

# Chapter 1

## Introduction

One of the underlying principles for the understanding of the structure of all living matter is that of spatial organization. At the cellular level, this occurs through the existence of membranes, the mediators of all interactions between cells and their external environment. In fact, the appearance of the external membrane may have been decisive for the origin of life, since it is rather unlikely that a self-replicating mixture of macromolecules could evolve to a higher organism without the enclosure by a membrane.

Experiments simulating the physical conditions of the primitive Earth demonstrated that the four main classes of organic molecules (amino-acids, sugars, nucleotides, and fatty acids) found in cells of all living organisms could have been generated under such conditions. It has also been verified that, in the pre-biotic period, nucleotide chains (polynucleotides) and amino-acid sequences (polypeptides) could have emerged.

Polypeptides, or proteins, and polynucleotides, in the form of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), are the most important components of today's cells. Polynucleotides are known to act as templates, specifying the sequence of nucleotides in the polymerization process of a new molecule. This is due to the fact that each one of the known nucleotide types (adenine (A), thymine (T), cytosine (C) and guanine (G)) binds preferentially to one of the others (that is, A binds preferentially to T, and C to G). The pairing of complementary nucleotides probably played a determinant role in the origin of life.

The information contained in nucleotide chains can be translated into the specific sequences of amino-acids. Due to the versatility of RNA molecules as well as to their catalytic properties, it is assumed that they led the primordial

protein synthesis.

The synthesis of specific proteins, under the control of a certain RNA type, and the posterior replication of this RNA, in a continuous process that would give rise to the first life forms could not have occurred without a compartmentalization of the molecules, preventing them from diffusing in the ‘pre-biotic soup’. The answer to the need of compartmentalization came in the form of an external membrane [1].

## 1.1 The chemical structure of cellular membranes

Although it has been known since the last century that cells are surrounded by a selectively permeable membrane, their molecular structure was described adequately only in the 1970’s, after the development of molecular biology.

The chemical composition of cellular membranes had already been known since 1890 [2], and their main components identified as being phospholipids and cholesterol, but only in the beginning of this century were the physical properties of these molecules investigated in more detail.

Phospholipids are special types of fatty acids. Such molecules are made of one or two long, chemically not very reactive hydrocarbon chains and a carboxylic head group, ionized in aqueous solution. The nonpolar hydrocarbon chains are hydrophobic, that is, they are not soluble in water, while the polar head group is said to be hydrophilic, and is readily soluble in water. Phospholipid molecules are thus said to be *amphiphilic*. The chemical structure of an amphiphilic molecule is depicted in Fig. 1.1. Mixtures of amphiphiles and water can assume a variety of thermodynamically stable phases. Examples are lipid monolayers in air/water interfaces, where the hydrophilic heads are dissolved in water, while the hydrophobic chains remain in contact with the air outside; lipid bilayers in water, where the nonpolar regions of two monolayers are isolated from water by the layers of hydrophilic heads; lamellar and micellar phases (see Fig. 1.2).

The physical properties of such mixtures are governed mainly by the *hydrophobic effect*. This can be understood as an interplay between entropy and electrostatic attraction between water molecules. Due to their polar nature, water molecules are bound to each other through hydrogen bonds. In

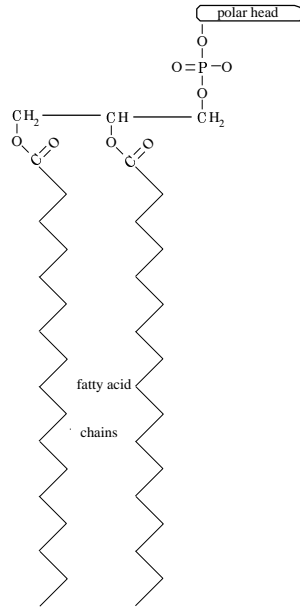


Figure 1.1: Schematic representation of a phospholipid molecule

spite of their weakness (they are approximately 20 times weaker than covalent bonds), hydrogen bonds are responsible for many of the physical properties of liquid water, such as its high surface tension and specific heat. Hydrogen bonds stabilize a regular structure of water molecules, even in liquid state. Ions and polar molecules can be accommodated in this structure, since they are also capable of establishing hydrogen bonds with the water molecules. They are therefore hydrophilic, or soluble in water. Nonpolar molecules, on the other hand, not being able to establish hydrogen bonds, disrupt the 'lattice' of water molecules. To minimize this energetically unfavorable effect, hydrophobic molecules aggregate, being thus insoluble in water [1].

