Theory of biomembranes

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Göteborg July, 2001

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1 Introduction

The cell membrane is a lipid membrane (see below) with various molecules, such as proteins and cholesterol molecules, attached or embedded. These membranes are the main component in biological systems, for instance the human brain consists of a network of membranes with a total surface area of $10^3 - 10^4$ m^2.

The basic ingredient of a biomembrane is the phospholipid molecule. The most important property of this molecule is that it is amphiphilic; one of its ends (the phosphatic head) is strongly attracted to water, thereby being hydrophilic, while the other end (the hydrocarbon tail) repels water and is therefore hydrophobic. This property of the lipid molecules make it energetically favourable for them, when being put in water, to form a closed bilayer with the phosphatic heads pointing outwards while the hydrocarbon tails are pointing inwards and are thereby kept from contact with the water. The typical thickness of a bilayer is 5-10 nm. A typical effective radius of the vesicle is 1-10 μm.

The interaction between molecules in a membrane (also referred to as a *vesicle*) is usually so weak that the bilayer is in a *fluid* state. The molecules are therefore free to diffuse along the membrane. A typical diffusion constant, D, for a phospholipid molecule is about 1 μ m^{2}s^{-1}. It therefore takes roughly one second for the molecule to go from one end of the bilayer to the other. On the other hand the time needed to go from one layer to the other (the so called flip-flop process) is rather long. It is therefore safe to assume that the molecules in the bilayer are bound to one layer, but behaves as a fluid within this layer.

Vesicles are found in a lot of different shapes depending on the environmental properties. The shapes are usually catagorized by noticing that the different shapes have different symmetry properties (catagorized by symmetry groups, see ([**?**])) and different number of holes (the so called genus, g). The biconcave shape of a typical red blood cell is shown in Fig 1. Its shape is invariant under rotations and reflections in the x-y plane as well as under reflection in mirror planes perpendicular to the x-y plane. The corresponding symmetry group is called $D_{\infty h}$. It has no holes and therefore $g = 0$.

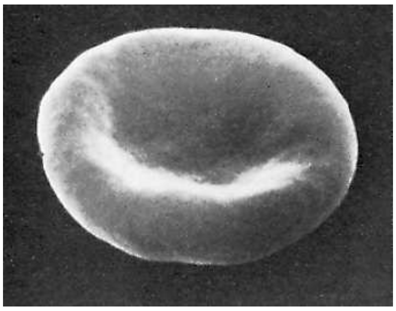

Figure 1: The typical biconcave shape of a red blood cell.

We will in this text only discuss the "macroscopic" properties of membranes. By macroscopic we mean that we only look at processes occuring on length scales such that it is possible to divide the membrane inot small area elements, dS, such that dS is small on the macroscopic scale but still contains a large number of molecules. It is instructive to consider a simple soap bubble. In zero gravity it is a spherical shell which is held together by the different forces between the molecules within the shell. In understanding many of its properties it is not necessary to understand the nature of interaction between the constituent molecules, but instead the shape of the bubble is determined by its elastic constants (which are macroscopic material constants). It turns out that a similar description is possible for vesicles, the elastic energy is however completely different from the one discussed above (due to the *fluidity* of the membrane).

Exercise 1
Figure out the symmetries of yourself. Also find out how the corresponding symmetry group is denoted (take a look in any textbook on group theory).

2 Mathematical preliminaries

This chapter is an attempt to develop the necessary mathematical concepts of curved surfaces in 3-dimensional Euclidean space needed for a thorough understanding of the rest of this text. The apparatus for dealing with curved surfaces is differential geometry and topology.

2.1 Surfaces

Consider a curve in 3-dimensional Euclidean space. A curve is fully characterized by one parameter, t, such as $t \rightarrow (x(t), y(t), z(t))$. In specifying a surface we need *two* parameters, u and v, to fully describe it

$$u, v \rightarrow (x(u,v), y(u,v), z(u,v)). \tag{1}$$

We also require that the dependence on the parameters should be smooth.

Example 1
The unit sphere is given by two parameters $0 < \Theta < \pi$ and $0 < \phi < 2\pi$ according to

$$\vec{x}(\Theta, \phi) = (\mathrm{sin}\Theta\mathrm{cos}\phi, \mathrm{sin}\Theta\mathrm{sin}\phi, \mathrm{cos}\Theta). \tag{2}$$

Example 2
An alternative parametrization of the unit sphere is

$$\vec{x}(x, y) = (x, y, \pm\sqrt{1-(x^2+y^2)}) \tag{3}$$

where the plus (minus) sign corresponds to the upper (lower) part of the sphere.

Example 3
The torus shown in Fig. 2. Its parametrization is $0 < u < 2\pi$ and $0 < v < 2\pi$ with

$$\vec{x}(u, v) = ((a + r\mathrm{cos}v)\mathrm{cos}u, (a + r\mathrm{cos}v)\mathrm{sin}u, r\mathrm{sin}v). \tag{4}$$

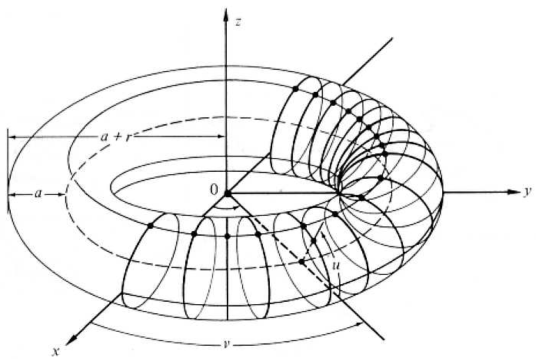

Figure 2: Parametrization of a torus

2.2 Topology

Topology is a way of characterizing surfaces according to which are continuously deformable into each other or not. Two surfaces, S_1 and S_2, which are continuously deformable into each other are said to be *homeomorphic*, denoted $S_1 \simeq S_2$. For instance the surface of a cube is homeomorphic to that of a sphere. The sphere is however not homeomorphic to the torus (try to continuously deform the torus in Fig. 2 to a sphere. You will not succeed.).

Homeomorphism between surfaces leads us to the concept of triangulation of a surface. Since two surfaces homeomorphic to each other are topologically equivalent we are free to choose some elementary building blocks when constructing a surface. The building blocks are usually taken to be triangles. For instance below in Fig. 3 a possible triangulation of a cylinder is shown. There are two mathematical requirement of a triangulation (to ensure that we do not choose too few triangles) that must be fulfilled:

- Two triangles must share at most one edge.
- Two triangles, which do not share any edges, must have at most one vertex (a vertex is a point where the edges of the triangles meet) in common.

In Fig. 3 our first impulse might be to use only two triangles. However because of the first requirement above this is not allowed since then these two triangles will share *two* edges. Four triangles are not allowed either because of the second requirement. However if we use six triangles both of the above requirement are fulfilled.

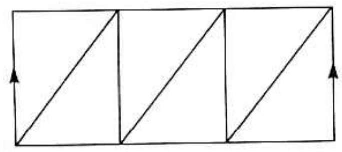

Figure 3: Possible triangulation of a cylinder. The outer edges marked with arrows are identified.

Exercise 2
Show that the triangulation in Fig. 3 satisfies the two mathematical requirements above.

Let us assume that we have a triangulations of two different surfaces, again denoted S_1 and S_2. How can we then determine if $S_1 \simeq S_2$ or not? It turns out that a necessary (but not sufficient) condition for homeomorphism is that the Euler characteristics, $\chi(S)$, defined by

$$\begin{aligned} \chi(S) &= (\text{number of vertices in } S) - (\text{number of edges in } S) \\ &+ (\text{number of faces in } S) \end{aligned} \tag{5}$$

is the same for the surfaces (or rather for the triangulations of the surfaces). If the two surfaces have different Euler characteristics they are therefore *not* homeomorphic (but the converse is not true). The Euler characteristic is said to be a *topological invariant*. It is not difficult to show that for a compact, connected surface

$$\chi(S) = 2 - 2g, \tag{6}$$

where g is the genus of the surface.

Example 4
From Fig. 3 we see that $\chi(S) = 6-12+6 = 0$ for a cylinder. Note that a cylinder is not a compact surface since it is unbounded.

Exercise 3
Find a triangulation of the sphere and the torus and show that Eqs. (5) and (6) agree.

2.3 Differential geometry

As we saw in section 2.1 a surface is completely specified in a region of 3d Euclidean space by *two* parameters. We therefore expect that it is possible to treat any surface as a "two dimensional entity" without any reference to 3d space. It is the aim of this section to develop the mathematical tools (differential geometry) that allow such a treatment. In particular we describe the first and second fundamental forms which allow a complete description of the surface.

