

Biological membranes. Structure, properties, functions

Abstract

Biological membranes, together with *cytoskeleton*, form the structure of living cell. *Cell* or *cytoplasmic* membrane surrounds every cell. The nucleus is surrounded by two nucleus membranes - external and internal. All the intracellular structures (mitochondria, endoplasmic reticulum, Golgi apparatus, lysosomes, peroxisomes, phagosomes, synaptosomes, etc.) represent closed *membrane vesicles*. Each membrane type contains a specific set of proteins - receptors and enzymes but the base of every membrane is a bimolecular layer of lipids (*lipid bilayer*) that performs in each membrane two principal functions: (1) a *barrier* for ions and molecules, and (2) structural base (matrix) for functioning of receptors and enzymes.

Introduction

Studying an electronic microscopic picture of the ultrafine section of living tissue, after its fixation and proper staining, fine double lines can be clearly seen that «pattern» the shape of cell and intracellular organelles (See [Fig. 1](#)). These are sections through biological membranes - finest films consisting of a double layer of lipid molecules and proteins built in to this layer. As a matter of fact, it is membranes, together with *cytoskeleton*, who forms the structure of living cells. *Cellular* or *cytoplasmic* membrane surrounds each cell. The nucleus is surrounded by two *nucleus* membranes: outer and inner. All the intracellular structures (mitochondria, endoplasmic reticulum, Golgi's apparatus, lysosomes, peroxisomes, phagosomes, synaptosomes, etc.) represent closed *membrane vesicles*.

History of studies on the properties and structure of membranes

The term «membrane» as an invisible film that surround a cell and serves as a barrier between cell contents and the environment and at the same time as a semipermeable partition through which water and some substances dissolved in it can pass, was first used obviously by botanists von Mol and independently K. Von Negeli (1817-1891) in 1855 for explanation of plasmolytic phenomena. Botanist W. Pfeffer (1845-1920) published his paper «Investigations of osmosis» (1877, Leipzig) where he postulated the existence of cell membranes basing on the similarity between cells and osmometers having artificial semipermeable membranes that had been prepared not long before by M. Traube. Further investigation of osmotic phenomena in vegetable cells by Danish botanist Ch. De Friz (1848-1935) laid the basis in the creation of physical chemical theories of osmotic pressure and electrolytic dissociation by Danish scientist J. Vant-Hoff (1852-1911) and by Swedish scientist V. Arrhenius (1859-1927). In 1888, German physicist and chemist W. Nernst (1864-1941) deduced the equation of diffusion potential. In 1890, German physicist, chemist and philosopher W. Ostwald (1853-1932) drew attention to a possible role of membranes in bioelectrical processes. Between 1895 and 1902, E. Overton (1865-1933) measured cell membrane permeability for many compounds and showed a direct relationship between the ability of these compounds to penetrate through membranes and their solubility in lipids. It was a clear indication that it is lipids who forms the film through which substances from surrounding solution pass to cell. In 1902, Yu. Bernstein (1839-1917) used the membrane hypothesis for explanation of the electric properties of living cells.

Gorter and Grendel showed in 1925 that the area of the monolayer of lipids extracted from erythrocyte membranes is two times larger than the total area of erythrocytes. They extracted lipids from hemolysed erythrocytes with/by acetone, evaporated the solution on the surface of water, and measured the area of the formed monomolecular lipid film. The results of these investigations suggested that lipids in membrane are arranged as a bimolecular layer. This supposition was verified by investigations of the electrical parameters of biomembranes (Cole & Curtis, 1935): high electrical resistance (approx. $10^7 \text{ Ohm} \cdot \text{m}^2$) and high electrical capacitance (0.51 F/m^2).

At the same time, there were experimental data that testified to the fact that biological membranes contained protein molecules as part of their composition. These contradictions in experimental results were removed by Danielli & Dawson who proposed in 1935 the so-called «sandwich»(butterbrod/bread-and-butter) model of biological membranes' composition that had been used in membranology, though with some small variations, for almost forty years. According to this model, proteins are located/dispersed in membranes on the surface of phospholipid layer.

