Some Similarities Between the Cell Membrane and Artificial Ion-Selective Membranes

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Abstract

There are presented some structural and functional similarities between the cell membrane and artificial selective membranes. The nervous cell membrane and artificial ion-selective membranes are taken as models and it is analyzed the way their behavior is influenced by some of their common properties. Based on the present theories in this field and also on some experimental data a few conclusions of interest are formulated that could be useful for the knowledge and mastership of the membrane phenomena. A special attention is paid to the interactions between the receptors in the membrane and certain chemical species present in the immiscible media it separates, particularly to those interactions considered to be at the origin of the information transfer at the membrane (both cellular and artificial) level. This particular aspect is of a great interest in biochemistry, biology, physical chemistry and analytical chemistry.

Keywords: cell membrane, artificial selective membrane, receptor, interactions

Introduction

By definition, an interface/membrane is constituted at the separation boundary of two immiscible media. So the very existence of an interface/membrane is conditioned by, such a situation. Thus, the membrane appears as a transition entity between the media it separates, and from the very beginning of its existence its physical and chemical properties differ from those characterizing each of these media. In certain circumstances due to the properties the membrane achieves in its close contact with both the adjacent media, it could become a real functional entity i.e. a host place for the very complex processes that occur at the transition space in these media [1-4]. In fact, such very complex processes are at the origin of what we often call the *membrane phenomena* among which of particular importance are those involved in the *information transfer* at this level [4-9].

A very complex and interesting natural membrane model is that of the cell membrane, a structural and functional entity built at the interface between the intracellular and extracellular media, of a special importance for the very existence and dynamics of the living matter. There are also interesting models among the artificial membranes, as it is the case of the selective ones.

A lot of structural and functional similarities have been identified between the nervous cell membrane, as a natural membrane, and the ion-selective liquid membranes as artificial ones [8], some of them referring to the membrane information transfer.

Some studies carried out until now try to point out the role that the interactions between certain membrane components and some chemical species in the adjacent media pay in the formation and dynamics of the membrane electrical potential as one of the most important elements involved in the information transfer mechanism at the cell level [1, 3, 5, 10].

The membrane uptake of the signals generated by different stimuli as well as their processing and transmission are fulfilled through certain mechanisms of high fineness and complexity, not well cleared up until now [10-12]. Such processes are fuelled or accompanied by partial transformation of the system energy [4, 9], with the conservation of its total energy, depending on the necessities related to the system's energetic equilibrium.

The structural and functional similarities between the natural and the artificial membranes allow one to use the results of the investigations carried out on one of these categories, more accessible experimentally, for better knowledge and mastership of the specific working mechanism of the other category, which might be less accessible from the point of view of research.

Some structural and functional similarities between the neuronal membrane and the ion-selective artificial liquid membranes considered to be relevant for the information transfer at the membrane level will be pointed out in the current study. A special attention will be paid to the role the interactions between certain "active membrane components" (receptors) and certain chemical species present in the adjacent media play in the accomplishment of the information transfer at the membrane level.

Actually the ideas this study started from are on one hand, the absence of unitary and pertinent theoretical and phenomenological approach of the membrane phenomena and on the other hand, the necessity to stress on the utility of a deep theoretical and phenomenological interdisciplinary treatment of such a very important and complex topic.

Structural Similarities

The neuronal membrane, as a structural and functional entity built at the interface between the intracellular and extracellular media, consists in a large variety of lipids and proteins allowing a good mutual adjustment in different conditions. Due to their structural diversity, and the availability for interaction given by their specific chemical functions the proteins are the active element in the cell membrane composition [1, 5]. In the cell membrane structure the lipid molecules are those contributing mainly to the accomplishment of the matrix the proteins are fixed in. With both hydrophilic and hydrophobic ends, the lipid molecules can be associated among themselves in quasi-compact structures/aggregates that resemble bi-lipid layers.

