ELSEVIER

Biophysical Chemistry 61 (1996) 29–35

Biophysical Chemistry

Theory of electric characteristics of the lipid/PVC/DOPP membrane and PVC/DOPP membrane in response to taste stimuli

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Received 12 January 1996; revised 22 February 1996; accepted 4 March 1996

Abstract

Electric characteristics of two kinds of membranes in response to NaCl and quinine were theoretically studied; one membrane composed of polyvinyl chloride (PVC) and dioctylphenylphosphonate (DOPP), and the other a lipid/PVC/DOPP membrane containing PVC, DOPP and a negatively charged lipid. We develop a theory by taking into account both the surface electric potential and the diffusion potential within the membrane and succeed in interpreting the observed data. On increasing the NaCl concentration, the lipid/PVC/DOPP membrane changes from weakly charged state to fully charged state by dissociation of H^+ from the lipids. The hydrophobic interaction between quinine and the PVC/DOPP membrane was strong enough to overcome the electric repulsion.

Keywords: Lipid membrane; Polyvinyl chloride; Plasticizer; Electric potential; Hydrophobic interaction; Chemical sensor

1. Introduction

In the accompanying paper [1], the response electric characteristics of two kinds of membranes are experimentally studied as a taste sensor [2–4]; one membrane composed of polyvinyl chloride (PVC) and dioctylphenylphosphonate (DOPP) as a plasticizer, and the other a membrane containing PVC, DOPP and a negatively charged lipid. These two membranes show an unusual behavior in response to NaCl and quinine. In usual polymer membranes such as the collodion membrane [5] and lipid-adsorbed membrane filter [6], the electric potential tends to be flat at high NaCl concentrations. This is known as a simple screening effect [7,8], and is considered mainly to originate from the surface electric potential [9], because the membrane resistance is as high as several $M\Omega\ cm^2$. However, the lipid/PVC/DOPP membrane also shows a membrane resistance of several $M\Omega$, and yet the electric potential is not flat or saturated, but the rate of change of electric potential increases at high NaCl concentrations [1,2].

Thus, the following questions arise: what is the origin of the difference of electric characteristics between lipid/PVC/DOPP membranes and usual polymer membranes, and why does the apparently noncharged PVC/DOPP membrane respond to cations and show cationic permeability [10–12]? Clarification of the electric characteristics of these

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PII S0301-4622(96)00026-9

membranes may contribute to developing an architecture for chemical or taste sensors by mimicking a part of biological membranes.

Here we develop a new theory by taking into account both electrostatic and hydrophobic interactions, and succeed to explain quantitatively the experimental data. The characteristic upward response of the lipid/PVC/DOPP membrane to NaCl is not caused by the usual screening effect but the change in its surface charge density owing to dissociation of protons from the membrane. The hydrophobic interaction between quinine and the PVC/DOPP membrane is so strong that the electric repulsion is overcome.

2. Theory

A schematic of the charged membrane system is shown in Fig. 1. The charged membrane separates two KCl solutions I and II. Aqueous solution II refers to the external solution which contains a taste substance. The membrane potential usually consists of the surface electric potential formed in the aqueous phase touching the membrane and the diffusion potential within the membrane, as shown in Fig. 1. In this theoretical model, therefore, the membrane potential is obtained from a sum of the surface potential and the diffusion potential, which are calculated individually.

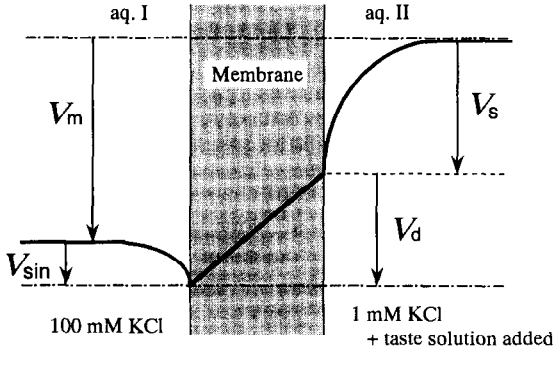

Fig. 1. The membrane electric potential in a charged membrane system. aq. I and II are internal and external solutions, respectively. A taste substance was added to the external solution, from which the membrane potential was measured as the origin.