Let us consider the tangent plane at some point p, see Fig.4. The vectors $\partial\vec{x}/\partial u$ and $\partial\vec{x}/\partial v$ are parallell to the surface and hence "span" the tangent plane. The basis $\{\partial\vec{x}/\partial u, \partial\vec{x}/\partial v\}$ is called the *coordinate basis* in the neighbourhood of p. Many entities of interest involve the local tangent plane. For instance consider the element of length, ds^2, in 3d Euclidean space:

$$ds^2 = \langle d\vec{x}, d\vec{x}\rangle = dx^2 + dy^2 + dz^2 \tag{7}$$

where $\langle .., ..\rangle$ denotes scalar multiplication. From the parametrization, Eq. (1), of a surface S we see that (using the chain rule: $d\vec{x} = (\partial\vec{x}/\partial u)du + (\partial\vec{x}/\partial v)dv$ -

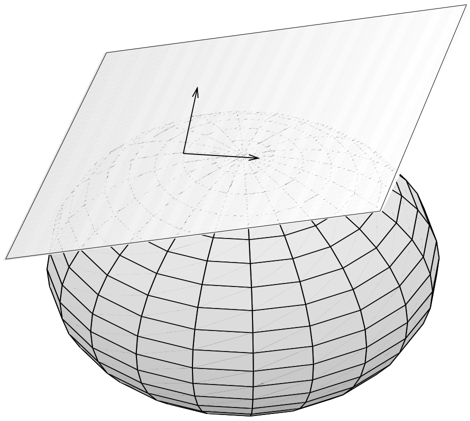

Figure 4: The tangent plane at a point on a sphere. The arrows indicate the tangent vectors $\partial\vec{x}/\partial u$ and $\partial\vec{x}/\partial v$.

expanding in the coordinate basis) the element of length between two infinitesimally close point on S is ($u^1 = u$ and $u^2 = v$)

$$ds^2 = \sum_{i,j} g_{ij} du^i du^j \tag{8}$$

where

$$g_{ij} = \langle \frac{\partial\vec{x}}{\partial u^i}, \frac{\partial\vec{x}}{\partial u^j} \rangle \tag{9}$$

Eq. (8) is called the *first fundamental form* and expresses the element of length in terms of the local coordinates u and v. In appendix B it is shown that ds^2 is an invariant, i.e independent of choice of parametrization of the surface. The 2×2 tensor g_{ij} is called the metric tensor (note that g_{ij} is symmetric, i.e. $g_{12} = g_{21}$). For the case of a *plane* surface with its normal parallell to the z-axis the length element is $ds^2 = dx^2 + dy^2$ and hence the metric tensor is

$$g_{ij} \equiv \eta_{ij} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{10}$$

The above tensor is sometimes called the *flat* metric tensor. The inverse of the metric tensor is often denoted g^{ij} and is hence a tensor that satisfies

$$\sum_j g^{ij} g_{jk} = \delta^i_k \tag{11}$$

where δ^i_k is the Kronecker delta.

Example 5
The element of length for a cylindrical surface (in cylindrical coordinates) is

$$ds^2 = dz^2 + \rho^2 d\phi^2, \tag{12}$$

where ρ (=constant) is the radius of the cylinder and ϕ is the angle of rotation around the z-axis. By simply making the reparametrization $z \to z, \rho d\phi \to t$ the element of length becomes $ds^2 = dz^2 + dt^2$ and hence the metric tensor in this parametrization is simply the flat one η_{ij}. Two surfaces for which it is possible to find parametrizations such that their first fundamental forms are the same are said to be *isometric*. The cylinder is hence isometric to the plane (the cylinder can be "unrolled" into a plane).

Let us now consider a special kind of transform of a surface that we will use in later sections - the *conformal transform*. A conformal transform is defined as a map of all points $\vec{x}$ on surface S to points $\vec{y}$ on another surface $\tilde{S}$ such that the element of length changes according to

$$d\tilde{s}^2 = \lambda^2 ds^2 \tag{13}$$

where λ is called the coefficient of conformality and is assumed to be a smooth function of $\vec{x}$. According to a theorem by Lioville the conformal transform are completely determined by the below three classes of transformations:

- *Rotations* and *translations* ($\vec{y} = \vec{x} - \vec{x}_0$). These transformations has $\lambda = 1$.
- *Dilations* (or *scale transformations*):

  $$\vec{y} = b\vec{x}, \tag{14}$$

  where b is constant. For dilations we have $\lambda = b$.
- The final distinct conformal transform is the *inversion*:

  $$\vec{y} = \frac{\vec{x} - \vec{x}_0}{|\vec{x} - \vec{x}_0|^2} + \vec{x}_0 \tag{15}$$

  Let us find the coefficient of conformality for the above inversion and let us for simplicity choose the inversion center at the origin, i.e. $\vec{x}_0 = 0$. We have ($r^2 = \langle \vec{x}, \vec{x} \rangle$):

  $$d\vec{y} = \frac{d\vec{x}}{r^2} - \frac{2\vec{x}}{r^3} dr \tag{16}$$

  where $dr = \langle \vec{x}, d\vec{x} \rangle$. The line element thus becomes

  $$d\tilde{s}^2 = \langle d\vec{y}, d\vec{y} \rangle = \frac{\langle d\vec{x}, d\vec{x} \rangle}{r^4} - \frac{4\langle d\vec{x}, \vec{x} dr \rangle}{r^5} + \frac{4dr\langle \vec{x}, \vec{x} \rangle}{r^6} = \frac{\langle d\vec{x}, d\vec{x} \rangle}{r^4} = \frac{ds^2}{r^4} \tag{17}$$

  We hence have that the coefficient of conformality for inversions is $\lambda = 1/|\vec{x} - \vec{x}_0|^2$.

The first fundamental form contains all necessary information for calculating metric properties such as arc length or area (but does not fully characterize the surface as seen in Example 5). Let us calculate the area element dS: the area of a small parallellogram on S is given by $|\partial\vec{x}/\partial u \times \partial\vec{x}/\partial v|$. Using the mathematical identity

$$|\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v}|^2 + \langle \frac{\partial \vec{x}}{\partial u}, \frac{\partial \vec{x}}{\partial v} \rangle^2 = |\frac{\partial \vec{x}}{\partial u}|^2 |\frac{\partial \vec{x}}{\partial v}|^2 \tag{18}$$

we find the area element

$$dS \equiv |\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v}|dudv = \sqrt{g_{11}g_{22} - g_{12}^2}dudv = \sqrt{g}dudv \tag{19}$$

where $g \equiv \det g_{ij}$. The area element is hence given by the square root of the determinant of the metric tensor. The area $\int dS$ of a region of S is an invariant (i.e. it is independent on the parametrization of the surface), see appendix B.

Exercise 4
Calculate the area of the sphere through the parametrizations given in Example 1 and 2 and show that they give the same value, i.e. that $\int dS$ is an invariant.

As we saw in Example 5 the first fundamental form does not completely characterize a surface. To do this we must go beyond metric properties of the surface and look into also the *curvature* of the surface. Let $\vec{x}(u,v)$ be a parametrization of S in the neighbourhood of a point p. The distance from a point $q = \vec{x}(u,v)$ to the tangent plane at $p = \vec{x}(0,0)$ is (see Fig. 5)

$$s = \langle \vec{x}(u,v) - \vec{x}(0,0), \hat{N}(p) \rangle \tag{20}$$

where $\hat{N}(p)$ is the normal to the tangent plane at p:

$$\hat{N} = (\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v})/|\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v}|. \tag{21}$$

Let us now Taylor expand around p according to:

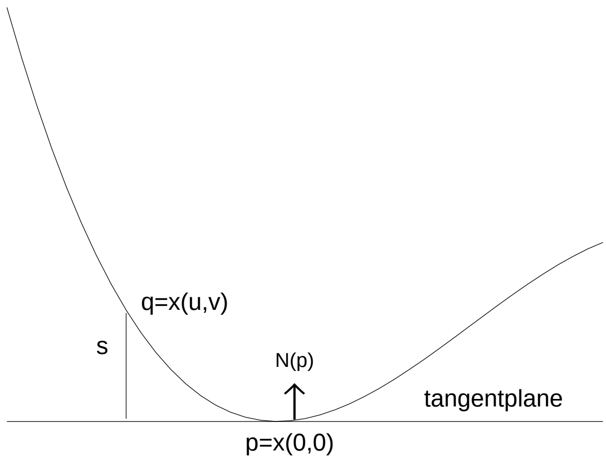

Figure 5: A cut through a surface along the normal.

$$\vec{x}(u,v) = \vec{x}(0,0) + \frac{\partial \vec{x}}{\partial u}du + \frac{\partial \vec{x}}{\partial v}dv + \frac{1}{2}[\frac{\partial \vec{x}^2}{\partial^2 u}(du)^2 + \frac{\partial \vec{x}^2}{\partial u \partial v}dudv + \frac{\partial \vec{x}^2}{\partial^2 v}(dv)^2] \tag{22}$$

Inserting this expansion into Eq. (20) and using the fact that the vectors $\partial\vec{x}/\partial u$ and $\partial\vec{x}/\partial v$ lie in the tangent plane at p we find ($u^1 = u$ and $u^2 = v$)

$$s = \underbrace{\frac{1}{2}\sum_{i,j} h_{ij} du^i du^j}_{\text{II}} \tag{23}$$

where

$$h_{ij} = \langle \frac{\partial \vec{x}^2}{\partial u^i \partial u^j}, \hat{N} \rangle \tag{24}$$

Π is called the *second fundamental form* and measures curvature of a surface. Π is an invariant as is shown in appendix B. In particular for a plane the normal distance to the tangent plane is everywhere zero and $\Pi \equiv 0$. The tensor h_{ij} is sometimes called the curvature tensor (note that h_{ij} is symmetric).

