A new approach to the rest potential of biological membranes

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Abstract

In a series of recent papers, Bonciocat et al., have shown that the faradaic current density of an electrode redox reactions occurring with combined limitations, of charge transfer and nonstationary linear, semi-infinite diffusion, is the solution of an integral equation of Volterra type. This integral equation has been transformed to describe the transport of ions through the interface between two immiscible electrolytic solutions. According to Goldman, Hodkin, Katz theory, the rest potential of a biological membrane is determined by the maintenance of different concentrations of the ions Na^+, K^+ and Cl^-, in the two aqueous solutions separated by the membrane. Using the integral equations (of Volterra type) for the ionic current densities i_{Na}, i_K, i_{Cl}, and applying the open circuit condition (i.e., $i_{Na} + i_K + i_{Cl} = 0$), the potential differences at the junctions: aqueous solution (I)/membrane, respective membrane/aqueous solution (II), have been obtained. To get the diffusion potential across the membrane, the Planck's theory has been used. The sum of these three contributions gives the expression of the rest potential (and a comparison with the Goldman–Hodkin–Katz formula is made, showing in what conditions they become identical formulae).
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1. Introduction

In a series of papers, Bonciocat et al., have shown that the faradaic current density of an electrode redox reaction $O + ne \leftrightarrow R$, which occurs with combined charge transfer and nonstationary, linear, semi-infinite diffusion limitations, is the solution of the following integral equation of Volterra type [1–6]:

$$i_F(t) = -\frac{i^0 N(t)}{\pi^{1/2}} \int_0^t \frac{i_F(u)}{(t-u)^{1/2}} du + \varphi(t) \qquad (1)$$

where

$$N(t) = \frac{\exp[-\beta n f \eta(t)]}{nF\sqrt{D_O} c_O} + \frac{\exp[(1-\beta) n f \eta(t)]}{nF\sqrt{D_R} c_R} \qquad (1')$$

and

$$\varphi(t) = i^0\{\exp[-\beta n f \eta(t)] - \exp[(1-\beta) n f \eta(t)]\}; \ f = \frac{F}{RT} \qquad (1'')$$

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$\eta(t)$ is the applied overtension at the moment of time t, u is a time before t, and the other quantities have the usual meanings: $i^0 = i^{00} c_O^{1-\beta} c_R^{\beta}$ the exchange current density of the electrode redox reaction and β its symmetry factor, D_O, D_R (and c_O, c_R) the diffusion coefficients (and the concentrations) of the electrochemical active species O and R. As for i^{00}, it represents the standard exchange current density of the electrode reaction.

By solving the above integral equation, it was possible to ground not only the nonstationary dc, and ac, methods already used in the experimental electrochemistry [1,7], but also new methods of direct and cyclic voltammetry, chromoamperometry and impedance spectroscopy [8–21].

The integral Eq. (1) may be easily transformed to describe the transport of ions through the interface between two immiscible electrolytic solution (ITIES). Indeed, consider a cation passing from an aqueous solution (I) to a nonaqueous solution (II). This passage is equivalent to an anodic electrode redox reaction $R \rightarrow O + ne$, the cation in solution (II) being the oxidized species O, and in solution (I) the reduced species R. This equivalence comes from the fact that both processes transport positive charges from left to right (i.e.,

solution (I) → solution (II), respective Me → solution). Of course, in the case of an anion, the passage is equivalent to a cathodic electrode redox reaction O + *n*e → R, the anion in solution (I) being the oxidized species, and in solution (II) the reduced species.

