_N$ are closed, of class $W^{2,2}$, have no transversal crossings and that $\sum_{i=1}^N \text{length}(\gamma_i) = M$, the value of the limit functional is given by*

$$\mathcal{W}(\Gamma) := \sum_{i=1}^{N} \mathcal{W}(\gamma_i).$$

If any of the conditions above is not satisfied the value of the limit functional is infinity.

Our results in fact show that the essence of lipid bilayer behaviour is captured by the mesoscale model:

- *Partial localisation:* Boundedness of $\mathcal{G}_\varepsilon$ along a sequence $u_\varepsilon, v_\varepsilon$ implies that the support of u_ε resembles a tubular ε-neighbourhood of a curve.
- *No Stretching:* All curves which belong to a system of curves with finite energy carry a constant density function (the constant being one).
- *No Fracture:* A curve which belongs to a system of curves with finite energy is necessarily closed.
- *Bending stiffness:* The Gamma-limit of the functional $\mathcal{G}_\varepsilon$ equals the generalised Elastica functional.

4. Ingredients of the proofs

The Monge-Kantorovich distance $d_1(u, v)$, which is part of $\mathcal{F}_\varepsilon(u, v)$, is characterised by an *optimal mass transport* problem.

Definition 5 For $(u, v) \in \mathcal{K}_\varepsilon$ the Monge-Kantorovich distance $d_1(u, v)$ is given by the minimal cost for transporting u to v,

$$d_1(u, v) = \min_S \int_{\mathbb{R}^2} |S(x) - x| u(x)\, dx$$

where the minimum is taken over all maps $S : \text{supp}(u) \to \text{supp}(v)$ which push u forward to v in the sense that

$$\int_{\mathbb{R}^2} \eta(S(x)) u(x)\, dx = \int_{\mathbb{R}^2} \eta(y) v(y)\, dy \quad \text{for all } \eta \in C^0(\mathbb{R}^2).$$

An optimal transport map S as above exists [6] and satisfies that

- the transport is along *transport rays*, which are line-segments in $\mathbb{R}^2$,
- two different transport rays can only intersect in a common endpoint.

Let the boundary of $\mathrm{supp}(u)$ be given by a collection of smooth closed curves γ_i with length L_i, $i = 1, ..., N$. We use these curves and the transport rays to parametrise the support of u, v and to compute $d_1(u, v)$. The key observation is that the transport problem above splits into one-dimensional mass transport problems in suitably defined *mass coordinates*. This coordinates depend on the local geometry, in particular on

- the angle between the ray directions and the tangential of a boundary curve,
- the rate of change of the ray directions.

The crucial estimate we prove is

$$\begin{aligned}\mathcal{G}_\varepsilon(u,v) \geq \sum_{i=1}^{N} \int_0^{L_i} \Big[\frac{1}{\varepsilon^2}\Big(\frac{1}{\sin\beta_i(s)} - 1\Big) M_i(s)^2 + \frac{1}{\varepsilon^2}\big(M_i(s) - 1\big)^2 \Big]\, ds \\ + \sum_{i=1}^{N} \int_0^{L_i} \frac{1}{4\sin\beta_i(s)} \Big(\frac{M_i(s)}{\sin\beta_i(s)}\Big)^4 \alpha_i'(s)^2\, ds \qquad (5)\end{aligned}$$

The quantities in this inequality are related to the geometry of u, v as follows:

- $\beta_i(s)$ corresponds to the angle between $\gamma_i'(s)$ and the ray through $\gamma_i(s)$,
- $\alpha_i'(s)$ corresponds to the derivative in $\gamma_i(s)$ of the ray directions,
- $M_i(s)$ represents the 'relative mass' over $\gamma_i(s)$.

The inequality (5) shows that for small $\varepsilon > 0$ the ray directions become perpendicular to the boundary curves, and the relative mass $M_i(s)$ is approximately one. The latter property is related to a constant thickness 2ε of the support of u and by the first property $\alpha_i'(s)^2$ is approximately the squared curvature of γ_i in $\gamma_i(s)$. In this way the last term in (5) motivates the bending energy in the limit.

Taking a sequence $(u_\varepsilon, v_\varepsilon)_{\varepsilon>0}$ with uniformly bounded values of $\mathcal{G}_\varepsilon$ we first derive that the boundary curves of $\mathrm{supp}(u_\varepsilon)$ are compact. We prove that their limit coincides with the limit of the measures $u_\varepsilon \mathcal{L}^2$. Finally from (5) we deduce the lower semicontinuity property belonging to the Gamma-convergence stated in Theorem 4.

