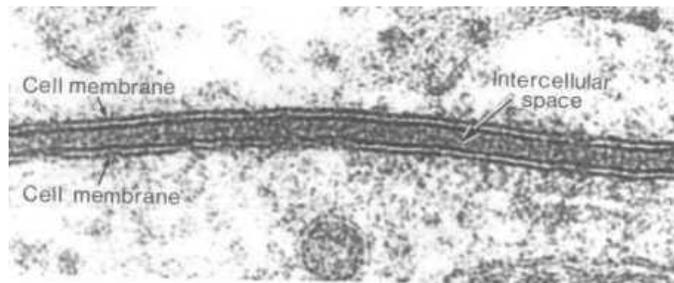


# 5 Biomembranes

## 5.1 Motivation

Biological membranes are thin, flexible, selectively permeable surfaces that separate cells and their organelles from their environments. Biomembranes form closed structures with an internal face oriented toward the interior of the compartment and an external face presented to the environment. Each type of cellular membrane has certain distinctive activities determined largely by the unique set of proteins associated with that membrane. We can distinguish two different types of membrane proteins (i) integral proteins, which partly or entirely penetrate the membrane, and (ii) peripheral proteins, which are laterally attached to one side of the membrane. Biomembranes are typically asymmetric, their interior and exterior faces can carry different proteins and have different properties.

Although biological membranes may have different properties and functions, all membranes share a common structural architecture that we will address in this chapter. They are rich in phospholipids, which spontaneously form a characteristic bilayer structures in water. Membrane proteins and lipids can diffuse laterally or sideways throughout the membrane, giving them their characteristic appearance of a fluid rather than a solid.

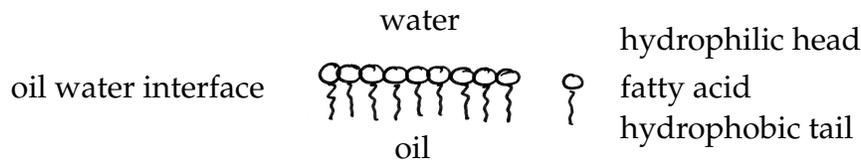


**Figure 5.1:** Electron microscopy of the cell membrane stained with osmium tetroxide illustrating the polar head groups with a light 2nm space of hydrophobic tails sandwiched between them, adopted from [1]

Given the variable composition of cellular membranes, how can we be that the phospholipid bilayer structure is common to all biomembranes? Electron microscopy of thin membrane sections provides the most direct evidence for the universality of the bilayer structure. Osmium tetroxide can be used for staining of phospholipids since it binds strongly to the polar head groups. A cross section of a single membrane stained with osmium tetroxide looks like a railroad track. Figure 5.1 shows two thin dark lines, the stained head group complexes, and a uniform 2nm light space of the hydrophobic tails sandwiched between them.

### 5.1.1 Lipid bilayers

In cell biology, the notion membrane is typically associated with the phospholipid bilayer and the proteins associated with it. In aqueous solutions, these proteins essentially display two kinds of non-covalent interactions which are referred to as hydrophobic and hydrophilic. Long polymer molecules typically tend to adopt conformations, in which non-polar residues are predominantly sequestered such that they avoid contact with water. The non-polar residues are said to be hydrophobic or water-avoiding. Polymer molecules favor conformations, in which the polar head groups are exposed to water. The polar head groups are referred to as being hydrophilic or water-loving. A typical example is the arrangement of fatty acids at an oil water interface, where the hydrophilic polar heads would typically be oriented towards the water phase while the hydrophobic tails would be oriented towards the oil phase, see figure 5.2.

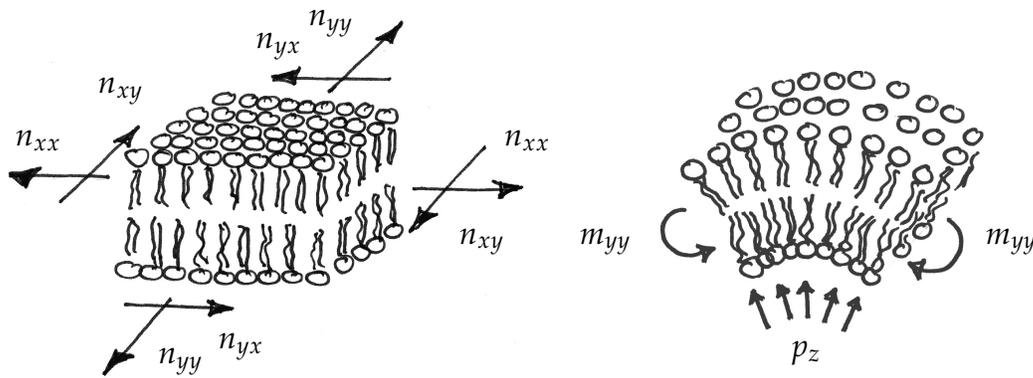


**Figure 5.2:** Oil water interface. Characteristic arrangement of fatty acid molecules with hydrophilic polar head group oriented towards the water phase and hydrophobic tail oriented towards the oil phase