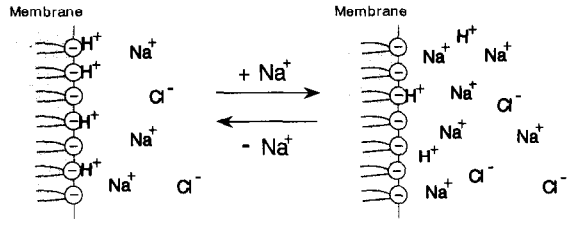

Fig. 2. The situation by which the surface electric charge density of the membrane is changed by H^+ dissociation from lipid molecules with the ion concentration in the bulk solution.

First, we describe the change in the surface potential with the ion concentration in the bulk solution. For this purpose, the change in the surface charge density must also be taken into account because of the hydrophilic group of lipid of the membrane contacting with the aqueous phase. It implies that the theory treats the situation where the surface electric potential is changed with H^+ dissociation from lipid molecules, which causes the change in electric charge density, as performed in some colloidal systems [8]. This situation is shown in Fig. 2.

The change in Gibbs free energy per lipid molecule with the above dissociation process in the lipid membrane is given from standard thermodynamics by Refs. [7,13]

$$dG = k_B T \ln\left[\frac{K}{[H^+]}\frac{\theta}{1-\theta}\right]d\theta \qquad (1)$$

where θ is the degree of H^+ binding to a lipid molecule at hydrophilic group, K is the dissociation constant, $[H^+]$ is the proton concentration in the bulk solution, k_B is Boltzmann's constant and T is the absolute temperature. We obtain an expression for the free energy in the charged membrane system as

$$G = \int_0^{\theta} k_B T \ln\left[\frac{K}{[H^+]}\frac{\theta}{1-\theta}\right]d\theta + A\int_0^{\sigma} V_s\, d\sigma \qquad (2)$$

where σ is the surface charge density, A is the occupied molecular surface area and V_s is the surface electric potential of the membrane. For simplicity, we assumed the membrane surface is regarded as a plane surface with the uniform charge density σ.

The charge density σ at the membrane surface is determined using the Gouy–Chapman theory of the electrical double layer; i.e. the ion distribution near

the membrane surface and the surface charge density are calculated by solving the Poisson–Boltzmann equation [7,8,13]. For 1:1 electrolyte the Gouy–Chapman theory leads to Eqs. (3) and (4).

$$\sigma = \kappa' \sinh\left(\frac{eV_s}{2k_BT}\right) \tag{3}$$

$$\kappa' = \frac{\epsilon}{2\pi}\frac{k_BT}{e}\kappa, \qquad \kappa = \sqrt{\frac{8\pi ce^2}{\epsilon k_BT}} \tag{4}$$

Here ϵ is the dielectric constant, e the elementary charge and c denotes the ion concentration in the bulk solution. A parameter, κ, is a characteristic value expressing the degree of spread of diffuse electrical double layer, and hence $1/\kappa$ can be regarded as the thickness of the diffuse double layer.

2.1. Case of NaCl

In general, NaCl affects the electrical double layer, and the surface electric potential can be changed. Using the degree of H^+ binding θ, the surface charge density σ can also be expressed by Eq. (5)

$$\sigma = -\frac{e}{A}(1-\theta) \tag{5}$$

If we eliminate σ from Eqs. (3) and (5), the following Eq. (6) is obtained.

$$\kappa' \sinh\left(\frac{eV_s}{2k_BT}\right) = -\frac{e}{A}(1-\theta) \tag{6}$$

By minimizing Eq. (2) with respect to θ by taking account of Eq. (5), we get Eq. (7)

$$\frac{\theta}{1-\theta} = \frac{[H^+]}{K}\exp\left(-\frac{eV_s}{k_BT}\right) \tag{7}$$

In Eqs. (6) and (7), two variables θ and V_s are unknown. Therefore, the surface potential V_s of the membrane can be calculated as a function of the ion concentration c in a similar way to a previous paper on polymer membranes composed of two lipid species [14].

