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# Fluid lipid membranes: From differential geometry to curvature stresses

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ABSTRACT

A fluid lipid membrane transmits stresses and torques that are fully determined by its geometry. They can be described by a stress- and torque-tensor, respectively, which yield the force or torque per length through any curve drawn on the membrane's surface. In the absence of external forces or torques the surface divergence of these tensors vanishes, revealing them as conserved quantities of the underlying Euler–Lagrange equation for the membrane's shape. This review provides a comprehensive introduction into these concepts without assuming the reader's familiarity with differential geometry, which instead will be developed as needed, relying on little more than vector calculus. The Helfrich Hamiltonian is then introduced and discussed in some depth. By expressing the quest for the energy-minimizing shape as a functional variation problem subject to geometric constraints, as proposed by Guven (2004), stress- and torque-tensors naturally emerge, and their connection to the shape equation becomes evident. How to reason with both tensors is then illustrated with a number of simple examples, after which this review concludes with four more sophisticated applications: boundary conditions for adhering membranes, corrections to the classical micropipette aspiration equation, membrane buckling, and membrane mediated interactions.



## 1. Introduction

Lipid membranes are amazing soft matter structures. Self-assembled from single molecules into fluid films just a few nanometers thick, they can stably span macroscopic lateral scales. Many of their characteristic energies (such as the aggregation energy per lipid or the bending rigidity) are about an order of magnitude bigger than thermal energy, hence membranes are stable against thermal fluctuations but soft enough to be easily deformed, for instance by proteins and the energies available biochemically from ATP hydrolysis. For the same reason undulations of lipid bilayers are readily noticeable in a microscope as "flickering," and they give rise to physically observable effects, for instance a long-range entropic repulsion between two fluctuating membranes. The strong drop in dielectric constant across just a few nanometers suffices to make membranes essentially perfect insulators for bare ionic charges, and they also constitute barriers over a range of permeabilities for a great many other solutes. Membranes hence compartmentalize space, but they can also change topology through fission and fusion events, which in turn can be exquisitely controlled by several classes of protein machineries. Mixed membranes show a variety of different phases and phase coexistence regions, and these can couple back to their morphology. All of these facets of membrane chemistry and physics have been widely studied over the past decades, and they are the topics of numerous contributions in this special issue. The present review focuses on the large scale: how to describe membranes in a way that is both mathematically elegant and efficient as well as physically intuitive.

One curious aspect of the way lipids assemble into bilayers is that the emergent area per lipid is a remarkably stiff degree of freedom: membranes are hard to stretch but easy to bend. Of course, stretching and bending are not dimensionally equivalent, so the meaning of "lower in energy" will have a length scale hidden in it. A better way to phrase the statement is therefore as follows: Take a flat membrane patch and stretch it by some dimensionless strain $s$, thus increasing its energy. Alternatively, curve it into a closed but tensionless spherical vesicle of radius $R$. If the two energies happen to be equal, what is the value of $R$? A simple calculation (see Section 3.2) gives the answer

$$R_s = \frac{1}{s}\sqrt{\frac{2(2\kappa+\overline{\kappa})}{K_A}}, \tag{1}$$

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where $\kappa$ and $\bar{\kappa}$ are the bending and Gaussian curvature modulus, respectively, and $K_A$ is the area expansion modulus. Inserting typical values for these material parameters and choosing a strain of $s = 1\%$ leads to $R \approx 80$ nm. Quite small strains correspond to fairly large curvatures (in the sense that this radius is only about 20 times bigger than the bilayer thickness, while a membrane's lateral size can easily exceed its thickness by three to four orders of magnitude).

For the purpose of the present review, the probably most remarkable aspect of fluid lipid membranes that follows from this observation is that on length scales not much bigger than their own thickness, their physical behavior can be described with astonishing accuracy by a purely geometric Hamiltonian—one that penalizes curvature. In the early 1970s this insight dawned on Canham (1970), Helfrich (1973) and Evans (1974), and the theoretical (and often closely linked experimental) work that followed from this idea ushered in a golden era for membrane science.

Unfortunately, curvature elastic surfaces come along with some challenging math. For instance, more than a decade passed between the discovery of the energy functional (Canham, 1970; Helfrich, 1973; Evans, 1974) and the appearance of its associated Euler–Lagrange equation in the physics literature (Ou-Yang and Helfrich, 1987, 1989).[1,2] This so-called "shape equation," in turn, is a formidable fourth order partial nonlinear differential equation, and finding a general analytic solution for this behemoth seems a forlorn hope. In the 1990s substantial efforts were devoted to numerically solving this (or a closely related) equation—mostly for the special case of axisymmetry (Svetina and Žekš, 1989; Seifert and Lipowsky, 1990; Lipowsky, 1991; Seifert et al., 1991; Jülicher and Lipowsky, 1993, 1996; Jülicher and Seifert, 1994; Miao et al., 1994), but occasionally also for the general case (Heinrich et al., 1993; Kralj-Igliç et al., 1993). The reader will find more details on this in existing reviews (Seifert and Lipowsky, 1995; Seifert, 1997).