## 1.2 Biological membrane models

In 1890 C.E. Overton, working on cells of plant root hairs, detected a strong correlation between the permeability of the membrane with respect to certain molecules and their solubility in lipids. He discovered that lipophilic molecules easily penetrate the cell, suggesting that the membrane is also

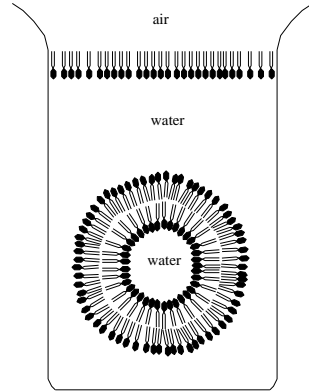


Figure 1.2: Schematic representation of amphiphiles in aqueous solution

composed of lipids. This was confirmed in 1925, with the experiments of Langmuir [2].

In 1925, E. Gorter and F. Grendel suggested that the basic membrane structure is a lipid bilayer. They dissolved the membranes of red blood cells in acetone, and spread them on a water surface to obtain a monolayer, and then compared its surface area to that of dried red blood cells observed under a microscope. From the comparison they concluded that the lipids in the membrane must be arranged in a bilayer [2].

One of the first models that tried to explain the different permeability and resistivity observed in artificial (pure lipidic) membranes and in biological membranes was proposed by H. Dawson and J. Danielli in the 50's [1, 2]. Their model assumed that membranes are composed not only of phospholipids, but also of proteins covering the bilayer on both sides, like a 'sandwich'. It was soon realized, however, that proteins, although present in the membrane structure, did not cover it completely.

In 1972, S. J. Singer and G. L. Nicolson [3] proposed the *fluid mosaic model* for the structure of biological membranes, which is the model currently accepted. According to their model, the membrane's constituent lipids are found in a fluid state. This means that the membrane may be considered as a two-dimensional lipid solution, with proteins dissolved in it. Both lipids and proteins within the membrane may diffuse freely. The fluid mosaic model is represented schematically in Fig. 1.3.

The basic function of biological membranes is that of allowing for the

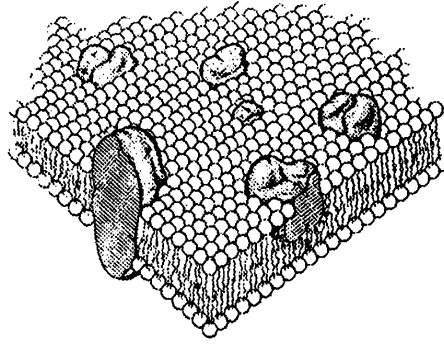


Figure 1.3: The fluid mosaic model.

existence of different intracellular compartments where the chemical reactions responsible for cell maintenance take place. Membranes act as a highly selective barrier for exchange of molecules between the cell and its external environment, as well as between intracellular compartments. They are also responsible for many other biological functions, such as signal transduction and mechanical support for polymer lattices, for example.

A complete understanding of the physical properties of biological membranes would require a thorough understanding of each of its components, followed by the challenging problems of membrane-membrane interactions, such as membrane fusion, pore formation, endo- and exocytosis and budding. The full system is current beyond the scope of analytical and numerical methods, and one must resort to simplified membrane models which render a physical, quantitative approach feasible.

### 1.3 Simplified membrane models

When trying to model the phase properties of membranes, a first approach is to extend the statistical mechanics of polymers to two (or more) dimensions. Polymers in solution show universal large scale properties, explained by the renormalization group [4], which have been extensively studied, both analytically and numerically [5]. The relative simplicity of the one-dimensional geometry of polymers allowed for considerable progress in the field.

Although the extension of these systems to two-dimensional structures

may seem natural, the statistical mechanics of the surfaces obtained in this way is far more complex than that of polymers. Since two-dimensional geometry is much richer than the restricted geometry of lines, membranes with distinct types of in-plane order (crystalline, hexatic, fluid) will, unlike polymers, display distinct long-range behavior, and consequently a richer set of universality classes [6].

### 1.3.1 Crystalline membranes

Crystalline membranes, sometimes termed *tethered* or *polymerized* membranes, are the natural generalization of linear polymer chains to two-dimensional structures. They possess in-plane elastic moduli as well as bending rigidity, and are characterized by a fixed connectivity. Such membranes are found in the cytoskeleton of cell membranes, the most studied example being the cytoskeleton of red blood cells. It is a fishnet-like network of triangular plaquettes formed primarily by the proteins *spectrin* and *actin*, bound to a fluid phospholipid bilayer[6].

The microscopic model describing crystalline membranes, the so-called ‘spring and bead model’, consists of beads connected by springs, forming a regular lattice. The model membrane is self-avoiding, since the beads cannot intersect each other.

A continuous model to describe a self-avoiding membrane corresponds to a generalization [7, 8] to two dimensions of the Edwards model [9] for polymers. While the Edwards model is amenable to treatment either by a direct renormalization method [4, 10, 11] or by identifying it with the  $N = 0$  limit of a scalar  $O(N)$  field theory [12], its generalization to membranes poses serious mathematical difficulties, which have only recently been overcome (for a review see [13] and references therein).