Consequently, to obtain the integral equation whose solution i_C expresses proportionally (as a current density) the flux of transport of a cation C^+ through the interface I/II, suffice to make in the integral Eq. (1) the following changes:

$$\eta(t) \to \eta_C(t)$$
$$i_F(t), i_F(u) \to i_C(t), i_C(u) \tag{2}$$

$$i^0 = i^{00} c_O^{1-\beta} c_R^{\beta} \to i_C^0 = i_C^{00} (c_C^{II})^{1-\beta_C} (c_C^{I})^{\beta_C}$$
$$D_O, D_R \to D_C^{II}, D_C^{I} \tag{2'}$$
$$n \to 1$$

i_C^0, i_C^{00} and β_C represents the kinetic parameters of the *hypothetical electrode reaction* by which one models the transport of C^+ through the interface I/II. β_C represents the symmetry factor of the energetic barrier determined by the electric double layer of the interface I/II, and the exchange current density i_C^0 is expressed in function of the standard exchange current density i_C^{00} and the concentrations of the cation C^+ in the two planes that delimitate the electric double layer. Concerning the expression of $\eta_C(t)$, it will be given latter at a convenient time.

In the case of an anion A^-, the necessary changes are:

$$\eta(t) \to \eta_A(t)$$
$$i_F(t), i_F(u) \to i_A(t), i_A(u) \tag{3}$$

$$i^0 = i^{00} c_O^{1-\beta} c_R^{\beta} \to i_A^0 = i_A^{00} (c_A^{I})^{1-\beta_A} (c_A^{II})^{\beta_A}$$
$$D_O, D_R \to D_A^{I}, D_A^{II} \tag{3'}$$
$$n \to 1$$

and i_A^0, i_A^{00}, β_A, c_A^{I}, c_A^{II} have similar meanings.

According to Goldman, Hodkin and Katz [22,23], the rest potential of a biological membrane is determined by the different concentrations of the ions Na^+, K^+ and Cl^-, in the two aqueous solution separated by the membrane. These concentrations are maintained at practically constant values by a mechanism, yet unknown, which play the role of a "Biological Potentiostat".

Thus, the electrochemical chain needed to obtain the rest potential of a biological membrane is illustrated in Fig. 1.

Using the integral equations (of Volterra type) having as solution the current densities i_{Na}, i_K, i_{Cl}, and applying the open circuit condition (i.e., $i_{Na} + i_K + i_{Cl} = 0$), the potential differences g_{m1}, and g_{m2} have been obtained. To get the diffusion potential across the membrane, the Planck's theory has been used, because it supposes a "constrained diffusion" through the liquid junction, by which the ionic concentrations in each section of the junction layer remain constant in time [24–28]. The sum of these three contributions gives the expression of the rest potential, and
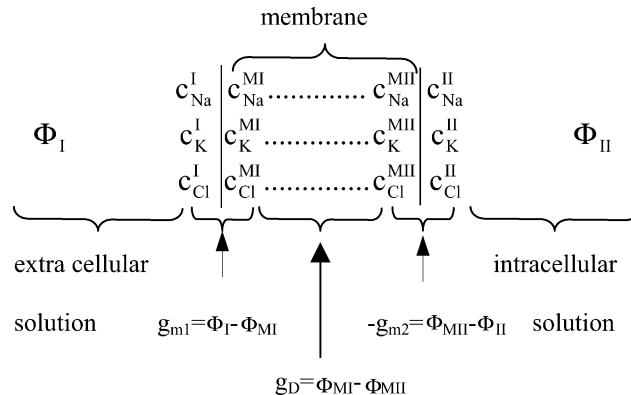

Fig. 1. The electrochemical chain showing the components of the rest potential of a biological membrane $g_m = \Phi_I - \Phi_{II} = g_{m1} - g_{m2} + g_D$.

a comparison with the Goldman–Hodkin–Katz formula is made, showing in what conditions they become identical formulae.

2. Results and discussions

2.1. The expressions of the electric tensions g_{m1} and g_{m2}

Let's consider the junction I/MI, where by MI we have denoted the beginning of the membrane (i.e., the part which is in contact with the extra cellular solution (I)).