2.2. Case of quinine

Since quinine is a hydrophobic molecule, it may be natural to consider that quinine ions are bound to the hydrophobic part of a membrane. Therefore, the surface charge density σ of the membrane is changed by this binding effect; proton binding to hydrophilic site and the quinine binding should be separately counted, whereas these two effects are not independent. The expression for σ is then given by Eq. (8)

$$\sigma = -\frac{e}{A}(1-\theta) + \frac{e}{A}\theta_q \tag{8}$$

where θ_q is the degree of binding of quinine ions. The degree of binding of quinine ions θ_q is dependent on the quinine concentration nearby the membrane surface and the electric charge condition of the membrane. Therefore, the expression for θ_q is given by Eq. (9)

$$\theta_q = a(1-\theta)^2 c_q \exp\left(-\frac{eV_s}{k_BT}\right) \tag{9}$$

where c_q is the bulk quinine concentration and a is a numerical parameter. The factor $(1-\theta)^2$ assumes that more quinine ions are bound to the membrane because of non-occupied sites of the surface at the first step of binding.

The surface charge density σ can be eliminated from Eqs. (3) and (8), and the equation similar to Eq. (6) can be obtained. In the present case, too, ions as H^+ (from H_2O) and K^+ (from 1 mM KCl) are contained in the aqueous medium; therefore, Eq. (7) holds.

Next, let us consider the diffusion potential V_d within the membrane. In charged systems shown in Fig. 1, K^+ ions, Cl^- ions and T^- ions usually diffuse into the membrane, where T^+ ions denote counterions caused by electrolyte of taste substances in the external solution. As a result, the diffusion potential is generated by the difference in the mobility of ions between cations and anions. The diffusion potential V_d within the membrane is calculated from the following Goldman–Katz Eq. [15,16].

$$V_d = \frac{k_BT}{e}\ln\left[\frac{\mu_K c_K^{ex} + \mu_{Cl} c_{Cl}^{in} + \mu_T c_T^{ex}}{\mu_K c_K^{in} + \mu_{Cl} c_{Cl}^{ex}}\right] \tag{10}$$

where μ_i denotes the product of the mobility of ion i within the membrane and the partition ratio of ion i to the two phases, which are the membrane and the external solution, and c_i the i ion concentration nearby the membrane surface, whose subscripts "ex"

and "in" represent the membrane surface on the side of external solution and that on the side of another solution across the membrane, respectively.

The membrane potential defined in Fig. 1 is explained by Eq. (11)

$$V_m = V_s + V_d - V_{sin} \quad (11)$$

where V_{sin} is the surface electric potential formed in the aqueous phase of another side across the membrane.

3. Results and discussion

The lipid/PVC/DOPP, which is negatively charged by H^+ dissociation from the lipid molecules, is sensitive to cations [1], and the PVC/DOPP membrane also responds to cations, although pure PVC and DOPP are both uncharged. PVC and DOPP are often used for ion-selective electrodes [17,18], and the membrane composed of PVC (and DOPP) shows cationic permeability [10–12]. Commercially available DOPP contains an impurity, e.g. negatively charged monooctylphenylphosphonate. PVC may be charged by sulfonate groups in PVC, which is generated by a persulfate radical initiator [17]. Hence we assume that the PVC/DOPP membrane is negatively charged by H^+ dissociation from monooctylphenylphosphonate, and apply the above theoretical model to the calculation for the PVC/DOPP membrane.

Theoretical results are compared with observed response potentials to NaCl and quinine in Fig. 3, where the dashed and solid curves represent the results for the lipid/PVC/DOPP membrane and the PVC/DOPP membrane, respectively. The theory and the observed data on response potentials of the membranes agree quantitatively for both NaCl and quinine. The theoretical curve of the response potential is taken relative to a standard potential calculated at pH 5.8, $T = 300$ K, $c = 1$ mM for 1 mM KCl solution without taste substances. The theoretical values of the standard potential of the lipid/PVC/DOPP and PVC/DOPP membrane are about -55 and -115 mV, respectively, while the observed absolute values were about -50 and -110 mV. The parameter values were chosen so as to explain the experimental results in the best fit as a whole within their reasonable ranges: $K = 10^{-4}$ M, $A = 120$ Å^2, $\mu_K = \mu_{Cl} = \mu_I = 0$ and $a = 150$ in the case of the lipid/PVC/DOPP membrane, $K = 10^{-3.5}$ M, $A = 1000$ Å^2, $\mu_{Cl}/\mu_K = 0.1$, $\mu_{Na}/\mu_K = 0.73$, $\mu_q/\mu_K = 8000$ and $a = 8000$ in the case of the PVC/DOPP membrane. The occupied molecular surface area A was estimated from the volume of the membrane and the quantity of used lipid or monooctylphenylphosphonate. We assumed that A was constant even when taste substances were adsorbed in the membrane as a first approximation.