From an energetic point of view, lipid bilayers show an attractive arrangement since they display both hydrophobic and hydrophilic interactions. The nonpolar fatty acid chains of the phospholipid molecules are sequestered together away from the water sandwiched between the polar head groups to maximize hydrophobic interactions. At the same time, the ionic polar head groups are in direct contact with the aqueous phase to maximize hydrophilic interactions. This dual nature of the molecules is referred to as amphiphilic.

For energetic reasons, each lipid bilayer has an inherent optimal microstructure with and optimal spacing between the lipid molecules. Any perturbation to this optimal arrangement disturbs this energetically favorable microstructure. The lipid bilayer thus exhibits an inherent resistance to deformations that cause shape changes. Typical examples are extension, for which the spacing between the head groups would increase throughout the membrane, or bending for which the head group spacing would increase on the outside while it would decrease on the inside, see figure 5.3.

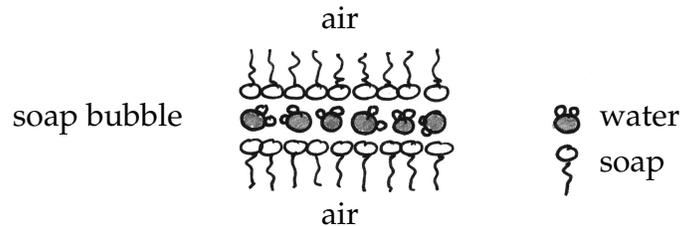
One of the key issues of this chapter is the identification of characteristic macroscopic parameters that display the nature of these intermolecular effects in a phenomenological way and account for the resistance of the cell membrane to extension, shear and bending. To this end, we will first look at a lipid bilayer structure that everybody can easily reproduce and elaborate at home, the structure of soap bubbles. When having understood how soap bubbles behave and how they can be described by mathematical equations, we will turn to elaborating the structural behavior of the cell membrane which is slightly more complicated but obey a similar set of equations from a mathematical point of view.



**Figure 5.3:** Infinitesimal element of the cell membrane subject to tension causing in plane deformation and shear (left) and bending causing out of plane deformation (right)

### 5.1.2 Soap bubbles

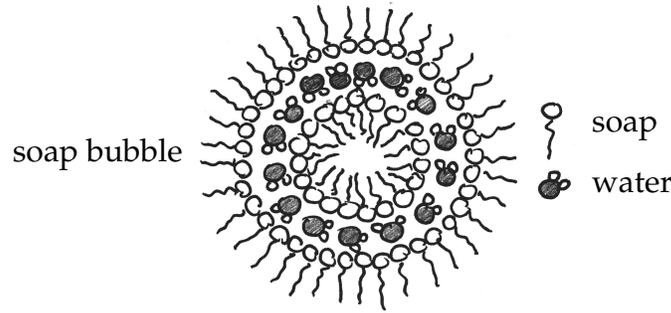
Soap bubbles are fascinating structures that display many similar features as the cell membrane. They can be used as model system to illustrate the qualitative behavior of a lipid bilayer. Soap bubbles are an excellent example of a self-assembled system. Their surface consists of a thin layer of water trapped between two layers of surfactant, typically soap. The surfactant possesses hydrophilic heads attracted to the thin water layer. Its hydrophobic tails form the inner and outer surface of the bubble as sketched figure 5.4. When being disturbed, the bubble pops.



**Figure 5.4:** Lipid bilayer of soap bubbles - characteristic arrangement of soap molecules with a thin water layer being sandwiched between the hydrophilic polar head groups while the hydrophobic tails are oriented to the non-polar air

The spherical shape of a soap bubble nicely displays the principle of energy minimization. Surface tension causes the bubble to form a sphere because this shape, as proposed by Archimedes and proven rigorously by Schwarz in 1884, is the minimal surface enclosing a fixed given volume. The spherical shape can be visibly distorted by additional external forces, you can easily test this by blowing against the bubble surface. If a bubble is subject to an environment without any additional external forces acting on it, however, it should always remain nearly spherical as displayed in figure 5.5.