At the cell membrane level, the proteins are mainly found in the form of enzymes, membrane carriers, constituents of the channels for some intermolecular complexes, *pharmaceutical receptors* etc., and play an important role in the economy of the cellular processes. There are intrinsic proteins (fully integrated in the membrane structure) involved especially in *transport processes* and extrinsic or peripheral proteins (attached to one of the membrane faces), frequently involved in *information transmission processes* at the cell level. Usually the extrinsic proteins play the role of *pharmaceutical receptors*.

The bounds nature between the extrinsic protein molecules and the other membrane components (lipids included) can be of electrostatic, hydrophobic, covalent (through the so called “lipid anchor”) nature or can be achieved through he physical-chemical attachment to other proteins in the membrane [5].

An artificial ion-selective liquid membrane is a structural and functional entity, which appears at the interface between two immiscible media. Usually one of these media is of organic nature (a mixture of a certain organic solvent and a certain chemical organic species) and the other is an aqueous one. When these two immiscible media come in contact, a new structural and functional entity appears at their separation boundary, which is the so-called artificial liquid membrane. The more or less selective character of such a membrane for a certain species in the aqueous adjacent medium is mainly given by the nature of the organic medium (the organic solvent and the organic solute). The structure of such a membrane is somehow similar to that of the cell membrane, with the molecules of the organic solvent playing mainly the role of lipids and the molecules of the organic solute (whose structure usually includes some active chemical functions, $-NH_2$ and halides included) with the role of proteins.

Functional Similarities

Among the main functions both the natural and the artificial membrane fulfill a particular importance for the current sturdy is that of a selective barrier between the media it separates [5].

The selectivity of the natural and artificial membranes, consisting in a discriminating behavior regarding the material transit (ions, simple molecules, macromolecules) or the information transfer at their level is one of most important characteristics of such structural and functional entities.

Receptors, Affinity, Selectivity and Interaction

Those factors, present in one or both media adjacent to the membrane, determining by their action any kind of reaction at the membrane level are known under the generic name of *stimuli*. Those membrane components more or less sensitive to different stimuli categories are generically called *receptors*. As for the artificial selective membranes such sensitive membrane components are known under different names, like: *charge carries*, *charge transporters*, *active components* and *mobile sites*. Taking into account that there are situations when the receptors are electrically neutral molecules and in other situations they do not excel through their mobility, in this paper we will generalize the term *receptor*, which we consider to be the most appropriate and to characterize in the most suitable way the essence, the role as well as the behavior of the respective molecular formations at the membrane level.

In the neuronal membrane the receptors appear as three-dimensional structured macromolecular systems, built on the skeleton of one of the main cell construction constituents (aminoacids, nucleotides, glucides, etc.) [1, 8, 10]. The structural elements and especially the chemical functions in the receptor molecule, their succession and spatial orientation in a three-dimensional force field are at the origin of a differentiated relation between the receptor and each of the substances present in the media adjacent to the membrane. In such conditions, a certain order of priority is naturally established among the “candidate” substances to the interaction with the receptor. This is actually the origin of what we currently call *receptor selectivity,* which further gives the *membrane selectivity*. Taking into account that to a great extent the chemical functions responsive for the artificial membranes selective behavior are the same with those in the nervous cell membrane and also the above mentioned structure similarities between the two types of membrane, the approach of the selectivity for the neuronal membrane can be easily extended to the artificial ion-selective membranes.

In the given context, the physical approach between the receptor and the substance at the membrane level is also of a great importance in facilitating or not the interactions between these two categories of chemical compounds, for both neuronal and ion-selective membrane.

The investigations carried out in this field until now have shown that the chemical-structural and energetic complementarities between the substance molecule and a certain receptor category are of great importance for fulfilling the physical approach between the two chemical entities. It can be said that even such complementarities are at the origin of what we are usually calling the *affinity* between the receptor and the substance, which actually facilitates the interaction between the two entities [8]. There are situations where due to the high selectivity of the (cell or artificial) membrane receptors, the membrane becomes a specific one (it is sensitive only to a certain chemical species in the adjacent media).