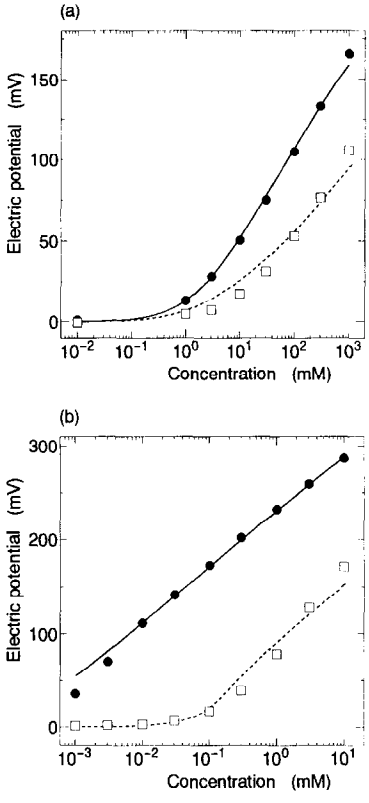

Fig. 3. Response potential of the lipid/PVC/DOPP membrane (□) and the PVC/DOPP membrane (●) to taste substances: (a) NaCl and (b) quinine, data from Ref. [1]. The dashed and solid lines represent the theoretical values of the lipid/PVC/DOPP membrane and the PVC/DOPP membrane, respectively.

Theoretical curves of the surface potential and the diffusion potential of both membranes to NaCl and quinine are shown in Fig. 4. In the responses of the lipid/PVC/DOPP membrane to NaCl and quinine, the surface potential contributes to most of the response potential. The diffusion potential is hardly

generated, because lipids packed densely in the membrane interfere with ion permeation. It implies that the lipid/PVC/DOPP membrane has a property that ions can hardly permeate through the membrane, whereas the inside of membrane is electrically connected because of hydrophilic part of lipids. However, the PVC/DOPP membrane may generate both the surface potential and the diffusion potential within the membrane. For NaCl, the response potential is caused by the change in the surface potential at low concentrations, whereas the diffusion potential plays an important role at high concentrations. For quinine, the main contribution to the response potential of this membrane changes from the diffusion potential to the surface potential with increasing quinine concentration due to binding with the membrane (see also Fig. 7).

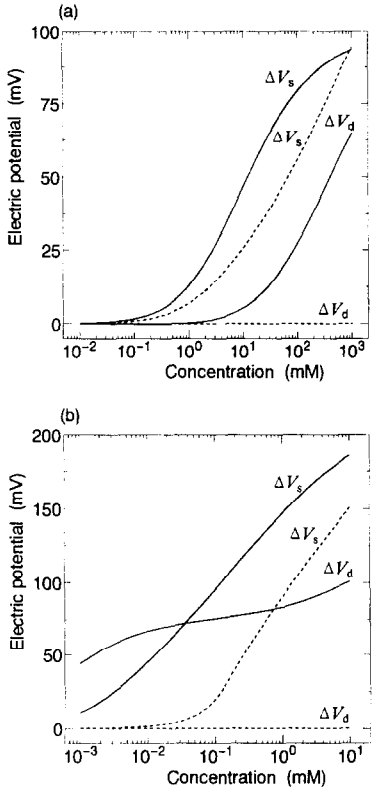

Fig. 4. Theoretical curves of the changes in the surface and diffusion potentials of the membrane, ΔV_s and ΔV_a respectively, to (a) NaCl and (b) quinine. The dashed and solid lines represent the theoretical results of lipid/PVC/DOPP membrane and PVC/DOPP membrane, respectively.