Functions of biological membranes

Functions of cytoplasmic and some intracellular membranes are listed in Table 1.

In all living cells, biological membranes carry out the function of «*barrier*» that divides the cell from the environment and the internal cell volume into comparably isolated «compartments». Partitions dividing cells into compartments are built of a double layer of lipid molecules (which is often called «*bilayer*») and are practically impermeable for ions and polar water-soluble molecules. But this lipid bilayer includes numerous built-in protein molecules and molecular complexes one of those have/possess the properties of selective «*channels*» for ions and molecules, and others - those of «*pumps*» capable to pump/transfer actively ions through membrane. The barrier properties of membranes and working of membrane pumps cause irregular/disbalanced distribution of ions between the cell and extracellular medium, which lies in the basis of the processes of intracellular regulation and signal transfer in the form of electrical impulse between cells.

A second function, common for all membranes, is the function of «mounting plate», or *matrix* on which there are proteins and protein groups that are disposed in a definite order and form/create systems of electron transfer, energy accumulation in the form of ATP, regulation of intracellular processes by hormones coming in from outside and intracellular mediations, recognizing of other cells and foreign proteins, light reception, mechanical effects, etc.

A flexible and elastic film which lay in the basis of all membranes also plays a definite *mechanical function* keeping the cell intact under mild mechanical loads and disturbances in/upsets of osmotic balance between the cell and environment.

Common for all membranes functions of barrier for ions and molecules and matrix for protein groups are mainly provided by the lipid bilayer that has in principle/general the same structure in all membranes. Nevertheless, the set of proteins is individual/unique for each membrane type which allows membranes to take part in carrying out different/various functions in different cells and cell structures. Some of these functions are listed in Table 1.

Table 1. Some functions of biological membranes.

Cells	Membranes	Function
All cells	Cell (cytoplasmic)	Active transport of K^+ , Na^+ , Ca^{2+} , maintaining of osmotic equilibrium
Majority of cells	Cell membranes	Binding of hormones and switching on of mechanisms of intracellular signalling
Nerve and muscle cells	Cell membranes	Generation of potentials of peace and action, distribution of action potential
Majority of cells (except erythrocytes)	Inner membrane of mitochondria	Transfer of electrons on oxygen and synthesis of ATP (oxidative phosphorylation)
Majority of cells (except erythrocytes)	Endoplasmic reticulum	Transfer of Ca^{2+} from cell juice into vesicles
Eye epythelium cells	Membranes of eye disks	Absorption of light quanta and generation of intracellular signal

Membrane structure

General scheme of membrane structure

According to modern information, all cell and intracellular membranes have similar structure: the base of the membrane is composed of a lipid double molecular layer (lipid bilayer) on the surface and inside of which proteins are disposed (See [Fig. 1](#)).

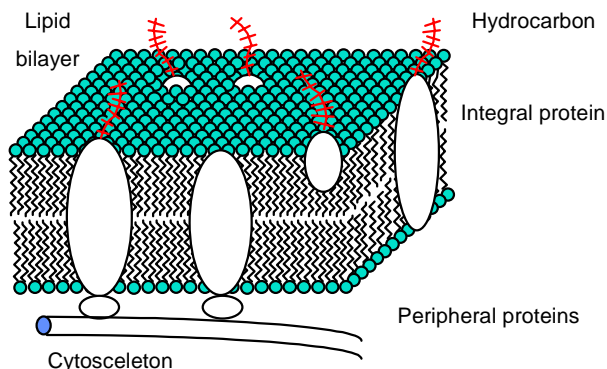


Fig. 1 The membrane structure

Membrane lipids

Membrane lipids

Lipid bilayers are formed by amphiphilic molecules of phospholipids and sphingomyelin in water phase. These molecules are called amphiphilic because they are composed of two parts which differ by their solubility in water: (1) polar «head» possessing high affinity for water, i.e. hydrophilic, and (2) «tail» that is formed by non-polar carbohydrate chains of fatty acids; this part of the molecule has low affinity for water, i.e. it is hydrophobic. Fig.2.