An interesting question to ask about soap bubbles is what is the radius  $r$  of a soap bubble that is blown up at a pressure  $\Delta p$ ? Here  $\Delta p = p^{\text{int}} - p^{\text{out}}$  would be the pressure difference between the inside and outside of the bubble. To answer this question, we consider spherical soap bubble with initial radius  $r$ , that has a surface of  $A = 4\pi r^2$  and a volume of  $V = \frac{4}{3}\pi r^3$ . The inflation of the surface induces an internal energy



**Figure 5.5:** Lipid bilayer of soap bubbles - characteristic arrangement of soap molecules with a thin water layer being sandwiched between the hydrophilic polar head groups while the hydrophobic tails are oriented to the non-polar air

$W^{\text{int}}$  which is assumed to be proportional to the increase in membrane surface  $A$ . In the simplest case,  $W^{\text{int}} = \gamma A$  where, for now,  $\gamma$  is introduced as a mere proportionality constant. Its unit is obviously force per length and its physical interpretation will be discussed later. The external work  $W^{\text{ext}}$  is equal to the pressure difference  $\Delta p$  acting on the enclosed volume  $V$ , such that  $W^{\text{ext}} = \Delta p V$ . The total energy  $W$  of the bubble thus consists of the internal energy  $W^{\text{int}}$  and the external energy  $W^{\text{ext}}$ .

$$W(r) = W^{\text{int}} - W^{\text{ext}} \quad \text{with} \quad \begin{aligned} W^{\text{int}} &= \gamma A = \gamma 4 \pi r^2 \\ W^{\text{ext}} &= \Delta p V = \Delta p \frac{4}{3} \pi r^3 \end{aligned} \quad (5.1.1)$$

The minimum of the overall energy  $W$  with varying bubble radius  $r$  is obviously equivalent to the vanishing first variation  $\delta W$  with respect to  $r$ .

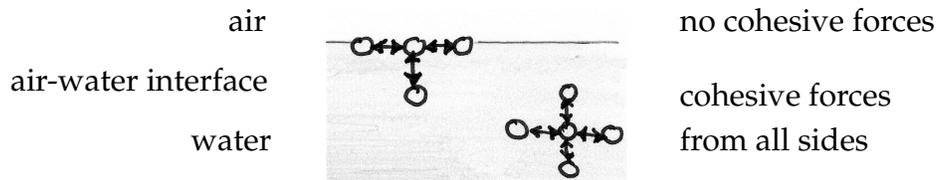
$$W(r) \rightarrow \min \quad \delta W(r) \doteq 0 \quad \text{with} \quad \begin{aligned} \delta W^{\text{int}} &= \gamma 8 \pi r \\ \delta W^{\text{ext}} &= \Delta p 4 \pi r^2 \end{aligned} \quad (5.1.2)$$

Evaluating the above equation  $\gamma 8 \pi r - \Delta p 4 \pi r^2 \doteq 0$  we obtain the following simple relation between the pressure difference  $\Delta p$  and the bubble radius  $r$

$$\Delta p = 2 \gamma \frac{1}{r} \quad (5.1.3)$$

which has been developed independently by Young and Laplace more than 200 years ago [7, 12]. In the literature, equation (5.1.3) is referred to as the Young-Laplace equation. The historical controversy about its development is documented by Müller & Strehlow [8]. We will see later how this equation for spherical membranes such as soap bubbles can be derived in a more rigorous form.

The cohesive forces between liquid molecules are responsible for the phenomenon which is referred to as surface tension. Cohesive forces between molecules are shared between all neighboring molecules. Unlike molecules in the bulk of the liquid, molecules close to the surface are surrounded by neighboring molecules from only one side. These molecules on the surface thus exhibit stronger attractive forces upon their nearest neighbors than do those on the inside. This enhancement of intermolecular attractive forces close to the surface is called surface tension, see figure 5.9.



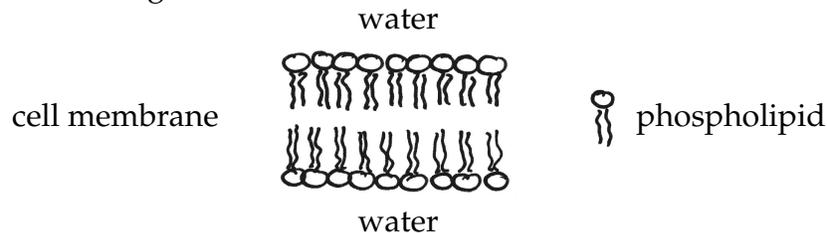
**Figure 5.6:** Air water interface - molecular interpretation of surface tension

More than a century ago, an illustrative set of experiments on surface tension was carried out by Boys [2]. You can easily visualize the effect of surface tension by carefully laying down a paper clip on a surface of water. Although the density of the paper clip should be higher than that of water and you would expect it to sink down, it actually floats on top of the water surface due to surface tension.