In principle there are infinitely many possible choices of basis vectors that span the tangent plane at some point p. We have so far used the coordinate basis which we introduced in connection to the first fundamental form. Let us now introduce a basis which is connected to curvature and hence the second fundamenal form. The normal vector field $\hat{N}$ introduced in Eq. (21) allow us to measures curvature along a curve on the surface; the normal $\hat{N}$ along a curve on a plane is everywhere a constant, whereas for a curved surface, $\hat{N}$ in general varies along the curve. Therefore the derivatives $\partial\hat{N}/\partial u$ and $\partial\hat{N}/\partial v$ are convenient measures of curvature since these entities yields zero for a plane. Furthermore the vectors $\partial\hat{N}/\partial u^i$ lie in the tangent plane at a point p, since from the normalization condition $\langle \hat{N}, \hat{N} \rangle = 1$ we obtain by differentiation $\langle \hat{N}, \partial\hat{N}/\partial u^i \rangle = 0$. The basis $\{\partial\hat{N}/\partial u, \partial\hat{N}/\partial v\}$ is thus an alternative basis to the coordinate basis which span the tangent space at p. Defining $h_i^j \equiv \sum_k g^{jk} h_{ik}$ it is straighforward to show that the above two bases are related according to [**?**]:

$$\frac{\partial \hat{N}}{\partial u^i} = -\sum_j h_i^j \frac{\partial \vec{x}}{\partial u^j} \tag{25}$$

i.e. related by the curvature tensor. The above relation is called the *Weingarten equations*.

Exercise 5
Prove Eq. (25).

Let us now proceed by introducing invariants related to curvature (see also appendix B). The matrix h_i^j relates two different sets of local basis vectors and from elementary linear algebra we know the determinant and trace of such a matrix are invariants, i.e.

$$K \equiv \det h_i^j = \det h_{ij} / \det g_{ij} \tag{26}$$

and

$$H \equiv \frac{1}{2} \mathrm{Tr} h_i^j = \frac{1}{2} \sum_i h_i^i = \frac{1}{2} \sum_{i,j} g^{ij} h_{ij} \tag{27}$$

are invariant under a reparametrization. The entity K is called the Gaussian curvature and H is the mean curvature at the point p. Since h_i^j is a symmetric matrix it can always be diagonalized. Denote the corresponding eigenvalues (the so called *principal curvatures*) by k_1 and k_2. We can then write the Gaussian and mean curvature according to

$$K = k_1 k_2 \tag{28}$$

and

$$H = \frac{k_1 + k_2}{2}. \tag{29}$$

The principal curvatures have simple geometrical interpretations: Let us imagine a curved surface, S, and let N be a plane which intersects S in such a way that the normal in a point p is parallell to N. The intersection between N and S is then a curve. The normal curvature, k_n, in this point p is defined as the inverse radius of a circle which tangents this curve at p. k_n comes with a sign: the normal curvature is negative if the surface bends "away" from the normal of the surface and positive otherwise. Now imagine a rotation of the plane N around the normal of S at p. We get a continuous set of curves, all having a specific k_n. The principal curvatures, denoted k_1 and k_2, are then the maximum and the minimum of this set of k_n. Note that when $K < 0$ the two curvatures k_1 and k_2 have different signs, this correspond to a saddle point. A remarkable property of the Gaussian curvature is that, although we defined it entirely with the help of the second fundamental form, it can be shown that (Theorema Egregium) that it is entirely expressible in terms of the metric (and derivatives thereof). K is hence invariant under isometries (see Example 5). The same is however not true for H as is seen in the below example.

Example 6

Using the above geometrical interpretation of H and K we find that for a plane we have $K_{\rm plane} = 0$ and $H_{\rm plane} = 0$. For a cylinder we get $K_{\rm cyl} = 0$ and $|H_{\rm cyl}| = 1/(2\rho)$. This proves that H is not invariant under isometries (and hence cannot be entirely expressible in terms of the metric).

Example 7

Let us calculate the Gaussian and mean curvature for a sphere of radius a. From the previous discussion we intuitively believe that $K = 1/a^2$ and $|H| = 1/a$. Let us now use the above formalism. We have

$$\vec{x}(\Theta, \phi) = a(\sin\Theta\cos\phi, \sin\Theta\sin\phi, \cos\Theta). \tag{30}$$

from which we obtain

$$\begin{aligned}
\frac{\partial \vec{x}}{\partial \Theta} &= a(\cos\Theta\cos\phi, \cos\Theta\sin\phi, -\sin\Theta), \\
\frac{\partial \vec{x}}{\partial \phi} &= a(-\sin\Theta\sin\phi, \sin\Theta\cos\phi, 0), \\
\frac{\partial^2 \vec{x}}{\partial \Theta^2} &= a(-\sin\Theta\cos\phi, -\sin\Theta\sin\phi, -\cos\Theta), \\
\frac{\partial^2 \vec{x}}{\partial \Theta \partial \phi} &= a(-\cos\Theta\sin\phi, \cos\Theta\cos\phi, 0), \\
\frac{\partial^2 \vec{x}}{\partial \phi^2} &= a(-\sin\Theta\cos\phi, -\sin\Theta\sin\phi, 0),
\end{aligned} \tag{31}$$

Let us first obtain the metric tensor. Using Eq. (9) we get

$$g_{11} = a^2(\cos^2\Theta\cos^2\phi + \cos^2\Theta\sin^2\phi + \sin^2\Theta) = a^2, \tag{32}$$

where the the trigonometrical identity has been used. Similarly

$$\begin{aligned} g_{12} = g_{21} &= 0 \\ g_{22} &= a^2 \sin^2\Theta. \end{aligned} \tag{33}$$

Notice that these result just give the well known expression for the length element in spherical coordinates: $ds^2 = a^2 dr^2 + a^2 \sin^2\Theta d\Theta^2$.

For the calculation of N we observe that

$$\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v} = a^2(\sin^2\Theta\cos\phi, \sin^2\Theta\sin\phi, \cos\Theta\sin\Theta) \tag{34}$$

so that

$$|\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v}| = a^2|\sin\Theta| = a^2\sin\Theta, \tag{35}$$

where again the trigonometrical identity has been used. From Eq. (21) we then find

$$\vec{N} = (\sin\Theta\cos\phi, \sin\Theta\sin\phi, \cos\Theta). \tag{36}$$

Let us now calculate the curvature tensor. From Eq. (24) we then obtain

$$h_{11} = -a(\sin^2\Theta\cos^2\phi + \sin^2\Theta\sin^2\phi + \cos^2\Theta) = -a. \tag{37}$$

Similarly

$$\begin{aligned} h_{12} = h_{21} &= 0 \\ h_{22} &= -a\sin^2\Theta. \end{aligned} \tag{38}$$

From Eq. (27) we then finally obtain

$$H = -\frac{1}{a}, \; 0 < \Theta < \pi \tag{39}$$

in agreement with our intuitive reasoning in the beginning of the example. The fact that H is negative corresponds to the fact that we have chosen our parametrization such that the normal point out from the sphere and hence the surface of the sphere bends away from the normal. From Eq. (26) we obtain the Gaussian curvature

$$K = \frac{1}{a^2}. \tag{40}$$

The fact that $K > 0$ shows the obvious fact that a sphere does not have any saddle points. Let us also calculate dS from Eq. (19) or Eq. (35). We easily find

$$dS = a^2\sin\Theta d\Theta d\phi. \tag{41}$$

Example 8

Let us also consider the torus with parametrization according to Example 3. We find

$$\begin{aligned} \frac{\partial \vec{x}}{\partial u} &= (-r\sin u\cos v, -r\sin u\sin v, r\cos u), \\ \frac{\partial \vec{x}}{\partial v} &= (-(a + r\cos u)\sin v, (a + r\cos u)\cos v, 0). \end{aligned} \tag{42}$$

We then have

$$|\frac{\partial \vec{x}}{\partial u} \times \frac{\partial \vec{x}}{\partial v}| = r(a + r\mathrm{cos}u) \tag{43}$$

after continuous use of the trigonometrical identity. From Eq. (19) we find

$$dS = r(a + r\mathrm{cos}u)dudv. \tag{44}$$

It is also easy to show that the mean curvature becomes

$$H = \frac{a + 2r\mathrm{cos}u}{2r(a + r\mathrm{cos}u)} \tag{45}$$

Exercise 6
a) Show Eq. (45).
b) An ellips is parametrized by $\vec{x}(u,v) = (a\mathrm{sin}u\mathrm{cos}v, b\mathrm{sin}usinv, d\mathrm{cos}u)$, where a, b and d are constants. Let $a = b$ and calculate dS, H and K.
c) Perform the same calculation for a hyperbolic paraboloid, parametrized by $\vec{x}(u,v) = (au\mathrm{cosh}v, bu\mathrm{sinh}v, u^2)$.