To obtain the integral equations corresponding to the cations Na^+ and K^+, we shall make the changes (2) and (2′) in the integral Eq. (1), but putting MI instead of II in their expressions. It thus results:

$$i_{Na}^{I}(t) = -Q_{Na}^{I}(t) \int_0^t \frac{i_{Na}^{I}(u)}{(t-u)^{1/2}} du + \varphi_{Na}^{I}(t) \tag{4}$$

$$i_{K}^{I}(t) = -Q_{K}^{I}(t) \int_0^t \frac{i_{K}^{I}(u)}{(t-u)^{1/2}} du + \varphi_{K}^{I}(t) \tag{4'}$$

Similarly, for the anion Cl^-, using the changes (3) and (3′) one gets:

$$i_{Cl}^{I}(t) = -Q_{Cl}^{I}(t) \int_0^t \frac{i_{Cl}^{I}(u)}{(t-u)^{1/2}} du + \varphi_{Cl}^{I}(t) \tag{4''}$$

where, for sake of simplicity, we have introduced the quantity $Q^I(t) = i^0 N^I(t)/\pi^{1/2}$. The superior index "I" indicates the *first junction*, i.e., I/MI.

In open circuit conditions:

$$i_{Na}^{I}(t) + i_{K}^{I}(t) + i_{Cl}^{I}(t) = 0 \tag{5}$$

and therefore,

$$\int_0^t \frac{Q_{Na}^I(u)i_{Na}^I(u) + Q_K^I(u)i_K^I(u) + Q_{Cl}^I(u)i_{Cl}^I(u)}{(t-u)^{1/2}} du$$

$$= \varphi_{Na}^I(t) + \varphi_K^I(t) + \varphi_{Cl}^I(t) \qquad (6)$$

An Abel integral equation has the form:

$$\int_0^t \frac{\Psi(u)}{(t-u)^\alpha} du = C(t); \ \alpha \in (0,1) \qquad (7)$$

and for $\alpha = 1/2$, its solution is [29]:

$$\Psi(t) = \frac{1}{\pi}\left[\frac{C(0)}{\sqrt{t}} + \int_0^t \frac{C'(u)}{(t-u)^{1/2}} du\right] \qquad (7')$$

Thus, Eq. (6) is an Abel integral equation and has the solution:

$$Q_{Na}^I(u)i_{Na}^I(u) + Q_K^I(u)i_K^I(u) + Q_{Cl}^I(u)i_{Cl}^I(u)$$

$$= \frac{1}{\pi}\left[\frac{\varphi_{Na}^I(0) + \varphi_K^I(0) + \varphi_{Cl}^I(0)}{\sqrt{t}}\right.$$

$$\left. + \int_0^t \frac{(\varphi_{Na}^I(t))' + (\varphi_K^I(u))' + (\varphi_{Cl}^I(u))'}{(t-u)^{1/2}} du\right] \qquad (8)$$

we shall accept that the human organism, by using a mechanism, yet nonelucidated, maintains the rest potential of the biological membrane at a constant value, i.e.,

$$g_m^I(t) \approx \text{const} = g_m^I(0) \qquad (9)$$

(the index "m", indicates that the rest potential is a *mixed* potential (because of the three ionic currents)). This hypothesis has an important consequence concerning the functions $\varphi_{Na}^I(t)$, $\varphi_K^I(t)$ and $\varphi_{Cl}^I(t)$. Indeed in their expressions enter the overtensions $\eta_{Na}^I(t)$, $\eta_K^I(t)$, $\eta_{Cl}^I(t)$, which have the usual meaning, i.e., the differences between the mixed potential $g_m^I(t)$ and the Nernst equilibrium tensions, corresponding to the three ions [28]. Therefore, these overtensions are constant, i.e.,

$$\eta_{Na}^I(t) = g_m^I(t) - g_{rev,Na}^I = g_m^I(0) - g_{rev,Na}^I = \eta_{Na}^I(0)$$

$$\eta_K^I(t) = g_m^I(0) - g_{rev,K}^I = \eta_K^I(0) \qquad (10)$$

$$\eta_{Cl}^I(t) = g_m^I(0) - g_{rev,Cl}^I = \eta_{Cl}^I(0)$$

and consequently $\varphi_{Na}^I(t)$, $\varphi_K^I(t)$, $\varphi_{Cl}^I(t)$, are constant too. Of course, we are interested in the case of small overtensions, which represent the usual situations in biological systems. Then (see Eq. (1'')):