Membrane lipids are mainly composed of phospholipids, sphingomyelins, and cholesterol. For example, in human erythrocyte membranes their contents are 36, 30, and 22%, respectively; 12% are glycolipids (A.Kotytk & K.Yanachek «Membrane Transport», Moscow, «Mir», 1980, p.45). Phosphatidylethanolamine molecule, whose structure is shown in **Fig.2**, can serve as an example of amphiphilic molecule. Phosphatidylethanolamine, like other phospholipids, represents chemically the esters of three-atom glycerol with two fatty acids; orthophosphate is bound to the third hydroxyl group; and a small organic molecule characteristic of each type phospholipids is bound to orthophosphate. In this very case it is ethanolamine, but it can also be choline, inositol, serine, and some other molecules. Figs.3,4,5.

The composition of membrane lipid layer also includes cholesterol and sphingomyelins, the latter are close to phospholipids by chemical structure and physical properties.

Amphyphilic molecules

Lipid bilayers are formed by *amphiphilic* molecules of phospholipids and sphingomyelin in water phase. These molecules are called amphiphilic because they are composed of two parts which differ by their solubility in water: (1) polar «head» possessing high affinity for water, i.e. *hydrophilic*, and (2) «tail» that is formed by non-polar carbohydrate chains of fatty acids; this part of the molecule has low affinity for water, i.e. it is *hydrophobic*.

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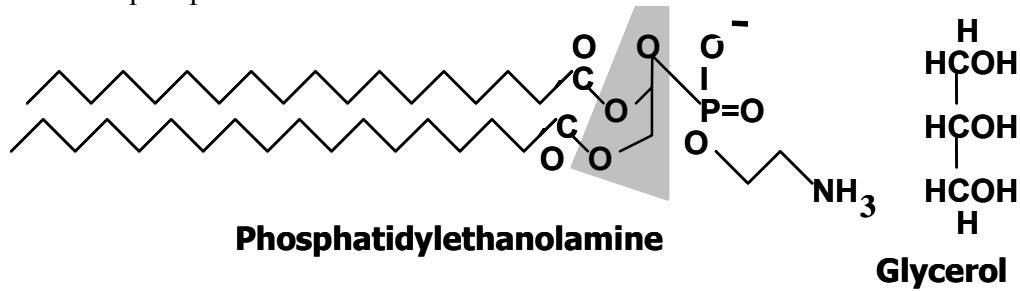


Fig. 2. A phospholipid molecule

In this very case it is ethanolamine, but it can also be choline, inositol, serine, and some other molecules ([Fig. 3](#)).