5. Conclusions

The mesoscale model investigated in this presentation reproduces some key properties of bilayer membranes. The mathematical analysis of the corresponding energy functional gives an example of stable partially localised patterns and yields a new approximation of the Elastica functional.

Our analysis is a starting point to investigate more realistic models. An extension to three-dimensions and the replacement of the Monge-Kantorovich distance term in $\mathcal{F}_\varepsilon$ by the more realistic 2-Wasserstein distance term is desirable. A characterisation of local minima of the functionals F_ε and their convergence as $\varepsilon \to 0$ are further interesting questions.

The energy $\mathcal{F}_\varepsilon(u, v)$ is a prototype of similar energies consisting of a nonlocal distance term and an interfacial energy, e.g. arising in models for block copolymers.

The detailed information we have obtained here supports also the understanding of more general energies.

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Lateral phase separation on biomembranes

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(joint work with Charles M. Elliott)

We are interested in separation phenomena on biomembranes with respect to the lipid composition resulting in intermembrane domains, called phases in the following. In addition to the classical bending energy (cf.[5]) a line energy describing the excess free energy of the phase boundary according to the model in [7] is taken into account. Denoting by Γ_i, $i = 1, 2$ the membranes occupied by each of the two phases and by $\gamma = \partial\Gamma_1 = \partial\Gamma_2$ the common boundary the free energy is

$$F_{\text{memb}} = \sum_{i=1}^{2} \int_{\Gamma_i} \frac{k_i}{2}\kappa^2 + \int_{\gamma} \sigma \tag{1}$$

where the k_i are the bending rigidities, κ is the curvature, and σ is the line energy density. Additional contributions to the bending energy from the Gauss curvature and a spontaneous curvature are neglected.

In biophysics, the goal has been to compute equilibrium shapes of membranes in dependence of the total membrane area $|\Gamma|$, the volume of the enclosed domain, the surface area ratio of the two phases, and the coefficients k_i, and σ, see [7, 6] for analytical and [9, 11, 8] for numerical studies. We want to contribute to this issue by providing a numerical tool based on a triangulation of the membrane on which isoparametric linear finite elements finite elements are defined and a diffuse interface model for the line energy. The idea is then to use [3] for fields on evolving surfaces and [4, 1] for Willmore flow in order to relax appropriate initial configurations to local minimisers by a gradient flow dynamics.

Computing the variation of (1) is based on deforming the space into which the two-phase membrane is embedded by a vector field $\boldsymbol{w} : \mathbb{R} \to \mathbb{R}$. Defining $\Gamma_i^s :=$

$\{\boldsymbol{x}+s\boldsymbol{w} \,|\, \boldsymbol{x} \in \Gamma_i\}$, $\gamma^s := \{\boldsymbol{x}+s\boldsymbol{w} \,|\, \boldsymbol{x} \in \gamma\}$, and the variation of F_{memb} in direction $\boldsymbol{w}$ by $\langle \delta F_{memb}, \boldsymbol{w}\rangle := \frac{d}{ds} F_{memb}(\Gamma_1^s, \Gamma_2^s, \gamma^s)|_{s=0}$ we may compute the Euler-Lagrange equation of (1) subject to the constraints on the areas of the two membranes and the enclosed volume (we refer to [10, 2] for the computation for open membranes). The constraints are taken into account with Lagrange multipliers denoted by λ_i, $i = 1, 2$, and p, respectively:

$$0 = k_i(\Delta_\Gamma \kappa + |\nabla_\Gamma \boldsymbol{\nu}|^2 \kappa - \tfrac{1}{2}\kappa^3) - \lambda_i \kappa + p \quad \text{on } \Gamma_i$$

where Δ_Γ is the Laplace-Beltrami operator on the surface Γ_i, ∇_Γ the surface gradient, and $\nabla_\Gamma \boldsymbol{\nu}$ the Weingarten map with a unit normal $\boldsymbol{\nu}$; on the common phase boundary γ we obtain the conditions

$$\begin{aligned} 0 &= \kappa_i, \quad i = 1, 2, \\ 0 &= k_i \nabla_\Gamma \kappa_i \cdot \boldsymbol{\tau}_i \, \boldsymbol{\nu}_i + \lambda_i \boldsymbol{\tau}_i - \sigma \boldsymbol{\kappa}_\gamma \end{aligned}$$

in addition to the conditions that the membranes Γ_i have to be attached to it; here, κ_i and $\boldsymbol{\nu}_i$ are the limiting values of κ and $\boldsymbol{\nu}$ when approaching γ from Γ_i, $\boldsymbol{\tau}_i$ the the external unit co-normal with respect to Γ_i, and $\boldsymbol{\kappa}_\gamma$ is the curvature vector of γ (direction of fastest length decrease).