$$\varphi_{Na}^I(t) = \varphi_{Na}^I(0) = -i_{Na}^{0I} f\eta_{Na}^I(0)$$

$$\varphi_K^I(t) = \varphi_K^I(0) = -i_K^{0I} f\eta_K^I(0) \qquad (11)$$

$$\varphi_{Cl}^I(t) = \varphi_{Cl}^I(0) = -i_{Cl}^{0I} f\eta_{Cl}^I(0)$$

where the minus sign comes from the convention used, i.e., negative (positive) overtensions, determine positive (negative) currents.

Coming back to Eq. (8), the integral term cancels and thus:

$$Q_{Na}^I(u)i_{Na}^I(u) + Q_K^I(u)i_K^I(u) + Q_{Cl}^I(u)i_{Cl}^I(u)$$

$$= \frac{f}{\pi}\frac{\varphi_{Na}^I(0) + \varphi_K^I(0) + \varphi_{Cl}^I(0)}{\sqrt{t}} \qquad (12)$$

Eq. (12) shows that:

$$Q_{Na}^t(t)i_{Na}^I(t) = -\frac{f}{\pi}\frac{i_{Na}^{0I}\eta_{Na}^I(0)}{\sqrt{t}}$$

$$Q_K^t(t)i_K^I(t) = -\frac{f}{\pi}\frac{i_K^{0I}\eta_K^I(0)}{\sqrt{t}} \qquad (13)$$

$$Q_{Cl}^t(t)i_{Cl}^I(t) = -\frac{f}{\pi}\frac{i_{Cl}^{0I}\eta_{Cl}^I(0)}{\sqrt{t}}$$

and further

$$\frac{i_{Na}^I(t)}{[i_{Na}^{0I}/Q_{Na}^I(t)]\eta_{Na}^I(0)}$$

$$= \frac{i_K^I(t)}{[i_K^{0I}/Q_K^I(t)]\eta_K^I(0)} = \frac{i_{Cl}^I(t)}{[i_{Cl}^{0I}/Q_{Cl}^I(t)]\eta_{Cl}^I(0)}$$

$$= \frac{i_{Na}^I(t) + i_K^I(t) + i_{Cl}^I(t)}{[i_{Na}^{0I}/Q_{Na}^I(t)]\eta_{Na}^I(0) + [i_K^{0I}/Q_K^I(t)]\eta_K^I(0)} = -\frac{f}{\pi\sqrt{t}}$$
$$\qquad\qquad + [i_{Cl}^{0I}/Q_{Cl}^I(t)]\eta_{Cl}^I(0)$$
$$\qquad (14)$$

Then, taking into account the open circuit condition (5), it follows:

$$\frac{i_{Na}^{0I}}{Q_{Na}^I(t)}\eta_{Na}^I(0) + \frac{i_K^{0I}}{Q_K^I(t)}\eta_K^I(0) + \frac{i_{Cl}^{0I}}{Q_{Cl}^I(t)}\eta_{Cl}^I(0) = 0 \qquad (15)$$

But, the overtensions $\eta_{Na}^I(0)$, $\eta_K^I(0)$ and $\eta_{Cl}^I(0)$ being small, we may approximate $N_{Na}^I(t)$, $N_K^I(t)$ and $N_{Cl}^I(t)$, by the constant expressions (see Eqs. (1'), (2') and (3')):

$$N_{Na}^I(t) \approx \frac{1}{F}\frac{\sqrt{D_{Na}^I(t)}c_{Na}^I(t) + \sqrt{D_{Na}^{MI}(t)}c_{Na}^{MI}(t)}{\sqrt{D_{Na}^I(t)D_{Na}^{MI}(t)}c_{Na}^I(t)c_{Na}^{MI}(t)}$$

$$N_K^I(t) \approx \frac{1}{F}\frac{\sqrt{D_K^I(t)}c_K^I(t) + \sqrt{D_K^{MI}(t)}c_K^{MI}(t)}{\sqrt{D_K^I(t)D_K^{MI}(t)}c_K^I(t)c_K^{MI}(t)} \qquad (16)$$

$$N_{Cl}^I(t) \approx \frac{1}{F}\frac{\sqrt{D_{Cl}^I(t)}c_{Cl}^I(t) + \sqrt{D_{Cl}^{MI}(t)}c_{Cl}^{MI}(t)}{\sqrt{D_{Cl}^I(t)D_{Cl}^{MI}(t)}c_{Cl}^I(t)c_{Cl}^{MI}(t)}$$