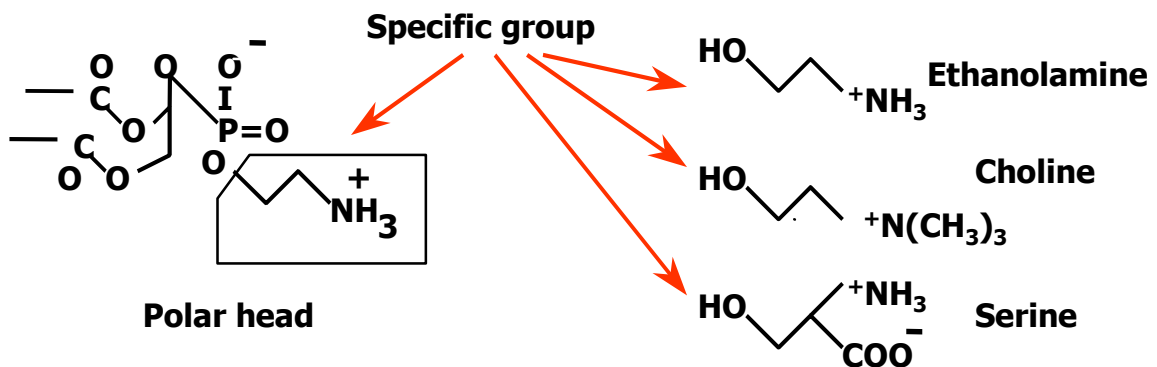


Fig. 3. Specific groups of phospholipids

Membrane proteins

Membrane proteins are usually divided into integral and peripheral. *Integral proteins* have vast *hydrophobic* areas on the surface and are insoluble in water. They are connected with membrane lipids by/with *hydrophobic interactions* and partially immersed into lipid bilayer, and they often pierce the bilayer leaving on its surface comparatively small hydrophilic areas. It is possible to separate these proteins from the membrane only with the help of detergents such as dodecyl sulfate or cholines which destroy lipid bilayer and transfer protein to soluble form (*solubilize* it) creating associates with it. All further operations on purifying integral proteins are also carried out in the presence of *detergents*.

Peripheral proteins are connected to the surface of lipid bilayer by electrostatic forces and can be washed out of the membrane by saline solutions.

Membrane lipid layer

The data of X-ray analysis and some other show that phospholipid molecules have a specific shape, namely, they resemble a cylinder, in which the diameter of the polar head is close to that of hydrophobic tale. The structure of a molecule is given in [Fig. 4](#).

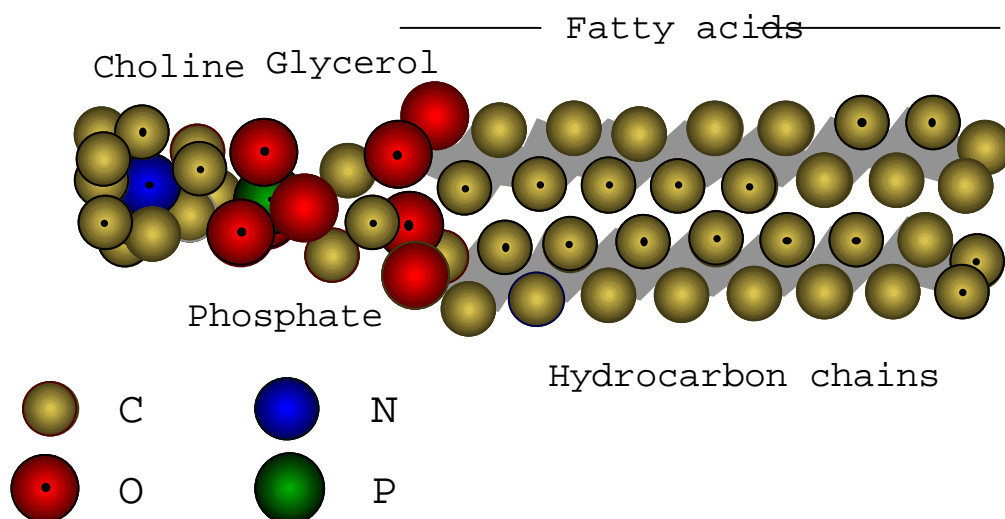


Fig. 4. Molecular model of phosphatidylcholine

A peculiar property of an amphiphilic molecules, including those of phospholipids, results in formation of a lipid bilayer and then liposomes in aqueous solutions. In the membrane, "fatty tails" of the molecules are hidden inside, while polar "heads" of the molecules are exposed to water environment ([Fig. 5](#)).

In aqueous environment amphiphilic molecules are spontaneously gathering together to form lipid bilayer, that in its turn is closing up, so making a vesicle (liposome) ([Fig. 5](#)).