As important as the extensive numerical results have been, they might also have contributed to a feeling that outside heavy numerics or perturbation theory little can be said about the general case. The shape equation expressed in some parametrization does not readily reveal its structure, and even though a first integral for the axisymmetric case had been found (Zheng and Liu, 1993), its physical meaning remained elusive. And yet, there exists a link between the symmetry of variational problems and the solutions of their associated Euler–Lagrange equations: Noether's theorem (Goldstein et al., 2002). Continuous symmetries, such as translations and rotations, go along with conservation laws and, in field theory, conserved currents that permit one to discuss exact properties of these solutions even if one cannot actually find them. The consequence for membranes is that there exist objects—the stress and the torque tensor—which are divergence free as evaluated on the surface of the membrane (Capovilla and Guven, 2002a,b, 2004; Capovilla et al., 2002). The resulting conservation laws hold even if the specific membrane shape has no discernible translation or rotation symmetry, for they are a consequence of the symmetry of the *Hamiltonian*, not of a specific *solution*.

The existence of stress- and torque-tensors, which are explicit functions of a membrane's geometry, affords profound insights not only into the nature of solutions, but also into questions of immediate practical relevance, such as: what force does a membrane respond with upon deformation? How does it adapt its shape when it adheres to a substrate or another membrane, and how does it remodel the other membrane in the latter case? And what types of forces does it transmit between multiple objects binding to it? Despite the stress tensor's intuitive physical meaning, physicists seem to be somewhat shy to use it, whereas for instance mechanical engineers have developed highly sophisticated frameworks largely unheard-of in the physics community (Jenkins, 1977a,b; Steigmann, 1999; Agrawal and Steigmann, 2008; Napoli and Vergori, 2010). I suspect the reasons are twofold: First, once physicists learn about Lagrangian or Hamiltonian Mechanics, the concepts of stress and force might appear a quaint remnant of the olden Newtonian days, best to be avoided. This of course is a luxury one can only afford in a world consisting of point particles, but not one that is populated with elastic continua.[3] And second, in order to express the stress tensor in a geometric language free of the idiosyncrasies of arbitrary surface parametrizations, one needs some differential geometry (of course, so do the engineers). And even though the amount necessary to understand virtually the entire framework from scratch is remarkably modest, it might still prove too much of an activation barrier.

It is the purpose of this review to provide a helping hand over this barrier. While there are excellent textbooks on differential geometry aplenty (Kreyszig, 1991; do Carmo, 1976, 1992; Willmore, 2012; Spivak, 1970, 1975a,b; Lovelock and Rund, 1989; Frankel, 2004; Schutz, 1980; Darling, 1994; Flanders, 1989), the bare minimum necessary to follow most of the reasoning and all of the subsequent applications can be condensed into a couple of pages. This review is aimed towards researchers who wish to learn more about these concepts, but who have no working experience with differential geometry and do not wish to invest several months to study the mathematical prerequisites before they can decide whether it is even worthwhile to adopt this framework. What follows will therefore be akin to a teaser trailer, focusing on the highlights in an abbreviated fashion, hoping to convince the reader that it's worthwhile to watch the whole movie (or, even better, read the book).

This review is organized as follows. Section 2 starts by summarizing the essential differential geometry of two-dimensional surfaces embedded in three-dimensional space. Beginning with a general purpose parametrization, metric and curvature tensor are introduced, and their connecting integrability conditions are developed. Along the way the issues of co- and contravariant components are clarified and the notion of a covariant derivative is introduced. In Section 3 these tools are used to derive the Helfrich Hamiltonian as the essentially unique large-wavelength limit of what physics and symmetry permit, and its phenomenological parameters are discussed in some detail, after a quick glance at thin plate theory. The relation between bilayer and monolayer physics is discussed within the framework of parallel surfaces, and a few comments on higher order corrections are made. Section 4 derives the stress tensor from first principles, beginning with a motivation for why membrane stresses differ from those in soap films or simple fluid surfaces. After revisiting the concept of a surface variation, and arriving at the classical shape equation by varying the geometry and ultimately the Helfrich Hamiltonian piece-by-piece,

[1] The work by Ou-Yang and Helfrich (1987, 1989) introduced the shape equation to physicists, but in other communities it had been well known. The special case $K_0 = 0$ was worked out a decade earlier by Jenkins (a mechanical engineer) (Jenkins, 1977a,b), and mathematicians knew it long before then (Thomsen, 1924; Blaschke, 1929; Willmore, 1965, 1982; White, 1973; Pinkall and Sterling, 1987). Since including $K_0$ does not incur any additional complications, these earlier publications deserve more credit than is usually given to them in the physics community.

[2] Even afterwards, a widely used axisymmetric specialization of the shape equations was claimed to be incorrect (Hu and Ou-Yang, 1993; Naito et al., 1993; Zheng and Liu, 1993), a criticism that was refuted on the basis that more attention needs to be given to the boundaries during functional variation (Jülicher and Seifert, 1994).

[3] The Landau/Lifshitz volume on elasticity (Landau and Lifshitz, 1999) pithily disabuses the reader of this misconception by introducing the strain tensor in Chapter 1 paragraph 1, and the stress tensor in paragraph 2; however, elasticity is no longer part of the standard physics curriculum.