The concentrations in the membrane being very small, as compared to the corresponding ones in the aqueous solution,

Eqs. (16) simplify to:

$$N_{Na}^I(t) \approx \frac{1}{F\sqrt{D_{Na}^{MI}(t)c_{Na}^{MI}(t)}}$$

$$N_K^I(t) \approx \frac{1}{F\sqrt{D_K^{MI}(t)c_K^{MI}(t)}} \tag{16$'$}$$

$$N_{Cl}^I(t) \approx \frac{1}{F\sqrt{D_{Cl}^{MI}(t)c_{Cl}^{MI}(t)}}$$

Further,

$$\frac{i_{Na}^{0I}}{Q_{Na}^I(t)} \approx \frac{\pi^{1/2}}{N_{Na}^I} = \pi^{1/2}F\sqrt{D_{Na}^{MI}c_{Na}^{MI}}$$

$$\frac{i_K^{0I}}{Q_K^I(t)} \approx \frac{\pi^{1/2}}{N_K^I} = \pi^{1/2}F\sqrt{D_K^{MI}c_K^{MI}} \tag{17}$$

$$\frac{i_{Cl}^{0I}}{Q_{Cl}^I(t)} \approx \frac{\pi^{1/2}}{N_{Cl}^I} = \pi^{1/2}F\sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}$$

and introducing in Eq. (15):

$$\sqrt{D_{Na}^{MI}c_{Na}^{MI}}\eta_{Na}^I(0) + \sqrt{D_K^{MI}c_K^{MI}}\eta_K^I(0)$$
$$+ \sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}\eta_{Cl}^I(0) = 0 \tag{18}$$

After using Eq. (10) to express the overtensions, Eq. (18) takes the form:

$$g_m^I(0) = g_{m1} = \omega_{Na}^I g_{rev,Na}^I + \omega_K^I g_{rev,K}^I + \omega_{Cl}^I g_{rev,Cl}^I \tag{19}$$

where the weight coefficients have the expressions:

$$\omega_{Na}^I = \frac{\sqrt{D_{Na}^{MI}c_{Na}^{MI}}}{\sqrt{D_{Na}^{MI}c_{Na}^{MI}} + \sqrt{D_K^{MI}c_K^{MI}} + \sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}}$$

$$\omega_K^I = \frac{\sqrt{D_K^{MI}c_K^{MI}}}{\sqrt{D_{Na}^{MI}c_{Na}^{MI}} + \sqrt{D_K^{MI}c_K^{MI}} + \sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}} \tag{19$'$}$$

$$\omega_{Cl}^I = \frac{\sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}}{\sqrt{D_{Na}^{MI}c_{Na}^{MI}} + \sqrt{D_K^{MI}c_K^{MI}} + \sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}}$$

To understand the meanings of the Nernst equilibrium tensions, which appear in Eq. (19), let us consider that the liquid junction I/MI *would be permeable only to Na$^+$ ions*. Then, these ions will *distribute* between the two phases, I and MI, much more quickly than they will diffuse across the membrane, between the phases MI and MII. Therefore, one may consider that the Na$^+$ ions reach an *equilibrium distribution*, described by the equality of their electrochemical potentials in the two phases, I and MI:

$$\mu_{Na}^{0I} + RT\ln c_{Na}^I + F(\phi_I)_{Na} = \mu_{Na}^{0MI} + RT\ln c_{Na}^{MI}$$
$$+ F(\phi_{MI})_{Na} \tag{20}$$