Depending on the amplitude of the effects the receptors are responsible for, at the level of the natural or artificial membrane, as a result of their interaction with the chemical species in the adjacent media, there are [1, 5, 8, 13]:

-*“primary receptors”,* whose interaction with a given substance result in the dominant effects of the latter on the membrane and consequently on the system it belongs to. Due to the type and the number of the chemical functions in the structure of the primary receptors, the ways they can interact with a certain substance are usually limited. So, the result of the receptor-substance interaction is also orientated to a well defined direction. In the case of the cell membrane, the primary receptor-substance interactions are those generating the “primary effects” of the substance. As for the artificial ion-selective membrane, when it is used as sensor in a ion-selective electrode (as part of an analytical system) this kind of interactions are those generating the main electrical signal according to the level of the concentration the respective substance is present in the analytical sample.

-*“secondary receptors”* whose interaction with a given substance generates its secondary effects at the membrane/system level. Consisting, most often, of different functional groups, situated or not on the same *trunk* with the primary receptors, the secondary receptors in the membrane allow more interaction alternatives with a certain substance in the adjacent medium. In a cell membrane such interactions are considered to be responsible for the secondary effects of the respective substance on the organism. When such receptors are present in the structure of an artificial ion-selective membrane used as sensor in a ion-selective electrode, most often such kinds of interactions distort the electrode answer relating to the substance concentration level in the analytical sample. For both the cell membrane and artificial ion-selective membrane, the effects of the secondary receptor-substance interactions can evolve independently, can cumulate among them or can mutually counteract each other.

-*“silent receptors”*, whose interaction with a certain the substance, although it takes place, does not lead to a perceivable change at the level of the membrane or to the system it belongs to. Though such interactions are practically not perceivable they can sometimes influence (positively or negatively) the availability of other receptor types in the same membrane to interact with a certain substance present in the adjacent media. Silent receptors can be found in cell and in artificial membranes alike.

As for the receptors availability for more or less selective interactions with substances present in the media separated by the membrane, there are:

- *"rigid receptors"*, that can be activated only when they get in contact with certain well-defined chemical species. There are situations in which such receptors are sensitive to only one of the optical isomers of the same substance. In the cell membrane, when the substance is as a drug, the interactions involving such receptors usually result in a high efficiency of this drug. As for an artificial ion-selective membrane, when used as sensor in an ion-selective electrode, such interactions result in a high selectivity of the electrode, when besides the substance (as analyte), the analytical sample contains also other quite similar chemical species.

-*"less rigid receptors"*, more or less sensitive to a large variety of substances in the adjacent media (thus, they are less selective). Such receptors, when present in a cell membrane, have many alternatives to interact with more substances characterized by similar or related chemical and physical proprieties, due to the same chemical function in the substance structure or by the means of different chemical functions in the receptor structure. As such interactions are less selective the results are often confuse, for both the cell and the artificial membrane.

As for the amplitude of the effects generated at the level of the systems they are taking place in (nervous cell and ion-selective membrane, respectively) the substance-receptor interactions are: [1, 5, 8, 13]:

-*efficient interactions*: those interactions generating perceivable effects at the membrane level and thus at the level of the system it belongs to. In the cell membrane case this type of interactions have as result, strong effects of a certain substance at the level of the cell, tissue etc. As for the ion selective artificial membrane such interactions result in an elevated electrical signal as a function of the analyte concentration.

-*silent interactions*: those interactions possible and feasible from the point of view of affinity and chemical-structural complementarity between the receptor and the substance, but with no perceivable effect in the expected direction, at the level of the host system. Comparatively with the "efficient interactions" they are also known as "inefficient interactions". Although they have no effects in the expected direction, on the host system state, the silence interactions are sometimes able to hamper or, on the contrary, to simulate the interaction between other substances present in the same medium and the same or other receptor categories in the membrane. At the cell membrane level such interactions could result in sensitization of the receptors to the action of other substances or, on the contrary, their temporary or forever annihilation by substances able to do it. As for the ion-selective artificial membrane such interactions lead more often to the so-called untypical interferences (those interferences cannot be explained by any of the accepted theories in this field), or they may result in the partial or total annihilation of the receptors by one or another of the chemical species in the analytical sample.