Exercise 7
Consider a parametrization of the form (compare Example 2)

$$\vec{x}(x,y) = (x, y, U(x,y)). \tag{46}$$

The function $U(x,y)$ is sometimes called a height function and gives the displacement of the surface from the x-y-plane. Show that in the limit of small first order derivatives the mean curvature is a harmonic function, i.e. show that

$$H \approx \nabla^2 U(x,y) \tag{47}$$

where $\nabla^2 = \partial^2/\partial^2 x + \partial^2/\partial^2 y$.

Topology describes surfaces according to which are continuously deformable into each other or not. Differential geometry, on the other hand, introduces different kind of *measures* on a surface, such as Gaussian and mean curvatures. A beautiful connection between topology and geometry is contained in the following theorem

THEOREM 1 (Gauss-Bonnet's theorem for compact surfaces)
Let S be a compact oriented surface in three-dimensional space , E^3. Then

$$\int_S K dS = 2\pi\chi(S). \tag{48}$$

Observe that K is the Gaussian curvature and hence the LHS of Eq. (48) is a purely geometrical entity. The RHS is on the other hand defined within topology.

Exercise 8
Calculate $\int_S K dS$ for a sphere and verify Eq. (48).

We have in this section shown that any quantity of interest (area, mean curvature, Gaussian curvature etc) for a surface can be obtained without "leaving" the surface; the first and second fundamental forms provide all the necessary information about the surface. We have also stated Gauss-Bonnet theorem which provides a connection between topology and differential geometry.

3 The elastic energy, $H_{\rm el}$

In this section we discuss the elastic energy of a fluid membrane. We find that the elastic energy H_{el} is essentially determined by the bending energy.

In elasticity theory one is concerned with the energy cost required to deform objects. In particular (neglecting entropic effects) the shape assumed by the object is the one of minimum elastic energy. When discussing membranes there are three distinct possible deformation, see Fig. 6 (i) *Stretching* - in this kind of deformation the area of the membrane is locally changed (ii) A *shearing* motion is an in-plane deformation which preserves the area (iii) *Bending* is a deformation in the normal direction of the membrane.

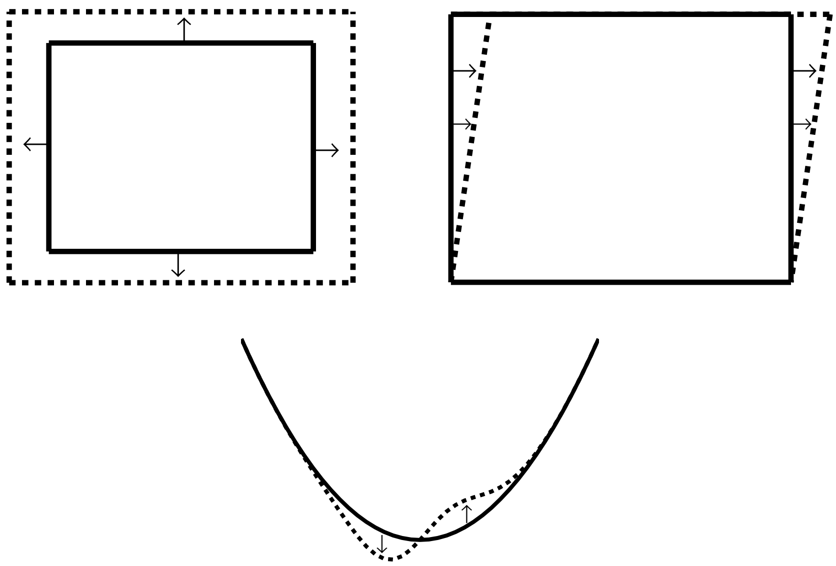

Figure 6: (top-left) A stretching deformation in the plane of a membrane (top-right) a shearing deformation in the plane of the membrane (bottom) a cut through a membrane undergoing a bending deformation.

We now follow [**?**] and [**?**] when writing the elastic energy of a closed vesicle. We make the following assumptions: (i) The membrane is in a 2-dimensional fluid state. This means that a shearing deformation cost a very small amount of energy and can be neglected. Mathematically the elastic energy should be independent on parametrization of the surface (reparametrization invariance). (ii) As always in elasticity theory we assume that the interaction holding the molecules in the membrane together is short-range and we hence neglect interactions between distant parts of the membrane. (iii) The membrane is smooth, which justifies the neglect of derivatives higher than the second. Furthermore it is obvious that the elastic energy (in the absence of walls) must be invariant with respect to rotations and translations of the object. It is then possible to show that the most general expression that satisfies the above criteria is:

$$H = H_{\rm stretch} + H_{\rm bend} \tag{49}$$

where

$$H_{\rm stretch} = \tau \int dS \tag{50}$$

(τ is called the area coefficient and has dimension of energy per area) and

$$H_{\rm bend} = \frac{\kappa}{2} \int (H - c_0)^2 dS + \bar{\kappa} \int K dS, \tag{51}$$

We have introduced c_0 called the spontaneous curvature which may be positive as well as negative and allows for bilayers that have chemically different outside than inside environment. The stretching energy is usually much larger than the bending energy, and the membrane can be considered as unstretchable. Therefore the $H_{\rm stretch}$-term is usually neglected from the expression from H and instead incorporated as a constraint that the area A is constant. The mean curvature, H, was defined previously [Eq. (27)] and K is the Gaussian curvature [Eq. (26)]. The above expression for the elastic energy is usually referred to as *the Helfrich elastic energy* (or Helfrich Hamiltonian). The last term can be rewritten using the Gauss-Bonnet theorem Eq. (48) (remember that the bilayer forms a closed surface) as

$$\oint K dS = 2\pi\chi(S) = 4\pi(1 - g), \tag{52}$$

where g is the genus (number of holes) of our surface and Eq. (6) has been used. The second term of the elastic bending energy, Eq. (51), is thus just a constant for a given genus and can be omitted in most cases (remember that two vesicles of different genus cannot be continuously deformed into each other). The elastic energy of a biomembrane is therefore determined by only *one* elastic constant, κ. Experimental values for κ typically ranges from a few to a few tens of $k_B T$.[**?**]

Exercise 9
Show that the bending elastic energy for a nearly flat surface can be written (with $c_0 = 0$):

$$H_{\rm bend} = \frac{\kappa}{2} \int \left[\nabla^2 U(x, y)\right]^2 dx dy \tag{53}$$

where $U(x, y)$ is the displacement from the flat surface at point (x,y).

Let us now consider some properties of the elastic energy of bending, Eq. (51), which will prove important in later discussions. First consider the following theorem:

THEOREM 2
Let S be a compact oriented surface in three-dimensional space , E^3. Then

$$T \equiv \int_S H^2 dS \tag{54}$$

is invariant under conformal transformations of E^3

As we saw in the previous section the conformal transform can be divided into rotations, translations, scale transformation and inversions. Let us prove that T is scale invariant. This property is easily verified noticing that $dS \rightarrow b^2 dS$ and that $H^2 = (k_1 + k_2)^2 \rightarrow (b^{-1}k_1 + b^{-1}k_2)^2 = b^{-2}H^2$. The full proof of the above theorem can be found in [**?**].

Example 12
It is easy to convince oneself that the unit sphere, S^2, parametrized according to Example 1 is invariant under Eqs. (14) and (15) (it is just a rigid movement, and hence does not change the *shape* of the sphere). Thus S^2 is mapped onto itself under the conformal transformations.