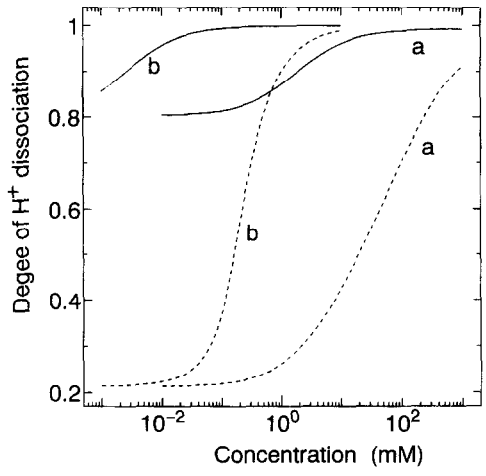

Fig. 5. The degrees of H^+ binding to the membrane for taste substances; a, NaCl and b, quinine. The dashed and solid lines represent the theoretical results of lipid/PVC/DOPP membrane and PVC/DOPP membrane, respectively.

In usual cases of fully charged membranes, Na^+ ions scarcely change the net electric charge density of a negatively charged membrane but affect the surface electric potential (i.e. the electric screening effect), and the electric potential tends to be flat at high NaCl concentrations [5,6]. Let us now consider the response characteristics for NaCl in Fig. 3(a), where electric potential changes of the lipid/PVC/DOPP and the PVC/DOPP membrane are not saturated at higher NaCl concentrations.

Fig. 5 shows the calculated results of degrees of H^+ dissociation from a lipid in the lipid/PVC/DOPP membrane and from monooctylphenylphosphonate in the PVC/DOPP membrane. In the lipid/PVC/DOPP membrane, H^+ ions are scarcely dissociated from the lipid at low NaCl concentrations, as found from low degree of H^+ dissociation of 0.21 in Fig. 5. This is because the occupied molecular surface area of used lipid is small owing to the membrane preparation; lipid is packed densely in the membrane. This dense packing inhibits the charging process (i.e. dissociation of H^+ from hydrophilic group of lipid), which causes a strong electric repulsion between charged molecules. The dissociation of H^+ ions is accelerated by the addition of NaCl. This implies the increase in the magnitude of surface electric charge density, as seen from in Fig. 6, where the calculated surface charge

density is shown as a function of NaCl or quinine concentration; i.e. the membrane becomes charged more negatively. Increasing NaCl concentration weakens the electric repulsion between lipids, and hence H^+ becomes dissociated.

Therefore, it is reasonable that the lipid/PVC/DOPP membrane is not electrically charged so much at lower ionic strength, and becomes more negatively charged by accelerating the dissociation of H^+ ions with increasing NaCl concentration. As a result, the rate of change in electric potential increases with NaCl, since the membrane becomes a more negatively charged membrane to increase the sensitivity to cations as Na^+.

The real occupied molecular surface area of monoester-type impurity in the PVC/DOPP membrane is large, because the percentage impurity was as low as 1% (data not shown). In the theoretical result of the PVC/DOPP membrane, H^+ ions are almost dissociated even at low NaCl concentrations, as seen from Fig. 5. Therefore, the PVC/DOPP membrane can have some negative charge, and responds sensitively to cations.

For quinine, the membrane potentials of the lipid/PVC/DOPP and PVC/DOPP membranes change more largely than that for NaCl, as seen from Fig. 3. Quinine hydrochloride is a hydrophobic molecule, however, it contains a positively charged

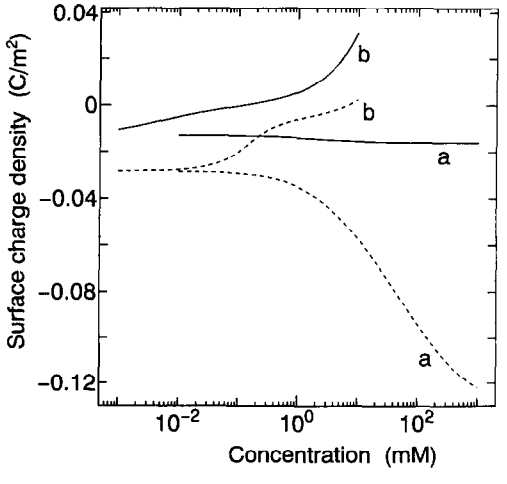

Fig. 6. The surface charge densities of the membrane for taste substances; a, NaCl and b, quinine. The dashed and solid lines represent the theoretical results of lipid/PVC/DOPP membrane and PVC/DOPP membrane, respectively.