The Competition Among Different Substances at the Receptors Level

A certain substance present in an adjacent medium to a (neuronal or artificial ion-selective) and a given receptor category in the membrane interacts between them in unique manner. When the adjacent to the membrane medium contains simultaneously more substances with affinity for the same membrane receptors category, the substances mutually influence their relation with the receptors. The molecules of all these substances enter in a tough competition to get a favorable position to interact with the receptors and their success depends on the extent their properties lend themselves to such interactions.

Depending on the nature of the relations established on the one hand, between the substance molecules found simultaneously in the adjacent medium to the membrane and, on the other hand, between them and different receptor categories populating the membrane, one can distinguish [1, 8, 13]:

-*competitive interactions*: when the molecules of two or more substances in the medium adjacent to the membrane are in competition to occupy favorable positions for the interaction with one and the same category of membrane receptors;

-*uncompetitive interactions*: when two or more substances in the adjacent medium to the membrane interact with different categories of membrane receptors. As for the effects at the membrane level such a situation may result in possible mutual influences between the given substances.

-*partially competitive interactions*: when two or more substances in an adjacent medium to the membrane interact with different functional groups belonging to the structure of one and the same membrane receptor category. The action of some of these substances on different functional groups in the receptor structure may have no one-self effect at the membrane level but it can change the availability of other functional groups of the receptors for the interaction with other substance(s) present in the medium adjacent to the membrane;

-*self-interactions*: when the molecules of the same substance, present in the medium adjacent to the membrane, interact simultaneously or subsequently with two or more functional groups in the structure of the same membrane receptor category. The rate between the frequency and the effectiveness of the substance interactions with a given functional group in the receptor structure and that of the interactions of the same substance with another functional group belonging to the same receptor depends on the substance concentration in the respective medium too.

Each mentioned interaction type has more alternatives, depending on the nature and the diversity of the receptor categories found in the membrane and of the nature and the number of the substances simultaneously found in the medium adjacent to the membrane.

The conclusion is that the simultaneous presence, in an medium adjacent to the membrane, of more substances characterized by a more or less marked affinity for certain membrane receptor categories may result in the stimulation as well as the partial or total annihilation of the respective receptors availability for the interaction with a given substance.

As for the cell membrane, the multitude and the diversity of substance-receptor interactions that may occur at its level, taking some particular aspects like: sensitization, antagonism, dualism, synergism and inhibition, are at the origin of the primary or secondary effects (on the cell, tissue or organism state), generated by the substance in such a relation with the receptors. In the case of the artificial ion-selective membranes used as sensors in the ion-selective electrodes such interactions are at the origin of the analytical answer of the electrode or at that of the interferences due to the other chemical species simultaneously present in the analytical sample.

The content of this paper, related to the aspects regarding the structure and behavior of the cell and artificial ion-selective membranes come to support the necessity and the utility of joining the studies on certain natural systems with that on the homologue artificial ones.

The current study should be considered as a modest attempt to an interdisciplinary approach of some of the membrane phenomena. It tried firstly to identify the “pair phenomena" taking place at the cell and at the artificial ion-selective membrane level, respectively. At a first glance for each of the two membrane categories, the finally identified pair phenomena may appear under different forms depending on the parameters of interest that can be measured or followed in a scientific investigation. Therefore, the identification of the pair phenomena is often a very difficult task but it is facilitated by an interdisciplinary approach of the topic. The authors conclusion is that this kind of approach of the topic under discussion could lead to good results in the common effort of the scientists to decipher, step by step, and to finally master the mechanisms of the membrane phenomena. Thus a necessary scientific basis for a correct approach of the membrane can be rounded, in an organized manner, as a very interesting and important structural and functional entity for many scientific and technical fields, and especially for medicine, biology, biotechnology and chemistry.

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