Example 13
The torus is parametrized according to Example 3. The transformation in Eq. (15) on the torus generates a one-parameter family of shapes: Choose the vector $\vec{x}_0$ according to $\vec{x}_0 = (\lambda\cos\Phi, \lambda\sin\Phi, 0)$ where Φ is fix (since changing Φ does not change the actual shape of the torus). Changing λ then moves the center of the torus creating a non-axisymmetric shape. The so called Clifford torus is in the next section shown to be a minimum geometry of genus 1 of the unconstrained Helfrich elastic energy with c_0=0. We thus expect the ground state of genus 1 vesicles to be degenerate (since all surfaces generated by $\vec{x}_0 = (\lambda\cos\Phi, \lambda\sin\Phi, 0)$ has the same energy). We will however see in the next section that putting the necessary physical constraints on the Helfrich Hamiltonian raise this degeneracy. However for genus 2 vesicles such a degeneracy is actually present and the membrane is fluctuating between different conformally equivalent shapes (this phenomena is called conformal diffusion).

4 Membrane shapes

In this section the geometries obtained by minimizing the Helfrich Hamiltonian are discussed. Depending on additional constraints three different models are discussed. The minimum elastic energy surfaces are given for genus 0,1 and 2.

Let us now discuss what physically relevant constraints we must put on our theory. Since there is no stretching in the vesicle its total area of the membrane must be taken to be a constant. The contained volume inside the membrane is also a constant on short time-scales. Because of the scale invariance discussed in the previous section the two constraints above are reduced to one. This constraint is usually taken to be the so called reduced volume, ν, defined by

$$\nu \equiv \frac{V}{4\pi R_0^3/3} = const, \tag{55}$$

where $R_0 = (A/4\pi)^{1/2}$ and A is the area of the membrane.

There are basically three slightly different models which are used when finding shapes of membranes (they differ in the additional constraints): Let us first consider *Spontaneous Curvature model*. The shape of the membrane is obtained by minimizing the Helfrich Hamiltonian under the constraint of constant reduced volume. Formally this is done by introducing Lagrange multipliers and minimize Eq. (51) which leads us to the equation

$$\delta(H_{\mathrm{bend}} + PV + \Sigma A) = 0, \tag{56}$$

where P is a Lagrange multiplier associated with constant volume and has dimension of pressure. Σ is the Lagrange multiplier associated with constant area and has dimension of force per length. Note that V and A are effectively related through Eq. (55). This equation is that of the Spontaneous Curvature model (SC). A surface which has different chemical composition of the inside and the outside of the surface is incorporated through a non-zero spontaneous curvature ($c_0 \neq 0$).

Exercise 10

Revise the technique of energy minimization with Lagrange multipliers. Find the minimum potential energy for a thin rope in a constant gravitational field. The length of the rope is constant and its ends are attached to two different walls.

So far we have not considered the microscopic structure of the membrane or the effect that the membrane has a finite lateral extension. Let us therefore examine if microscopic effect may give a contribution to the Helfrich Hamiltonian. For the reasoning below to be correct we need to assume that $c_0 = 0$ (the connection between the models below and the Spontaneous curvature model with $c_0 \neq 0$ is actually very subtle). Let us assume a flat surface and then bend it slightly. As we have seen before this gives rise to the curvature term T, but there is also a correction which is explained below. When bending a membrane the outer monolayer is stretched and the inner one is compressed, thus the number of lipids per unit area is increased on the inner surface and decreased on the outer surface. If the molecules were free to wander between the layers they would wander from the inner to the outer surface to smoothen the densities (thereby minimizing the energy). However the lipids in the monolayers cannot go from one layer to the other on small time scales (the number of lipids in each layer is conserved) and conclusively we cannot reach the equilibrium. The difference between the case when the lipids are free to go between the layers (thus reaching the "true" minimum) and the case where they are bound to one monolayer is contained in the *Area-difference-elasticity model* (ADE) whose Hamiltonian is

$$H_{\mathrm{ADE}} = \frac{1}{2}\kappa T + \frac{\kappa\pi}{8A_0 d^2}(\triangle a - \triangle a_0)^2 \tag{57}$$

where d is the bilayer thickness, $\triangle a_0$ is the unbent area difference between the layers and $\triangle a$ is the bent area difference.

A special case of the ADE model is the *Bilayer Coupling model* (BC). This model introduces the 'hard' constraint of having a constant area-difference of the inner and outer surface. This is incorporated through a Lagrange multiplier,

μ. The minima equation in the BC-model then takes the form

$$\delta(\frac{1}{2}\kappa T + PV + \Sigma A + \mu\triangle a) = 0, \tag{58}$$

Compare Eq. (56). $\triangle a$ can be written as an integral of the mean curvature (to first order) according to

$$\triangle a = 2d\oint H dS, \tag{59}$$

where d is the layer thickness.

Exercise 11
For a thin spherical shell the area differenece between the outer and the inner area is $\triangle a = 4\pi(r+d)^2 - 4\pi r^2 \approx 8\pi r d$. Show that is is in agreement with Eq. (59).

Let us now consider the special case of genus 0 vesicles (no holes) and in particular consider the following theorem

*T*HEOREM 3
Let S be an embedded *closed* surface in three-dimensional space , E^3. Then

$$T \equiv \int_S H^2 dS \tag{60}$$

takes its unique minimum if S is the sphere.

For a proof of this theorem (except for uniqueness) see appendix C. The full proof can be found in [**?**]. Surfaces which minimize T as defined above are called *Willmore surfaces*. The above theorem then states that the sphere and its conformal transforms (we showed in Example 12 that the sphere is its own conformal transform) are the only Willmore surface of genus 0. Examples of Willmore surfaces of genus 1 and higher can be found in [**?**] and [**?**].

Example 14
Let us as an example calculate T for the sphere and thereby obtain the exact minimum energy. The sphere has $H^2 = 1/a^2$ as was shown in Example 7 and $dS = a^2 \sin\Theta d\Theta d\phi$. We thus have

$$T = \frac{1}{2\pi}\int_0^{2\pi}\int_0^{\pi} \sin\Theta d\Theta d\phi = 2. \tag{61}$$

Notice the expected independence of the radius of the sphere [because of the scale invariance, see Eq. (14)].

Comparing Eqs. (51) and (60) we might "naively" assume that (for genus zero and with no spontaneous curvatature) only spherical vesicle shapes are allowed in Nature. The non-spherically in our model arises when we introduce our constraints, $(c_0, \nu) = const$ in the Spontaneous Curvature model and $(\triangle a, \nu) = const$ in the Bilayer Coupling model. After the introduction of these constraints the theorem 3 no longer applies and instead Eqs. (56) or (58) have to be solved. The solutions to these equations give rise to different shapes depending on the constraints, thus naturally defining phase spaces $\Gamma(c_0, \nu)$ and $\Gamma(\triangle a, \nu)$. The phase space in the Spontaneous Curvature model for genus 0 vesicles is given in Fig. 7 (this figure is taken from [**?**]).

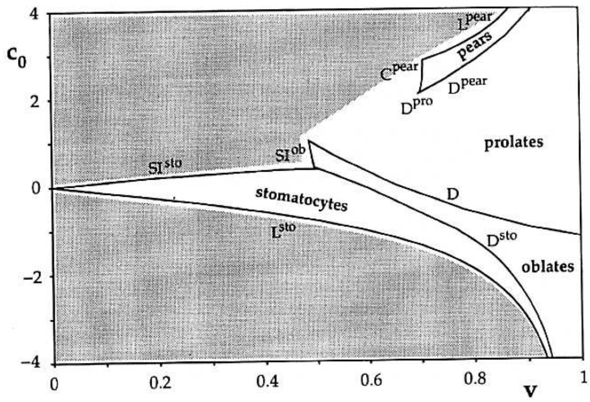

Figure 7: Phase space diagram in the Spontaneous Curvature model for genus 0 vesicles. Taken from [**?**]. In the shaded area, the shape of lowest energy has not been determined. A prolate is the shape you obtain by rotating an ellips around its major axis. By rotating around the minor axis you get an oblate shape. The stomatocytes are cup-shaped vesicles.

As seen in Fig. 7 various shapes are obtained depending on the constraints. In one region of the phase space stomatocytes are the mimima free energy surface. The red blood cell in Fig. 1 is an example of a stomatocyte. Other shapes that occur are oblates, prolates and pear shaped vesicles.

Exercise 12
Calculate T for an ellips and show that T is minimized if the ellipticity $e^2 \equiv 1 - a^2/d^2$ is zero (e^2=0), i.e. by a sphere.

We continue by investigating genus 1 vesicles. There is a conjecture by Willmore ([**?**]) that T defined in Eq. (54) is minimized by the so called Clifford torus among genus 1 shapes. Clearly the Clifford torus, defined as a torus with $c \equiv r/a = 1/\sqrt{2}$, (unlike the sphere in the previous section) is not the unique minima of genus 1 shapes since all shapes that are conformally invariant are also minima of T (see Example 13).