**Surface tension** Surface tension is typically measured in force per length related to the units dynes per cm. Since  $1 \text{ dyne} = 10 \text{ mN}$ ,  $1 \text{ dyne/cm} = 1 \text{ mN/m}$ . Alternatively, especially in thermodynamics, the notion surface energy is used instead. Surface energy is measured in ergs per length squared, where one erg, the force of one dyne exerted for a distance of one cm is equal to gram centimeter squared per second squared  $\text{g cm}^2/\text{s}^2$  or, equivalently,  $10^{-7}$  joules. The surface tension of water at room temperature is  $\gamma^{\text{water}} = 72 \text{ dynes/cm}$ , ethanol has a lower surface tension of  $\gamma^{\text{ethanol}} = 22 \text{ dynes/cm}$  and mercury has a surface tension as large as  $\gamma^{\text{mercury}} = 465 \text{ dynes/cm}$ .

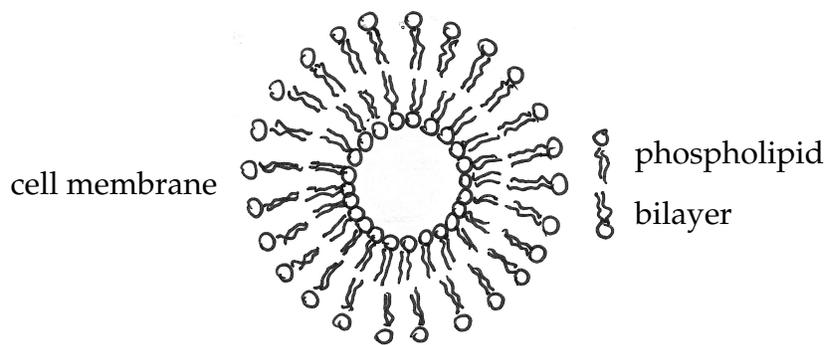
### 5.1.3 Cell membranes

The most intriguing of all biomembranes is the cell membrane, a semipermeable phospholipid bilayer common to all living cells. This lipid bilayer which is approximately 6 nm thick consists of a variety of different biopolymers the most common of which are proteins, lipids and oligosaccharides.



**Figure 5.7:** Lipid bilayer of the cell membrane - characteristic arrangement of phospholipid molecules with hydrophilic polar head groups being oriented towards the aqueous phase while the hydrophobic tails are oriented towards the non-polar inside

On the inside, the lipid bilayer serves as attachment for the cytoskeleton which is primarily responsible to control the cell shape, see figure 5.7. On the outside, the cell membrane plays an important role in attaching to the extracellular matrix. Specific proteins embedded in the cell membrane can act as molecular signals and to allow for cell to cell interaction. In fungi, bacteria and plants, the cell membrane is further surrounded by the cell wall. In an aqueous environment, the intact cell membrane seeks



**Figure 5.8:** Lipid bilayer of cell membrane - characteristic arrangement of phospholipid molecules with hydrophilic polar head groups being oriented towards the aqueous phase while the hydrophobic tails are oriented towards the non-polar inside

to attain its lowest energy level. Accordingly, the nonpolar aminoacid residues of its proteins and the fatty acid chains of its phospholipids will typically be sequestered furthest away from the aqueous solvent. The ionic and polar head groups of the proteins, the lipids and the oligosaccharides, in turn, will seek to be in contact with water, see figure 5.8. Perhaps the most important lesson learned from the study of pure phospholipid bilayer membranes is that they spontaneously seal to form closed structures that separate two aqueous compartments. In the configuration of a plain sheet with ends in which the hydrophobic interior are in contact with water, bilayers are unstable. Their typical spherical architecture with no ends is the most stable state of a phospholipid bilayer.

## 5.2 Energy

From a structural mechanics point of view, biomembranes are characterized through their very thin structure. As you have seen, the lipid bilayer of the cell membrane has a thickness of approximately 6 nm. The typical dimensions of a cell are at least of the order of  $\mu\text{m}$ . Therefore, it is quite common to treat biomembranes as shell structures. In general, the notion of shells is associated with thin, curved structures that are subjected to loads that can cause in plane stretches and shear and out of plane bending. A special case of shells, a flat shell of zero curvature, would be referred to as a plate. Shells are structural elements for which one dimension, the thickness, is much smaller than their two other dimensions, the length and the width. Based on this dimensional restriction, specific kinematic assumptions can be made that significantly reduce and simplify the set of governing equations of three dimensional continua.

### 5.2.1 The Kirchhoff Love theory

The kinematic assumptions that seem reasonable for biomembranes are based on the classical von Kármán theory. The von Kármán theory implies that the displacements are small, while the rotations of the shell's mid surface can be moderate. Of course,