Model membranes

Studies on the physical properties of membrane lipid layer are carried out mainly on artificial membrane structures of two types formed by synthetic phospholipids or lipids extracted from biological sources: (1) liposomes and (2) bilayer lipid membranes (BLM).

Liposomes

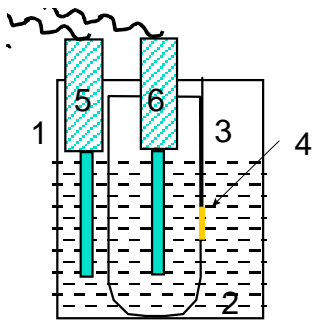
Liposomes are lipid vesicles that are formed from phospholipids in water solutions. In order to obtain liposomes, a phospholipid dissolved in alcohol is injected into a large-volume water solution; insoluble in water phospholipids create small vesicles whose walls are composed of lipid bilayer (***unilayer liposomes***).

The phospholipid solution can first be dried from a solution in an organic solvent (for example, in chloroform) in a tube. Then water solution should be added into the tube and shaken well. Lipids pass into the water solution, now in the form of ***multilayer*** liposomes. Liposome suspensions are usually used in studies on the physical properties of lipid bilayer such as viscosity, surface charge, or dielectric permittivity, as well as for investigation of permeability for uncharged molecules.

Bilayer Lipid Membranes (BLM)

In studies on ion permeability of the lipid layer of membranes BLM are used.

For preparation of BLM (see [Fig. 6](#)), an electrolyte-containing glass was used into which a teflon cup with an orifice ($D = 1\text{mm}$) in its wall was put.



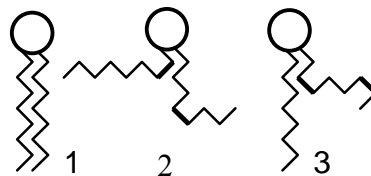
- 1 – A glass with an electrolyte solution (2).
- 3 – Teflon tube with a hole (4).
- 4 – BLM.
- 5 и 6 – non-polarizable electrodes.

A small drop of a solution of phospholipid in liquid hydrocarbon, heptane or hexane is introduced/injected into the orifice using a capillary tube ([Fig. 7, A](#)).

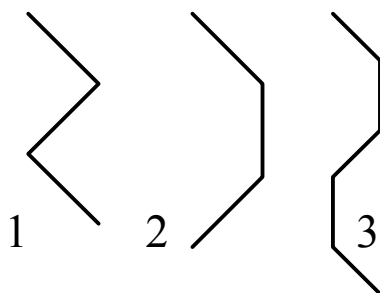
The polar heads of phospholipids are directed into water phase, and nonpolar hydrocarbon chains of fatty acids merge into a homogeneous viscous phase in the inner side of lipid membranes. This film is alike by many properties with the lipid layer of biomembranes.

The mobility of hydrophobic tails of phospholipid molecules in the lipid bilayer of membranes

The carbon atoms in hydrocarbon backbone of the phospholipid fatty acids are connected to each other by ordinary bounds, around which, as on an axis, the different sites of the molecule can rotate. This rotation results in that the hydrophobic chain can be in the most various configurations, as it is shown in Fig. 8 and 9.



As a result of such rotation, the fatty acid chains seem to be flexible, though actually they could not be bent in common sense of this word: they only can turn around of the bonds between atoms, which results in a bend of a molecule as a whole.



- 1-*all-trans*-configuration; 2- *ghosh*-configuration;
- 3- *double ghosh*-configuration.

Kinks

The ability of fatty acids to change their configuration is of primary importance for dissolution of various molecules and ions in a lipid layer and for their diffusion through membrane lipid phase. Sometimes two adjacent loops of fatty acid chains may form a sort of the cave, named a *kink*. The *kinks* are formed as a result of thermal movement of phospholipid molecules, and ions can diffuse through the lipid layer of the membrane, jumping from one kink to another. It is schematically represented in [Figure 10](#).