Example 15
Let us calculate T for the torus and see that the Clifford torus has lowest energy. According to Example 3 the torus can be parametrized according to

$$\begin{aligned} x &= (a + r\cos u)\cos v \\ y &= (a + r\cos u)\sin v \\ z &= r\sin u \end{aligned} \tag{62}$$

From Example 8 the mean curvature is

$$H = \frac{a + 2r\cos u}{2r(a + r\cos u)} \tag{63}$$

The area element is

$$dS = r(a + r\cos u)dudv \tag{64}$$

Inserting this into the expression for T, Eq. (54), we have

$$\begin{aligned} T &= \frac{1}{2\pi}\int_0^{2\pi}\int_0^{2\pi}\frac{(a + r\cos u)^2}{[2r(a + r\cos u)]^2}r(a + r\cos u)dudv \\ &= \frac{1}{8\pi r}\int_0^{2\pi}du\int_0^{2\pi}dv\frac{(a + 2r\cos u)^2}{a + r\cos u} = \frac{1}{4c}\int_0^{2\pi}\frac{1}{1 + c\cos u}du \\ &+ \int_0^{2\pi}\frac{\cos u}{1 + c\cos u}du + c\int_0^{2\pi}\frac{\cos^2 u}{1 + c\cos u}du = \frac{\pi}{2c(1 - c^2)^{1/2}} \end{aligned} \tag{65}$$

where we have defined $c \equiv r/a$. Let us now minimize this expression with respect to c. We have

$$\frac{dT}{dc} = -\frac{\pi}{2c^2(1 - c^2)^{1/2}} + \frac{\pi}{2(1 - c^2)^{3/2}} = 0 \tag{66}$$

The solution becomes

$$c = \frac{1}{\sqrt{2}} \tag{67}$$

which is the Clifford torus. Inserting Eq. (67) into Eq. (65) we obtain the minimum energy (which is larger than the minimum energy for the genus 0 minimum, see Eq. (61))

$$T_{min} = \pi \tag{68}$$

If we constrain our theory we conclude that this will raise the conformal degeneracy, that is for a given reduced volume the shape of the membrane is unique.

Let us now study genus 2 vesicles and we will see that an interesting phenomena called *conformal diffusion* occurs. Mathematically there is a conjecture by Lawson that the minima of T (Willmore surface) for genus 2 surfaces is the Lawson surface L and its conformal transforms (see Fig. 8). This conjecture was numerically verified in [**?**]. As we saw in section 3.2 a conformal transformation is parametrized by a vector $\vec{x}_0$. In Example 13 we observed that the conformal transformations of the torus are generated by one parameter, λ, and the degeneracy is therefore one-fold. It turns out that the degeneracy of the Lawson surface is 3-fold. This has the remarkable consequence that given two constraints to the theory this is not enough to completely raise the conformal degeneracy. If we for instance imagine a phase-space in the BC-model $\Gamma(\triangle a, \nu)$ there should be a region, denoted W, where there are many shapes with the same energy *and* the same constraints. In this region of the phase space the membrane is free to fluctuate (a kind of diffusion process) between these shapes since going from one shape to another does not cost any energy. This phenomena is called

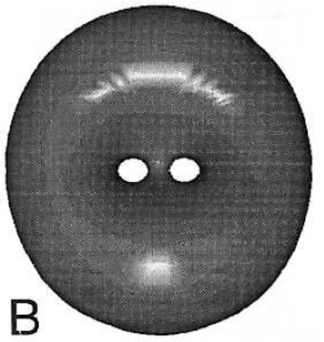

Figure 8: A conformal transform of the Lawson surface.

conformal diffusion. The elastic energy of a genus 2 vesicle is an example of a system which has a continuous set of ground states, which are connected by zero-energy paths. Such systems can be found in other areas of physics as well, in for instance solid state physics spin-waves and transverse phonons are well-known examples.

A full numerical investigation of genus 2 vesicles was performed in [?]. Their results for the BC phase space is shown in Fig. 9. Observe that there is just a finite region of phase space where conformal diffusion is allowed.

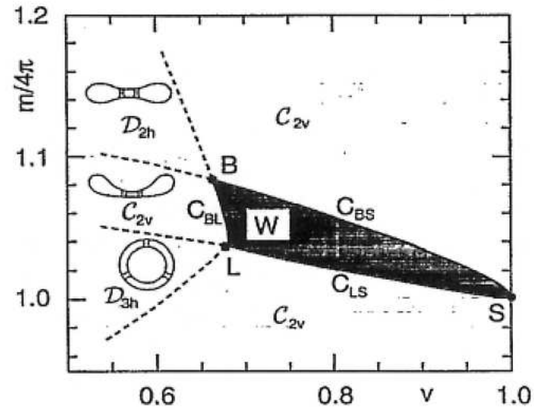

Figure 9: Phase space diagram in the Bilayer Coupling model for genus 2 vesicles. Taken from [?].

The existence of conformal diffusion was experimentally observed in 1995 (see [?]) and verifies the above theoretical results. Note that the existence of conformal diffusion effectively puts a limit to the number of physically relevant constraint to 3 to our models, since if we increase the number of constraints further the conformal degeneracy would be raised, which is not observed.

5 Adhesive interaction, H_{surf}

In this section we investigate the interaction between a surface and a membrane.

Consider a vesicle which interacts with a surface. If this interaction is attractive it can lead to a bound state of the vesicle on the surface. In a simple model this interaction can be incorporated by a simple free energy contribution

$$H_{\text{surf}} = -WA^* \tag{69}$$

where $W \geq 0$ is the contact potential for adhesion and A^* is the contact area. How large the area of adhesion becomes is, like in the previous section, a competition between gain in surface energy, H_{surf}, and loss in elastic energy. A larger membrane is more likely to adhere to a surface than a smaller one, since due to the scale invarinace Eq. (14) H_{bend} is (for the same shape) independent on the size of the membrane, whereas $|H_{\text{surf}}|$ increases with larger size of the membrane. A further complication is, however, the effect of entropy. Since a membrane bound to a surface has less possible configurations (the part bound to the surface cannot fluctuate) there is in general an effective entropic repulsion, which competes with surface energy and elastic energy. This repulsion is usually referred to as the *steric* repulsion. The case of weak and strong adhesion is illustrated in Fig. 10.

Figure 10: A membrane bound to an attractive surface, (a) weak adhesion, (b) strong adhesion, (c) repulsed membrane

6 Electric field interaction, H_{elec}

In this section we investigate the interaction between an electric field and a membrane.

An electric field, $\vec{E}(\vec{x}, t)$, interacts with a dielectric by inducing a polarization, $\vec{P}(\vec{x}, t)$, in the medium (see Fig. 11). Assuming a constant temperature and the polarization to be a linear function of the external field the electromagnetic part of the free energy is:

$$H_{\text{elec}} = -\frac{1}{2}\int \vec{E}(\vec{x}) \cdot \vec{P}(\vec{x}) d^3x. \tag{70}$$

We have also assumed that the charges producing the electric field are sufficiently far from the dielectric, so as not to interact with the induced polarization field. Note that $\vec{P}(\vec{x})$ is usually not simply related to $\vec{E}(\vec{x})$, because the

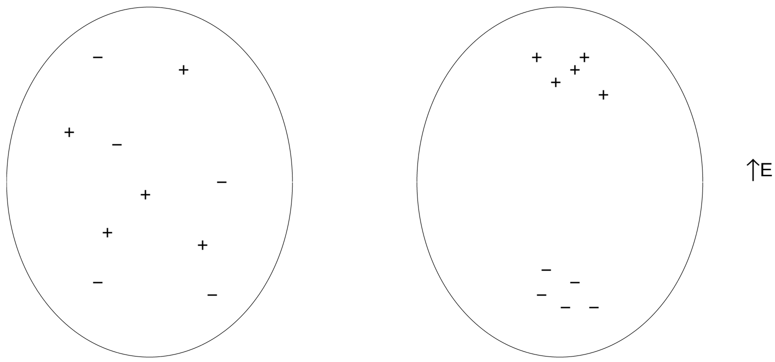

Figure 11: An external electric field induces a polarization in a dielectric object. (left) a neutral object without external field (right) the same object in an external electric field.

induced dipoles interact with each other as well as with the external electric field. $\vec{P}(\vec{x})$ must in general be obtained self-consistently by solving Maxwell's equations.

