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Cell membranes, Lipid Bilayers, and the Elastica Functional

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We study an energy functional that arises in a simplified two-dimensional model for lipid bilayer membranes. We demonstrate that this functional, defined on a class of spatial mass densities, favours concentrations on 'thin structures'. Stretching, fracture and bending of such structures all carry an energy penalty. In this sense we show that the models captures essential features of lipid bilayers, namely *partial localisation* and a *solid-like behaviour*.

Our findings are made precise in a Gamma-convergence result. We prove that a rescaled version of the energy functional converges in the 'zero thickness limit' to a functional that is defined on a class of planar curves. Finiteness of the limit value enforces both optimal thickness and non-fracture; if these conditions are met, then the value of this functional is given by the classical Elastica (bending) energy.

1 Introduction

In this note we investigate a new model for cell membranes. For more detailed informations, a precise statement of the full result and a complete proof we refer to [5].

1.1 Lipid Bilayers

Cell membranes shield the interior of the cell from the outside and are typically formed by lipid bilayers. Their main component is a lipid molecule which consists of a head and two tails. The head is hydrophilic, while the tails are hydrophobic. This difference in water affinity causes lipids to aggregate in structures as shown in Fig. 1, reducing energetically unfavourable tail-water interactions. Despite the structured appearance of the bilayer, there is no covalent bonding between any two lipids; the bilayer structure is entirely the result of the hydrophobic effect.

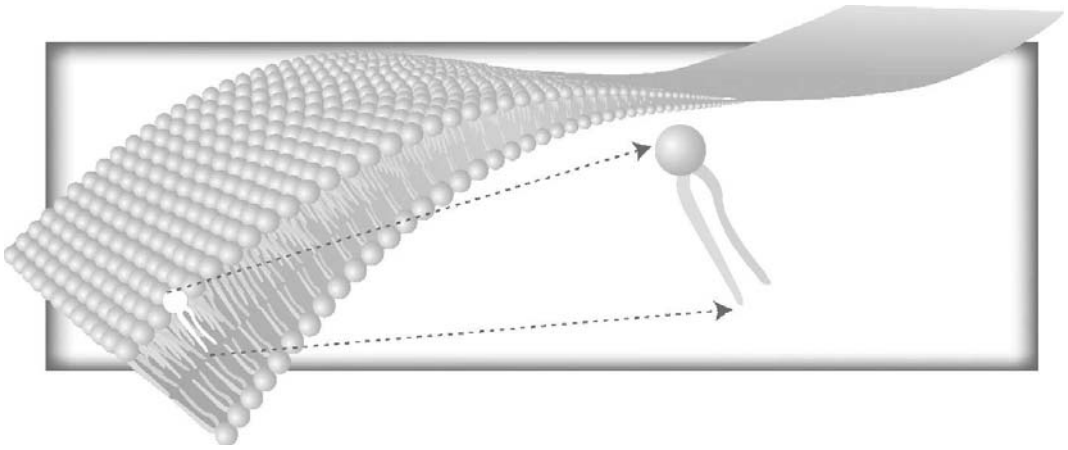

Fig. 1 Lipid molecules aggregate into macroscopically surface-like structures

1.2 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.

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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 [2, 4, 3]. 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 [6].

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

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

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

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

Here $d_1(\cdot,\cdot)$ is the Monge-Kantorovich distance as defined in Definition 4.1, $\varepsilon > 0$ is a small parameter and $M > 0$ is fixed.

Despite of 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 partial 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

Here we motivate and informally describe our main results.

3.1 Motivation: Special structures

To gain some insight into the properties of $\mathcal{F}_\varepsilon(u,v)$ one can study particular choices of u, v which allow to compute the value of $\mathcal{F}_\varepsilon$.

1. A **disc:** concentrate all the mass of u into a disc in $\mathbb{R}^2$, of radius $R \sim \varepsilon^{1/2}M^{1/2}$, surrounded by the mass of v in an annulus. Since $d_1(u,v)$ is approximated by an 'average transport distance' multiplied by the total mass M this gives
$$\mathcal{F}_\varepsilon(u,v) \sim \varepsilon^{-1/2}M + \varepsilon^{1/2}M^{1/2}$$
2. A **strip**: take the support of u to be a rectangle of width $t\varepsilon$ and length M/t, flanked by two strips of half this width for $\operatorname{supp} v$. Then
$$\mathcal{F}_\varepsilon(u,v) = \frac{t}{2}M + \frac{2}{t}M + 2t\varepsilon.$$

Comparing the two one observes that the strip structure has lower energy, for small ε, than a spherical one. For the strip structure we find that there is a preferred thickness given by 2ε and that the energy is at least $2M$ plus 'higher order terms'.

This is a first indication that $\mathcal{F}_\varepsilon$ may favour partial localisation.

Explicit calculations can also be done for *ring structures*. There one observes that the curvature of the structures create an energy penalty on the order $O(\varepsilon^2)$. This gives a hint how $\mathcal{F}_\varepsilon$ is related to a bending energy.

3.2 Statement of the results

We study the behaviour of th 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 3.1 *Take any sequence $(u_\varepsilon, v_\varepsilon)_{\varepsilon>0} \subset \mathcal{K}_\varepsilon$ with small energy in the sense 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 transversally intersect.*

Theorem 3.2 *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 self-intersections and that $\sum_{i=1}^N \operatorname{length}(\gamma_i) = M$, 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 4.1 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 $S : \operatorname{supp}(u) \to \operatorname{supp}(v)$ 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 [1] 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

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

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 3.2.

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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