Thus,

$$(\phi_I - \phi_{MI})_{Na} = g_{rev,Na}^I = \frac{1}{F}(\mu_{Na}^{0MI} - \mu_{Na}^{0I}) + \frac{RT}{F}\ln\frac{c_{Na}^{MI}}{c_{Na}^I} \tag{21}$$

expresses the Nernst equilibrium tension that appears in Eq. (19). The first term on the right hand side represents the *standard* Nernst equilibrium tension:

$$g_{rev,Na}^{0I} = \frac{1}{F}(\mu_{Na}^{0MI} - \mu_{Na}^{0I}) \tag{21$'$}$$

Similarly, if the junction would be permeable only to K$^+$ ions:

$$(\phi_I - \phi_{MI})_K = g_{rev,K}^I = \frac{1}{F}(\mu_K^{0MI} - \mu_K^{0I}) + \frac{RT}{F}\ln\frac{c_K^{MI}}{c_K^I} \tag{22}$$

$$g_{rev,K}^{0I} = \frac{1}{F}(\mu_K^{0MI} - \mu_K^{0I}) \tag{22$'$}$$

In the case of a junction permeable only to Cl$^-$ ions, the equality of the electrochemical potential in the phases I and MI writes:

$$\mu_{Cl}^{0I} + RT\ln c_{Cl}^I - F(\phi_I)_{Cl} = \mu_{Cl}^{0MI} + RT\ln c_{Cl}^{MI} - F(\phi_{MI})_{Cl} \tag{23}$$

and therefore,

$$(\phi_I - \phi_{MI})_{Cl} = g_{rev,Cl}^I = \frac{1}{F}(\mu_{Cl}^{0I} - \mu_{Cl}^{0MI}) + \frac{RT}{F}\ln\frac{c_{Cl}^I}{c_{Cl}^{MI}} \tag{24}$$

$$g_{rev,Cl}^{0I} = \frac{1}{F}(\mu_{Cl}^{0I} - \mu_{Cl}^{0MI}) \tag{24$'$}$$

In fact, the liquid junction is permeable to all three ions and, for this reason, an intermediate electric tension establishes, which is given by Eq. (19) and represents the *weighted mean* of the individual Nernst equilibrium tensions $g_{rev,Na}^I$, $g_{rev,K}^I$, $g_{rev,Cl}^I$, with the *weight coefficients* given by Eq. (19$'$).

Coming back to Eqs. (14) and (17) it results (see also Eq. (10)):

$$i_{Na}^I(t) = -\frac{f}{\pi\sqrt{t}}\frac{i_{Na}^{0I}}{Q_{Na}^I(t)}\eta_{Na}^I(0)$$
$$\approx -\frac{f}{\pi\sqrt{t}}\pi^{1/2}F\sqrt{D_{Na}^{MI}c_{Na}^{MI}}(g_m^I(0) - g_{rev,Na}^I)$$
$$i_K^I(t) \approx -\frac{f}{\pi\sqrt{t}}\pi^{1/2}F\sqrt{D_K^{MI}c_K^{MI}}(g_m^I(0) - g_{rev,K}^I) \tag{25}$$
$$i_{Cl}^I(t) \approx -\frac{f}{\pi\sqrt{t}}\pi^{1/2}F\sqrt{D_{Cl}^{MI}c_{Cl}^{MI}}(g_m^I(0) - g_{rev,Cl}^I)$$

An important conclusion comes out from Eq. (25): in the expressions of the current densities do not appear kinetic parameters (i.e., i_{Na}^{0I}, β_{Na}, etc.), as it should be, because we have supposed that the ionic species distribute very quickly between the phases I and MI, i.e., without charge transfer limitations and therefore the kinetic behavior of the modeling electrode reactions should be that of reversible electrode reactions.

