Selective Interaction Model and Photoreceptor Cell Membrane

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Abstract. A mathematical model is proposed in order to describe, from the thermodynamic point of view, the changes in the photoreceptor cell membrane induced by light stimuli. The phenomenological background is the increase of the fly microvillar membrane ionic conductivity as a consequence of Ca^{++} - Na^{+} affinity modification under light action. On the basis of the analogy with the model of protein interaction in mixed solvents, the model is focused on the selective interaction between ion channels gates and two ionic ligands. Three possible theoretical cases are examined.

Key words: Selective interaction, Mathematical modeling, Photoreceptor

1. Introduction

The scientific world in general tends to accept that the mathematical framework for the study of biological systems, more complex than the physical, needs to be much more carefully worked out because of the fragmentary character of the information that is obtainable from the investigated reality.

The research preoccupations authors of this paper are the processing of visual information at the level of the invertebrate eye, both experimentally and theoretically. In this paper we report a mathematical model of photoreceptor cell membrane behavior under light action. The model of protein selective interaction with a mixed solvent [5, 6] is taken as a starting point and a phenomenological analogy with the interaction of some proteic sites of the visual cell membrane with a mixture of ions is pointed out. This thermodynamic model applied to fly eye bioelectrogenesis emphasizes the existence of at least two types of ionic channels, already reported in the literature [3]. It also suggests the non-homogenous response of the fly visual cell membrane to light stimuli.

2. Phenomenological Background

Light absorption at the level of the photosensitive principal pigment, rhodopsin, induces biochemical and physiological modifications, starting with the opening of membrane Na^{+} channels. This phenomenon is explained [3] by an increase of membrane affinity for Na^{+} ions and simultaneous decrease of its affinity for Ca^{++} ions. Then both internal and external ion concentrations change, the membrane elec-

tric potential varies, new voltage dependent ion channels open, ion concentrations change further and a membrane action potential is generated. Electroretinograms are often used to record the eye response to different lighting conditions [1, 7, 8]. The aim of this paper is to offer a more detailed mathematical description of the visual cell membrane affinity modification for Na^+ and Ca^{++} ions.

3. The Model of Protein Interaction with a Mixed Solvent

The model proposed in the present paper for describing some aspects of phototransduction is based on the theory concerning the attachment of ligands to molecular sites in the case of protein solvating in mixed solvents [5, 6]. In agreement with this theory, interaction between protein molecules and two components of an aqueous solution of urea or guanidine chloride, for example, occurs at the level of some independent sites, with a discontinuous distribution at the macromolecule surface. It is supposed that the protein molecules can be found in two interconvertible energetic states, A and B, differing by the number of binding sites:

The protein site occupancy by the two types of molecules composing the solvent, that is the 'principal solvent' – the water, noted by '1' and salt molecules dissolved in the water and noted by '3', is explained on the basis of some thermodynamic presumptions and is treated as a competitive process between '1' and '3' with respect to the binding sites of the macromolecule (noted by '2').

The *selective interaction intensity* or the *selective interaction* of the protein sites with the molecules 3 is defined as a function Γ_{23} , which has a term corresponding to the molecular type ligands and a second term corresponding to the ionic ligands (the Donan component). The first term is the derivative of the 2–3 interaction energy relative to the molecules 3 activity in the solution while the second term depends on the protein sites electric charge and the molecules 3 molar concentration in the solution.

It is possible to demonstrate [6] that the *selective interaction* has a significance related to the *supplementary number of molecules 3 bonded at the membrane surface* in comparison with the high distance zones of the mixed solvent.

4. The Selective Interaction Model Applied to Fly Eye Phototransduction

In the case of invertebrate phototransduction investigated *via* the above model, the membrane ion channel gates (corresponding to the notation '2') are taken as the binding sites, which are able to interact with the Na^+ and Ca^{++} ions from the proximal external medium. The Ca^{++} ions (type 1 ligands) behave as ligands able to block the ion channels gates, while the Na^+ ions (type 3 ligands) acts as opening gate ligands. The two distinct membrane states, corresponding to dark and light states respectively, are defined by the two configuration states of the

principal visual pigment: rhodopsin, involving a membrane low energy state (A) and metharhodopsin, responsible for the membrane high energy state (B). The reversal from one to the other is an equilibrium of type (1). The enhancement of bounded Na^+ ion concentration, by Ca^{++} ion replacement, determines the opening of the light ion channel gates and membrane conductance increases.