Our approach for the phase separation employs an order parameter $c : \Gamma \to \mathbb{R}$ to distinguish the phases. The line energy is replaced by a Ginzburg-Landau functional

$$F_{\mathrm{GL}} = \int_\Gamma f, \quad f := \frac{\sigma\varepsilon}{2} |\nabla_\Gamma c|^2 + \frac{\sigma}{\varepsilon} \psi(c)$$

where ∇_Γ is the surface gradient and $\psi(c)$ is a double-well potential with minima in -1 and 1 corresponding to the two phases. The constraints on the surface areas of the two phases and their ratio become a constraint on the total area and one of the form $\int_\Gamma h(c)$ with a monotone function h satisfying $h(0) = 0$, $h(1) = 1$. The bending rigidity becomes a function of the order parameter $k(c)$ where one will require that $k(1) = k_1$ and $k(-1) = k_2$.

To set up a dynamics that decreases the energy one may define the evolution of c and then, by computing the time derivative of the membrane energy, deducing an appropriate definition for the membrane velocity. Exemplary, we restrict the membrane velocity to be in normal direction (let $v_{\boldsymbol{\nu}}$ denote the scalar normal velocity in direction $\boldsymbol{\nu}$) and postulate a Cahn-Hilliard type equation for c:

$$\begin{aligned} \partial_t^\circ c - c\kappa v_{\boldsymbol{\nu}} &= \Delta_\Gamma \mu, \\ \mu = \delta_c F_{memb} &= -\varepsilon\sigma \Delta_\Gamma c + \tfrac{\sigma}{\varepsilon} \psi'(c) + \tfrac{1}{2} k'(c) \kappa^2, \end{aligned}$$

where ∂_t° stands to the normal time derivative or, in this case, the material derivative. In this approach, c is a conservative surface quantity whence $\int_\Gamma c$ is kept constant during the evolution. Computing $\frac{d}{dt} F_{memb}$ then yields the following law for the normal velocity:

$$(2) \quad v_{\boldsymbol{\nu}} = -\Delta_\Gamma\big(k(c)\kappa\big) - k(c)|\nabla_\Gamma \boldsymbol{\nu}|^2 \kappa + (f - \mu c)\kappa + \nabla_\Gamma c \otimes \nabla_\Gamma c : \nabla_\Gamma \boldsymbol{\nu} + \lambda\kappa - p$$

where λ is a Lagrange multiplier for the area constraint and $A : B = \sum_{ij} A_{ij} B_{ij}$.

Discretising (2) as described in [1] yields a system of the following form in every timestep to compute the new coordinates $\underline{x}^{m+1}$ of the mesh nodes:

$$I^m \underline{x}^{m+1} = \underline{r}^m + \lambda^{m+1} \underline{k}^m + p^{m+1} \underline{n}^m.$$

Solving $(I^m)^{-1}\underline{r}^m$, $(I^m)^{-1}\underline{k}^m$, and $(I^m)^{-1}\underline{n}^m$ one may consider $\underline{x}^{m+1}$ as a function of λ and p, and a Newton iteration can be performed in order to compute appropriate reals λ^{m+1} and p^{m+1} such that the constraints are fulfilled. In a second step the new field c^{m+1} on the new surface can be computed as described in [3]. Some numerical tests have been performed. Exemplary, in Fig. 1 the results for a cigare shaped initial surface are depicted. Further investigations of such procedures, in particular simulations for quantitative comparisons with the results in [7] are planned for the future.

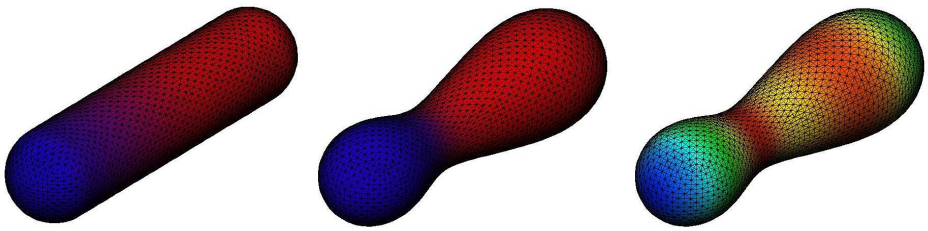

FIGURE 1. Left: initial surface triangulated with 9216 triangles and 4610 nodes and initial profile of c, values between -1 (blue) and +1 (red). Middle: relaxed surface with c profile. Right: relaxed surface with curvature, values between -4.2 (blue) and -1.7 (red).

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