A vesicle placed in an electric field may be deformed.[**?**, **?**, **?**, **?**] This is related to the fact that it is possible to increase the number of induced dipoles in the direction of the external field (and hence H_{elec}) by a deformation of the vesicle. How large deformations a vesicle allow is determined by the elastic constant, κ. The elastic energy is scale invariant [the same for small object and large object, only depending on the shape, see Eq. (14)], whereas H_{elec} in general is larger for large object (more induced dipoles). It is therefore easier do deform a large object using electric fields than to deform a small one. Magnetic induction can cause deformations as well.[**?**]

From Eq. (70) it is clear that a mobile object in an *inhomogeneous* electric field will in general try to move towards higher field intensities. This is due to the fact that at high field intensities both $\vec{E}(\vec{x})$ and $\vec{P}(\vec{x})$ are maximized, assuming the polarization to be in the same direction as the electric field. This effect is used in so called *optical tweezers*. This device is used to move and manipulate dielectric objects such as cells. An optical tweezer consists of a focused laser beam that creates a high field intensity in a small region of space (the focal point). The dielectric object moves to this high intensity region in order to minimize its free energy and there becomes trapped. By moving the focal plane (sufficiently slow so that viscous forces are small) it is possible to move the cell.

A Covariant derivative

Let us now introduce the covariant derivative, ∇_i. The covariant derivative find many applications in analysis of surfaces (see for instance appendix C). This operator has the following properties: When operating on an invariant or *scalar* ϕ it is just the ordinary partial derivative:

$$\nabla_i \phi = \frac{\partial \phi}{\partial u^i} \tag{71}$$

When operating on a vector V_i the covariant derivative gives:

$$\nabla_i V_j = \frac{\partial V_j}{\partial u^i} - \sum_k \Gamma_{ij}^k V_k \tag{72}$$

where the so called *connection* is

$$\Gamma_{ij}^k = \frac{1}{2} \sum_l g^{kl} (\frac{\partial g_{lj}}{\partial u^i} + \frac{\partial g_{li}}{\partial u^j} - \frac{\partial g_{ij}}{\partial u^l}) \tag{73}$$

We see that the connection is symmetric in the lower indices, i.e. $\Gamma_{ij}^k = \Gamma_{ji}^k$. One may furthermore show that the covariant derivative acting on the metric tensor gives zero result, i.e.

$$\nabla_i g_{jk} = 0 \tag{74}$$

which we leave as an exercise to prove.

Exercise 12
Prove Eq. (74).

The covariant derivative on a vector Eq. (72) has the same transformation as the metric tensor, see appendix B (having this transformation property is actually sometimes used as a *definition* of a tensor). The covariant derivative has a simple geometrical interpretation: Consider a vector field V_i (i=1,2) in the tangent plane of the surface. The covariant derivative $\nabla_j V_i$ then gives the normal projection of $\partial_j V_i$ onto the surface.[**?**]

B Change of coordinates

A surface may in general be parametrized in many different ways and in particular one parametrization may not be enough to cover the entire surface (see Example 2 for instance). It is therefore important to investigate how different entities change under a reparametrization (change of coordinates) of the surface. Furthermore entities that are independent on parametrization, so called *invariants* or *scalars*, play an important role in differential geometry and we will in this appendix find a number of such invariants.

Consider a surface S and let us assume that we have two different parametrizations of the surface, $\vec{x}(u, v)$ and $\vec{x}(\bar{u}, \bar{v})$. We can then in general find a map

$$\begin{aligned} \bar{u} &= \bar{u}(u, v) \\ \bar{v} &= \bar{v}(u, v) \end{aligned} \tag{75}$$

from the (u, v)-plane to the $(\bar{u}, \bar{v})$-plane (change of coordinates).

Let us start by investigating how entities related to the first fundamental form change under such a reparametrization. For the coordinate basis we can apply the chain rule to obtain ($u^1 = u$, $u^2 = v$, $\bar{u}^1 = \bar{u}$ and $\bar{u}^2 = \bar{v}$)

$$\frac{\partial \vec{x}}{\partial \bar{u}^j} = \sum_k \frac{\partial \vec{x}}{\partial u^k} \frac{\partial u^k}{\partial \bar{u}^j} \tag{76}$$

For the differential in the $(\bar{u}, \bar{v})$-plane we have

$$d\bar{u}^i = \sum_m \frac{\partial \bar{u}^i}{\partial u^m} du^m \tag{77}$$

Using Eq. (76) we find that the metric, Eq. (9), transforms according to:

$$\bar{g}_{ij} = \langle \frac{\partial \vec{x}}{\partial \bar{u}^i}, \frac{\partial \vec{x}}{\partial \bar{u}^j} \rangle = \sum_{k,l} \frac{\partial u^k}{\partial \bar{u}^i} \frac{\partial u^l}{\partial \bar{u}^j} g_{kl} \tag{78}$$

For the inverse metric we must then have [to certify Eq. (11)]

$$\bar{g}^{ij} = \sum_{k,l} \frac{\partial \bar{u}^k}{\partial u^i} \frac{\partial \bar{u}^l}{\partial u^j} g_{kl} \tag{79}$$

We are now in a position to find our first invariant:

$$\begin{aligned} d\bar{s}^2 &= \sum_{i,j} \bar{g}_{ij} d\bar{u}^i \bar{u}^j = \sum_{i,j,k,l,m,n} \frac{\partial u^k}{\partial \bar{u}^i} \frac{\partial u^l}{\partial \bar{u}^j} \frac{\partial \bar{u}^i}{\partial u^m} \frac{\partial \bar{u}^j}{\partial u^n} g_{kl} du^m du^n \\ &= \sum_{kl} g_{kl} du^k du^l = ds^2 \end{aligned} \tag{80}$$

where we have used $\partial u^i/\partial u^j = \partial \bar{u}^i/\partial \bar{u}^j = \delta_i^j$. ds^2 is thus an invariant independent on the parametrization of the surface. Now denote by $\partial(u,v)/\partial(\bar{u},\bar{v})$ the Jacobian for the change of parameters. The the area element, Eq. (19), is

$$d\bar{S} = \sqrt{\bar{g}} d\bar{u} d\bar{v} = \sqrt{g} |\frac{\partial(u,v)}{\partial(\bar{u},\bar{v})}| d\bar{u} d\bar{v} = \sqrt{g} du dv = dS \tag{81}$$

hence the area element is also an invariant under reparametrization of the surface. We leave as an exercise to the reader to show the following result for the covariant derivative, Eq. (72):

$$\bar{\nabla}_i \bar{V}_j = \sum_{k,l} \frac{\partial u^k}{\partial \bar{u}^i} \frac{\partial u^l}{\partial \bar{u}^j} \nabla_i V_j \tag{82}$$

i.e. the covariant derivative operating on a vector transforms just like the metric tensor.

Exercise 13
Prove Eq. (82).

Let us now consider entities related to the second fundamental form. Let us start with the normal:

$$\bar{N} = \frac{\partial(u,v)/\partial(\bar{u},\bar{v})}{|\partial(u,v)/\partial(\bar{u},\bar{v})|} \frac{\partial \vec{x}/\partial u \times \partial \vec{x}/\partial v}{|\partial \vec{x}/\partial u \times \partial \vec{x}/\partial v|} = \pm N \tag{83}$$

where the plus (minus) sign correspond to a positive (negative) Jacobian. Consider the two bases $\{\partial \vec{x}/\partial u, \partial \vec{x}/\partial v, N\}$ and $\{\partial \vec{x}/\partial \bar{u}, \partial \vec{x}/\partial \bar{v}, \bar{N}\}$. A positive Jacobian then corresponds to a transformation between two right-handed or two left-handed systems. Using the above result it is straighforward to show that the curvature tensor, Eq. (24), transforms according to

$$\bar{h}_{ij} = \pm \sum_{k,l} \frac{\partial u^k}{\partial \bar{u}^i} \frac{\partial u^l}{\partial \bar{u}^j} h_{kl} \tag{84}$$

The proof that the second fundamental form, Eq. (23), is invariant under a reparametrization (except for a possible change of sign),

$$\bar{\text{II}} = \pm \bar{\text{II}}, \tag{85}$$

is then identitical to the proof that ds^2 is invariant. Using Eq.(79) together with Eq. (84) we then similarly find that the mean curvature, Eq. (27), has the same value after a reparametrization except for a possible sign change:

$$\bar{H} = \pm H \tag{86}$$

Let us finally show that the Gaussian curvature, Eq. (26), is an invariant. We have

$$\bar{K} = \frac{\det \bar{h}_{ij}}{\det \bar{g}_{ij}} = \frac{\det h_{ij}}{\det g_{ij}} = K \tag{87}$$

where we have used Eqs. (78) and (84).

C Calculus of variation

In this appendix we introduce the notion of normal variation and describe the calculus of variation of curved surfaces. In particular we find the variation of the Helfrich Hamiltonian.