So, from the thermodynamic point of view, at the absolute temperature T , the two membrane states are characterized by the free energies G_A and G_B (the Gibbs thermodynamic potentials), [4], taken also as chemical potentials μ) and:

$$\Delta G = \Delta G^0 \Leftrightarrow RT \ln K, \quad (2)$$

$$\Delta G^0 = G_A^0 \Leftrightarrow G_B^0, \quad (3)$$

$$\Delta G = G_A \Leftrightarrow G_B, \quad (4)$$

where K is the equilibrium constant for the reaction (1) and the index '0' marks the standardized conditions, such as reference temperatures and pH, usually physiological values. For an infinitely low percentage of ion channel gates in comparison to the number of the interacting ions, one can write the relations (5) and (6) for infinitely diluted solutions:

$$G_A = G_A^0 + RT\beta_{A3}, \quad (5)$$

$$G_B = G_B^0 + RT\beta_{B3}, \quad (6)$$

where the terms $RT\beta$ represent the free energies of the sites (corresponding to the states A and B respectively) which are interacting with the 'active' component of the ion system, i.e. the Na^+ ions which are capable of replacing the Ca^{++} ions. The Gibbs potentials G_A^0 and G_B^0 contain the energies of interaction with the ions of type '1', so that:

$$\Delta G = \Delta G_0 + RT\Delta\beta_{23}. \quad (7)$$

The evaluation of $\Delta\beta_{23}$ can be carried out utilizing a qualitative, intuitive approximation, based on a partition function Z and according to the Shellman [6] procedure addressing proteins dissolved in aqueous solutions of an active molecular species (capable of protein degradation). Taking into account first a single site, the function Z can be written as a sum of terms proportional to the relative probabilities that the site remain unoccupied, occupied by an ion of the type 1 or by a 3 type ion:

$$Z = 1 + \lambda_1 q_1 + \lambda_3 q_3. \quad (8)$$

That is:

$$\Delta\beta_{23} = \Leftrightarrow RT \ln Z, \quad (9)$$

where q_1 and q_3 are the partition functions for an ion 1 or 3 bonded to the membrane site, while λ_1 and λ_3 are the absolute activities of the two ion species.

Working with the activities expressed as functions of the molar fractions, A_1 and A_3 , so that $\lambda_1/\lambda_1^0 = A_1$ and $\lambda_3/\lambda_3^0 = A_3$ respectively (where the index ^{0} marks the activities in the standardized conditions) and taking as negligible the probability that the site remains non-occupied, we obtain:

$$\begin{aligned} \Leftrightarrow RT \ln Z &\cong \Leftrightarrow RT \ln(\lambda_1 q_1 + \lambda_3 q_3) \\ &= \Leftrightarrow RT \ln \lambda_1^0 q_1 \Leftrightarrow RT \ln(A_1 + \kappa A_3) \end{aligned} \quad (10)$$

where $\kappa = (q_3 \lambda_3^0 / q_1 \lambda_1^0)$ has the meaning of an equilibrium constant for the site interaction with the ions 1 and 3, that is a constant of selective association of ions 3 in comparison with ions 1. The term $\Leftrightarrow RT \ln \lambda_1^0 q_1$ signifies site interaction with the ions 1 when the ions 3 are absent, as one can see from the conditions $A_3 = 0$ and $A_1 = 1$. The term $\Leftrightarrow RT \ln(A_1 + \kappa A_3)$ is associated with free energy modifications induced by the active (competitive) presence of the ions 3.

The variation of the ions 3 interaction energy when passing from the state A to the state B is given by the sum over all the binding corresponding sites:

$$\Leftrightarrow \Delta \beta_{23} = \sum_i^B \ln(A_1 + \kappa_i A_3) \Leftrightarrow \sum_j^A \ln(A_1 + \kappa_j A_3). \quad (11)$$

The two sums differ not only in the number of sites but also in the difference between the κ_i and κ_j , the values of the rate between the partition functions q_1 and q_3 . The number of binding sites can be larger in the B state as a consequence of some new ion gated channel aggregation under the light action. The compensation of the term $\Leftrightarrow RT \ln \lambda_1^0 q_1$ by the two sums in (10), corresponds to the situation when bounded ions 3 are negligible so that the number of sites bonded to ions 1 is the same in both membrane states, A and B.

In the next section we further detail the phenomenon of substitution of calcium ions by sodium ions as a consequence of transformations induced by light action, the mathematical description being based on the selective interaction phenomenon taken as a modification of the rate between the Ca^{++} and Na^+ concentrations at the membrane external face (bounded ion concentration) relative to those characterizing the zones situated at higher distances from the membrane external surface (free ion concentration).

Applying the protein interaction model, we use the definition of *selective interaction intensity* or *selective interaction* of the membrane sites with the ions 3 to be the function Γ_{23} [6]:

$$\Gamma_{23} = \Leftrightarrow (\partial \beta_{23} / \partial \ln A_3)_{\text{T.P.}, m_3} \Leftrightarrow D(|\mathbf{Z}|, m_3), \quad (12)$$

where the first term corresponds to the molecular type ligands and the second is the Donnan component of the selective interaction in the case when the ligands are ions.