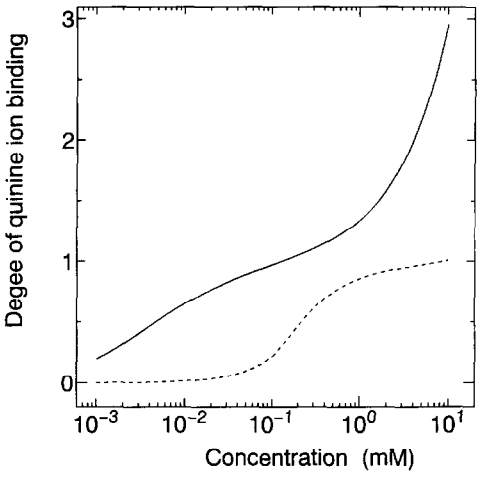

Fig. 7. The degree of quinine ion binding to the membrane as a function of quinine concentration. The dashed and solid lines represent the theoretical results of lipid/PVC/DOPP membrane and PVC/DOPP membrane, respectively.

hydrophilic part too. Hence quinine ions are bound to the hydrophobic part of negatively charged membranes, and lead to large changes in the membrane potential. The degree of binding of a taste substance with the membrane may be dependent on the following two factors; the balance between hydrophilicity and hydrophobicity of the taste substance, and the electrostatic and hydrophobic interaction between the membrane and the taste substance.

Fig. 7 shows the calculated results of degrees of binding of quinine ions to the lipid/PVC/DOPP and PVC/DOPP membranes. Quinine ions are bound to the PVC/DOPP membrane more strongly than to the lipid/PVC/DOPP membrane. The surface charge density of the PVC/DOPP membrane is changed from a negative value to a positive value at high quinine concentrations by the quinine binding effect. These results indicate that the PVC/DOPP membrane is a strong hydrophobic membrane with a slight amount of electric charge. The interaction between quinine ions and the hydrophobic part of the PVC/DOPP membrane may be so strong as to overcome the electric repulsion. In the lipid/PVC/DOPP membrane, the dissociation of H^+ ions from lipids in the membrane is accelerated with increasing quinine concentration, as seen from Fig. 5; the degree of binding of quinine ions increases at the same time. The hydrophobic interac-

tion between quinine and the lipid/PVC/DOPP membrane is generated to some extent, although it is not as strong as that in the case of the PVC/DOPP membrane.

Here, the molecular surface area A was assumed as constant even if quinine was bound with the membrane. It seems that A can be changed by this binding process. At present, however, the quantitative estimate is not easy. Study of transient response of membrane potential with abrupt increase in quinine concentration may be effective for investigation of change of A.

In the present work, electric characteristics of the lipid/PVC/DOPP membrane and PVC/DOPP membrane were studied theoretically. As a result, it was suggested that the surface electric potential is dominant in the membrane potential of the lipid/PVC/DOPP membrane, whereas both the surface and diffusion potentials cannot be neglected in the PVC/DOPP membrane. Furthermore, it was shown that the lipid/PVC/DOPP membrane changes from a weakly charged state to a fully charged state by dissociation of H^+ from lipids with increasing NaCl concentration. The PVC/DOPP membrane was shown to be a weakly charged membrane with the strongly hydrophobic property.

Acknowledgements

The authors would like to give sincere thanks to Mr. T. Nojiri and Mr. K. Kina in Dojindo Laboratory Corp. and Dr. M. Watanabe in Engineering Branch, Center of Advanced Instrumental Analysis in Kyushu University for chemical analysis of DOPP. They also thank to Mr. H. Akiyama and Miss K. Chishaki in Kyushu University and Mr. K. Sato and Mr. H. Ikezaki in Anritsu Corporation for discussions throughout the present work.

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