The nonlinear coupling of in-plane strain modes and out-of-plane height modes of crystalline membranes leads to nontrivial and surprising properties. Fluctuations at finite temperature in a crystalline membrane produce random corrugations in random directions whose effect is to stiffen the bending rigidity and soften the bulk shear moduli. As a consequence, these systems may be found in three quite different phases: a collapsed compact phase, a flat phase and an intermediate crumpled swollen phase [13].

A simpler model for crystalline membranes is obtained by allowing self-intersections of the membrane. Calculations and numerical simulations show that such ‘phantom’ membranes are found in a flat phase, if their bending

rigidity is large enough, and in a crumpled phase for smaller rigidities [6, 13].

### 1.3.2 Hexatic membranes

Unpolymerized lipid bilayers at sufficiently low temperatures are an example of membranes whose molecules, instead of being tied together by covalent bonds, are bound together by the much weaker Van der Waals forces [14]. If such a surface is constrained to be flat, its low temperature phase becomes eventually unstable due to a proliferation of defects. According to the celebrated Kosterlitz-Thouless argument [15], the entropy of a dislocation grows logarithmically with the system size. A crystal melts when the contribution of the entropy of dislocations to its free energy, at a sufficiently high temperature, becomes larger than their energy cost. If a two-dimensional crystal is allowed to buckle into the third dimension, an extraordinary reduction in the energy cost of disclinations can be obtained [16, 17]. This is possible because the energy of disclinations can be compensated by curvature. This is also true for the energy of dislocations, which becomes a constant, independent of the system size. The entropy term in the Kosterlitz-Thouless argument dominates at all nonzero temperatures, the resulting phase being a fluid with hexatic order.

The positions of the molecules forming a so-called hexatic membrane are strongly correlated, and they may exhibit in-plane crystalline order, forming a kind of two-dimensional solid. The stretching elasticity associated with this order conspires with the bending rigidity to make the membrane flat at long distances [16]. One may thus observe a *crumpling transition* [18], separating the flat phase from a crumpled phase.

In spite of displaying in-plane orientational order, hexatic membranes are fluid membranes, and their mathematical description is very different from those with crystalline order. Since, due to the fluidity of these membranes, the description cannot depend on internal degrees of freedom, the free energy must be invariant under reparametrizations of internal coordinates, that is, it should depend only on geometrical quantities. The corresponding free energy was first formulated by Canham [19] and Helfrich [20], and includes only curvature energy. Hexatic membranes have an additional degree of freedom, namely the bond angle, introduced as an extra vector field defined on the surface.

The statistical mechanics of the above mentioned model for hexatic membranes was worked out by David *et al* [21]. They showed the existence of a

‘crinkled phase’, more rigid than a crumpled phase, but more crumpled than a flat one. This phase exists within a radius of gyration controlled by a Flory exponent that varies continuously with the hexatic stiffness. Both disclination unbinding transitions and finite crumpling transitions are possible in hexatic membranes [14, 22].

### 1.3.3 Fluid membranes

Fluid membranes have rather special elastic properties. Since the shear modulus within a fluid membrane is zero, there are only two types of elastic deformations for such a membrane: stretching and bending [19, 20, 23]. The stretching is also limited, since fluid membranes start to rupture as soon as their surface area is changed by about one percent [24]. If the membrane is able to exchange lipid molecules with its surrounding aqueous environment, the elastic forces generated by a stretching deformation act only for a short time, until the change in the surface area is compensated by incorporating more molecules to the membrane. Similarly, elastic forces arising due to curvature effects are compensated by a rearranging of lipid molecules, since they flow freely within the membrane. The surface tension of such membranes is thus vanishingly small.

In principle, a fluid surface that does not experience any lateral tension but undergoes thermally-excited fluctuations starts to behave as a random surface without any average orientation as soon as its size exceeds a certain length scale, the so-called persistence length [25]. This length scale depends exponentially on the ratio of the bending rigidity of the membrane and the temperature. For lipid bilayers, this ratio is usually large [26, 27], implying that the persistence length exceeds their largest accessible size. Therefore, under normal circumstances, lipid bilayers appear to be flat.

Nevertheless, fluid membranes still exhibit thermal fluctuations, such as bending undulations or protrusion modes. These shape fluctuations have a strong effect on the interaction between the membranes. Actually, the simple fluid membrane model proposed by Canham [19] and Helfrich [20], mentioned in the previous section, displays a surprisingly rich phase behavior if the topology of the membrane is allowed to vary [28].

The physics of fluid membranes is a complex and fascinating subject in itself. Due to its relevance in many physical and biological systems and its potential applications in material science, the experimental and theoretical understanding of fluid membranes is one of the most active areas in soft



condensed matter physics.

In the following we shall concentrate on the investigation of fluid membranes. In the next chapter the Canham-Helfrich model will be discussed in detail, and some results concerning the physical properties of the membranes described by it will be reviewed.

