Preface

The plasma membrane is a fundamental element of the cell, constituted mainly by phospholipids, sterols, and membrane proteins.

Biological membranes carry out the function of a barrier between the living cell and the environment and between intracellular compartments and the cytosol. The lipid bilayer regulates the transport of molecules and their concentration inside cells. It is a semipermeable structure, which allows the entry of small hydrophobic molecules, like oxygen and carbon dioxide. Small polar molecules, like water and ethanol, can cross the bilayer, but they do it more slowly. By contrast, the diffusion of charged ions, water-soluble molecules, or large molecules is avoided. The passage of these substances is regulated by specific transport proteins, selective channels for ions and molecules, or pumps capable to actively transfer molecules across the bilayer. Other transmembrane proteins are receptors for extracellular signaling molecules, which are critical for controlling cellular properties and behavior, like hormones, neurotransmitters, growth factors. Other receptors are enzymes, whose role is to start a metabolic cascade of intracellular reactions when stimulated. Furthermore, some proteins, or protein groups, are disposed in the membrane in a definite order, to create a system of electron transfer and energy accumulation in the form of ATP.

When the structure of the lipid membrane is damaged, the intracellular content is released outside the cell, causing rapidly its death. This can be exploited to kill bacterial cells using membrane-damaging agents. A possibility is represented by antimicrobial peptides (AMPs), which are able to perturb bacterial membranes, altering their selective permeability and leading bacteria to death.

In this thesis, the study of peptide-membrane interactions has been carried out using model membranes. It has been shown, indeed, that peptides feature the same activity on these systems. The most common membrane model is represented by lipid vesicles (liposomes), a simple but realistic system for physical and chemical studies of a variety of phenomena. The lipid assembling process that leads to vesicle formation is completely spontaneous; thus, liposomes are easy and fast to obtain.

The main advantages in the use of AMPs are that they are not toxic for eukaryotic cells, and that, with the membrane as their principal target, the raise of bacterial resistance against them seems unlikely. In the first part of this thesis, studies on the mechanism of membrane perturbation by AMPs will be presented.

The problem of AMPs selectivity will be also analyzed in detail. Selectivity is the capability of AMPs to distinguish between bacterial and mammalian cells, and to be toxic only for the former. The structural features that are essential for selectivity have not been clarified, yet; they will be investigated in Sect. 4.2 of Chap. 4 of this work.

The cell membranes represent a barrier also to the diffusion of drugs. In many cases, their internalization can be enhanced with the help of a carrier. Some peptides, called cell-penetrating peptides (CPPs), have the capability to cross-biological membranes, without damaging them, even when they are conjugated with a large cargo, i.e., constituted by a drug molecule. Section 4.3 of Chap. 4 will be dedicated to the possibility to modulate the biological activity of a CPP, to obtain a peptide with both penetrating and bactericidal functions.

The study of biological membranes is a fundamental topic of biology and biophysics. However, the particular characteristics of this system make it interesting also in different fields, like polymer science and nanoscience.

Due to its impermeability, the lipid membrane represents the envelope of a segregated environment. A chemical reaction can be carried out in this closed compartment, without occurring in the outer solution. In the second part of this thesis, liposomes will be exploited as nanotemplates for the photopolymerization of a hydrogel, allowing the formation of nanometric particles that can be used as drug delivery nanodevices for enzymatic therapies. The novelty of this approach resides in the fact that these nanoparticles have not been designed for the release of the enzyme in the organism, but to keep it within the gel, protecting it against inactivating factors, but allowing at the same time its catalytic function.

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