$RT\beta_{23}$ is the modification of the excess free energy correlated with the selective interaction of the channel gates 2, Z is the membrane site electric charge and m_3 is the ions 3 molar concentration at high distance from the membrane; T and P are the absolute temperature and the pressure constant values, while m_3 is also constant in the extracellular proximal medium.

As already mentioned above *selective interaction* has the significance of the *supplementary number of ions 3 bonded at the membrane surface* in comparison with the long distance zones of the mixture of ions 1 and 3.

It is necessary to take into account that the chemical activities A_1 and A_3 together with the molar fractions χ_1 and χ_3 , satisfy the Gibbs–Duhem equation for T and P , and constant [2] in the case when the two ion type concentrations are much higher than the binding site concentration, so that from:

$$\chi_1 d \ln A_1 + \chi_2 d \ln A_2 + \chi_3 d \ln A_3 = 0, \quad (13)$$

results:

$$\Leftrightarrow \chi_1 / \chi_3 = d \ln A_1 / d \ln A_3 = (\partial A_1 / A_1) / \partial \ln A_3 \quad (14)$$

and

$$\Gamma_{23} = \sum_j [(\Leftrightarrow \chi_3 A_1 / \chi_1) + \kappa_j A_3] / (A_1 + \kappa_j A_3) \Leftrightarrow D(|Z|, m_3), \quad (15)$$

the sum being carried out for the sites in the membrane states A or B.

If the chemical activities are given as a function of the molar fractions using the activity coefficients, f_i :

$$A_i = f_i \chi_i, \quad i = 1, 3 \quad (16)$$

then:

$$\Gamma_{23} = \sum_j (\Leftrightarrow f_1 + \kappa_j f_3) \chi_3 / (f_1 \chi_1 + \kappa_j f_3 \chi_3) \Leftrightarrow D(|Z|, m_3) \quad (17)$$

or:

$$\Gamma_{23} = \sum_j (\kappa'_j \Leftrightarrow 1) \chi_3 / [1 + (\kappa'_j \Leftrightarrow 1) \chi_3] \Leftrightarrow D(|Z|, m_3), \quad (18)$$

where $\chi_1 + \chi_3 = 1$ and $k'_j = f_3 k_j / f_1$ and Γ_{23} is taken as a ‘practical’ equilibrium constant.

This constant indicates how many times larger is the rate for the average number of ions 3 moles bonded to a site, n_3 , and the number of ions 1 moles, n_1 , in

STATE A

Figure 1. Schematic representation of fly visual cell membrane in the states A and B. The Ca^{++} ions are represented by the symbol $\circ$ while the symbol $\bullet$ represents the Na^+ ions.

comparison with the rate for m_3 (the ions 3 molar concentration) and m_1 (the ions 1 molar concentration) defined at higher distances from the membrane surface:

$$k'_j = r_{b3}/r_3, \quad (19)$$

where: $r_{b3} = n_3/n_1$ and $r_3 = m_3/m_1$. So, k'_j makes the comparison between the ionic mixture compositions at the membrane surface and in the proximal medium.

5. Discussion and Conclusion

The relation (19) offers the possibility of three distinct situations:

- (a) $k'_j < 1$, membrane negative *selective interaction* with the ions 3 in comparison with ions 1;
- (b) $k'_j = 1$, *non-selective membrane interaction* relative to the two ion types;
- (c) $k'_j > 1$, membrane positive *selective interaction* with the ions 3 in comparison with ions 1.

In the present case, the B membrane state, induced by the bonded ions 3 concentration increasing as a consequence of light action, can be assigned to a *positive selective interaction* with the ions 3, so that $k'_j > 1$ and $\Gamma_{B3} > 0$ (the Donan weight is relatively small).

The A membrane state can be, theoretically, any one of the three cases, with the condition: $\Gamma_{A3} < \Gamma_{B3}$.

If the A membrane state is assigned to case (a), then in darkness, the membrane surface is characterized by a relative deficit of ions 3 in comparison to the long distance zones.

In Figure 1 is shown a schematic representation of the case (a).

If the A membrane state is assigned to case (b), then the rate for the two type ion concentrations in darkness is the same at short as well as at long distance from the membrane surface.

If the A membrane state is assigned to case (c), then a threshold phenomenon seems to occur, i.e. only when the ion 3 concentration at the membrane surface exceeds a certain value, yielded by light action, do the ion channel gates open.

Experimental investigations are expected to provide the correct description of ionic statistical behavior at the microvillar membrane surface, not excluding the possibility that the three cases co-exist.

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