Let us now investigate how a small deformation of the surface changes its properties (such as area, curvature etc). For this purpose consider the *normal variation* of a surface given by:

$$\vec{x}(u_1, u_2, t) = \vec{x}(u_1, u_2) + t\Phi(u_1, u_2)\hat{N} \tag{88}$$

i.e. we consider a small deformation in the normal direction of the surface $\vec{x}(u_1, u_2)$. $\Phi(u_1, u_2)$ is an arbitrary differentiable function and t is a parameter. When investigating how different properties of a surface change when $\vec{x}(u_1, u_2) \to \vec{x}(u_1, u_2, t)$ it is convenient to introduce the operator

$$\delta = \frac{\partial}{\partial t}|_{t=0} \tag{89}$$

i.e. δ picks out the component linear in t for the entity we choose to study. Let us now investigate the results obtained by operating with δ on different entities and let us for notational simplicity introduce the short-hand notation $\partial_i \equiv \partial/\partial u^i$. We have

$$\begin{aligned} \delta\vec{x} &= \Phi\hat{N} \\ \delta(\partial_i\vec{x}) &= \delta(t\partial_i\Phi\hat{N} + t\Phi\partial_i\hat{N}) = \partial_i\Phi\hat{N} + \Phi\partial_i\hat{N} \end{aligned} \tag{90}$$

For the metric we have

$$\begin{aligned}\tilde{g}_{ij} &\equiv \langle \partial_i \vec{x} + \delta(\partial_i \vec{x}), \partial_j \vec{x} + \delta(\partial_j \vec{x}) \rangle \approx g_i j + t\Phi \langle \partial_i \vec{x}, \partial_j \hat{N} \rangle + t\Phi \langle \partial_i \hat{N}, \partial_j \vec{x} \rangle \\ &= g_{ij} - 2t\Phi h_{ij} \end{aligned} \tag{91}$$

where have have used the fact that the normal is orthogonal to $\partial_i \vec{x}$, i.e. $\langle \partial_i \vec{x}, \hat{N} \rangle = 0$, which by differentiation gives

$$\langle \partial_i \vec{x}, \partial_j \hat{N} >= -\langle \hat{N}, \partial_i \partial_j \vec{x} \rangle = -h_{ij} \tag{92}$$

Hence the variation of the metric tensor becomes

$$\delta g_{ij} = -2\Phi h_{ij} \tag{93}$$

i.e. the variation of the metric tensor is proportional to the curvature tensor. By differentiating the defintion of the inverse metric, Eq. (11), we find

$$\sum_j \delta g_{ij} g^{jk} = -\sum_j g_{ij} \delta g^{jk} \tag{94}$$

hence [using Eq. (93)]

$$\delta g^{ij} = 2\Phi \sum_{k,l} g^{ik} g^{jl} h_{kl} \tag{95}$$

The variation of the area element, see Eq. (19), is a bit more tricky to obtain. As a preliminary we prove the following result for some arbitrary matrix M

$$\ln(\det M) = \mathrm{Tr}(\ln M) \tag{96}$$

Proof:
Determinants and traces are independent of basis. For simplicity choose a diagonal one.

$$\begin{aligned} M &= \begin{pmatrix} M_{11} & & \\ & \ddots & \\ & & M_{nn} \end{pmatrix} \\ \ln M &= \begin{pmatrix} \ln M_{11} & & \\ & \ddots & \\ & & \ln M_{nn} \end{pmatrix} \end{aligned}$$

$$\begin{aligned} RHS &= \mathrm{Tr}(\ln M) = \sum_i \ln M_{ii} = \ln(\prod_i M_{ii}) \\ &= \ln(\det M) = LHS \end{aligned}$$

which completes the proof.
For the variation of the area element we then have

$$\delta \sqrt{g} = \frac{1}{2} \sqrt{g} \sum_{p,q} g^{pq} \delta g_{pq} \tag{97}$$

Proof:
The variation of $\sqrt{g}$ is

$$\delta\sqrt{g} = -\frac{\delta g}{2\sqrt{g}} \tag{98}$$

To obtain a relation for δg it is convenient to study the variation of $\ln g$. It is

$$\delta \ln g = \frac{1}{g}\delta g$$

but it can also be written (repeated indices are assumed summed over below)

$$\begin{aligned}
\delta \ln(g) &= \delta \ln(\det g_{mn}) = \ln(\det(g_{mn} + \delta g_{mn})) - \ln(\det g_{mn}) \\
&= \ln(\det(g_{mn}(1 + g^{mn}\delta g_{mn}))) - \ln(\det(g_{mn})) \\
&= \ln(\det(g_{mn}) + \ln(\det(1 + g^{mn}\delta g_{mn}))) - \ln(\det(g_{mn})) \\
&= \ln(\det(1 + g^{mn}\delta g_{mn}) = \mathrm{Tr}(\ln(1 + g^{mn}\delta g_{mn})) \\
&\approx \mathrm{Tr}(g^{mn}\delta g_{mn}) = g^{mn}\delta g_{mn}
\end{aligned}$$

where we have used relation Eq. (96) and the power series expansion of the logarithm $\ln(1+x) \approx x - \frac{x^2}{2} + ...$ Combining these two relations we obtain

$$\delta g = g g^{mn}\delta g_{mn} \tag{99}$$

Inserting Eq. (99) into Eq. (98) we obtain

$$\delta\sqrt{g} = \frac{1}{2}\sqrt{g} g^{pq}\delta g_{pq} \tag{100}$$

which proves our assertion.
Finally combing Eqs. (93) and (97) we find

$$\delta\sqrt{g} = -\Phi\sqrt{g}\sum_{pq} g^{pq} h_{pq} = -2\Phi\sqrt{g}H \tag{101}$$

where we have used the definition of the mean curvature, Eq. (27). The variation of the area element is hence proportial to the area element itself and the mean curvature. Surfaces which have $H \equiv 0$ therefore have vanishing variation of the area element and are called *minimal surfaces*. Let us finally consider the variation of the curvature tensor h_{ij}. The calculation is a bit lengthy and we here only state the result which is[**?**]

$$\delta h_{ij} = \nabla_i \nabla_j \Phi - \Phi \sum_{k,l} g^{kl} h_{li} h_{kj} \tag{102}$$

where ∇_i is the covariant operator defined in Eqs. (71) and (72). With the result given by Eqs. (93),(95), (101) and (102) most problems of interest can be treated.

For closed vesicles we can obtain the change in *volume* V of the object. The change in volume is simply obtained (to first order) by multiplying the "original" area element dS by the normal displacement and we hence have

$$\delta V = \delta \int dV = \oint \Phi dS. \tag{103}$$

This result is useful in the variational problems given in Eqs. (56) or (58).

Let us consider the variation of the mean curvature (we assume that repeated indices are summed over below)

$$\begin{aligned}\delta H &= \frac{1}{2}\sum_{i,j}\delta(g^{ij}h_{ij}) = \frac{1}{2}(\delta g^{ij}h_{ij} + g^{ij}\delta h_{ij}) = \Phi h_i^j h_j^i + \frac{1}{2}g^{ij}\nabla_i\nabla_j\Phi - \frac{1}{2}\Phi h_i^j h_j^i \\ &= \frac{1}{2}(\triangle\Phi + \Phi\mathrm{Tr}h^2) = \frac{1}{2}[\triangle\Phi + \Phi(k_1^2 + k_2^2)] = \frac{1}{2}\triangle\Phi + \Phi(2H^2 - K) \qquad (104)\end{aligned}$$

where $\triangle \equiv \sum_j g^{ij}\nabla_i\nabla_j$ and we have used the fact that h_{ij} has eigenvalues k_1 and k_2 together with Eqs. (26) and (27).

Let us now as an application of the calculus of variation consider the variation of the Helfrich Hamiltonian, $\int H^2 dS$ for a *closed surface*. We have

$$\begin{aligned}\delta\int H^2 dS &= \int 2H\delta H dS + \int H^2\delta dS = \int H[\triangle\Phi + 2\Phi(2H^2 - K)]dS \\ &\quad -2\int H^2\Phi H dS = \int [\triangle H + 2H(H^2 - K)]\Phi dS \qquad (105)\end{aligned}$$

where we have used Eqs. (101) and (104) together with Green's theorem for a closed surface[**?**]

$$\int \Psi\triangle\Phi dS = \int \Phi\triangle\Psi dS \qquad (106)$$

In particular we now notice that the minimum of $\int H^2 dS$ is obtained for surfaces satisfying

$$\triangle H + 2H(H^2 - K) = 0 \qquad (107)$$

We notice that since the sphere has $H = -1/a$ and $K = 1/a^2$ the sphere minimizes the Helfrich Hamiltonian, which then proves (except for uniqueness) theorem 3 in the main text. The mimimum equation corresponding to Eq. (107) for *non-closed* surfaces has also been investigated, see for instance [**?**].

Exercise 15

Use the results in this appendix to prove that the minima equation, Eq. (56), in the spontaneous curvature model becomes

$$P - 2\Sigma H + \kappa(H - c_0)(H^2 - K + c_0 H) + \frac{\kappa}{2}\triangle H = 0 \qquad (108)$$

The solution of the above equation then gives realistic membrane shapes. For a review see [**?**].