It is obvious that by making in the above equations the changes:

$$I \rightarrow II \text{ and } MI \rightarrow MII$$

one gets the corresponding equations, valid for the liquid junction II/MII. For sake of simplicity, we give only a part of them:

$$g_m^{II}(0) = g_{m2} = \omega_{Na}^{II} g_{rev,Na}^{II} + \omega_K^{II} g_{rev,K}^{II} + \omega_{Cl}^{II} g_{rev,Cl}^{II}$$

$$\omega_{Na}^{II} = \frac{\sqrt{D_{Na}^{MII}} c_{Na}^{MII}}{\sqrt{D_{Na}^{MII}} c_{Na}^{MII} + \sqrt{D_K^{MII}} c_K^{MII} + \sqrt{D_{Cl}^{MII}} c_{Cl}^{MII}} \quad (26)$$

etc.

$$g_{rev,Na}^{0II} = \frac{1}{F}(\mu_{Na}^{0MII} - \mu_{Na}^{0II})$$

$$g_{rev,K}^{0II} = \frac{1}{F}(\mu_K^{0MII} - \mu_K^{0II}) \quad (26')$$

$$g_{rev,Cl}^{0II} = \frac{1}{F}(\mu_{Cl}^{0II} - \mu_{Cl}^{0MII})$$

and

$$i_{Na}^{II}(t) = -\frac{fF}{\pi^{1/2}\sqrt{t}}\sqrt{D_{Na}^{MII}} c_{Na}^{MII}(g_m^{II}(0) - g_{rev,Na}^{II}) \quad (27)$$

etc.

2.2. The expression of the diffusion potential across the membrane

The deduction of Planck's formula is given in the references cited [24–28]. It refers to the diffusion potential which establishes at the contact between two electrolytic solutions I/II, but it may be also used to get the diffusion potential between the two ends of a single electrolytic solution, within which the ionic concentrations change with the distance. Here, we give this famous formula in its general form and afterwards, we apply it to get the diffusion potential between the two ends of the membrane, i.e., MI and MII. Thus, for univalent ions:

$$g_D = \phi_{MI} - \phi_{MII} = \frac{RT}{F} \ln \xi \quad (28)$$

where ξ results by solving the equation:

$$\frac{U_{II}^+ - \xi U_I^+}{\xi V_{II}^- - V_I^-} = \frac{\ln(C_{II}/C_I) + \ln \xi}{\ln(C_{II}/C_I) - \ln \xi} \frac{C_{II} - \xi C_I}{\xi C_{II} - C_I} \quad (29)$$

in which,

$$U_I^+ = \sum_{k,odd} c_k^I u_k; \quad U_{II}^+ = \sum_{k,odd} c_k^{II} u_k \quad \text{(cations)} \quad (29')$$

$$V_I^- = \sum_{k,even} c_k^I u_k; \quad V_{II}^- = \sum_{k,even} c_k^{II} u_k \quad \text{(anions)} \quad (29'')$$

$$C_I = \sum_{k,odd} c_k^I = \sum_{k,even} c_k^I; \quad C_{II} = \sum_{k,odd} c_k^{II} = \sum_{k,even} c_k^{II} \quad (29''')$$

As one sees, the Planck's theory considers that the ionic mobility u_k remain constants along the liquid junction.

In our case:

$$C_{MI} = c_{Na}^{MI} + c_K^{MI} = c_{Cl}^{MI}; \quad C_{MII} = c_{Na}^{MII} + c_K^{MII} = c_{Cl}^{MII} \quad (30)$$

$$U_{MI}^+ = c_{Na}^{MI} u_{Na}^M + c_K^{MI} u_K^M; \quad U_{MII}^+ = c_{Na}^{MII} u_{Na}^M + c_K^{MII} u_K^M \quad (30')$$

$$V_{MI}^- = c_{Cl}^{MI} u_{Cl}^M; \quad V_{MII}^- = c_{Cl}^{MII} u_{Cl}^M \quad (30'')$$

and after some algebraic operations:

$$\frac{c_{Na}^{MII} u_{Na}^M + c_K^{MII} u_K^M - \xi(c_{Na}^{MI} u_{Na}^M + c_K^{MI} u_K^M)}{c_{Cl}^{MII} u_{Cl}^M - \xi c_{Cl}^{MI} u_{Cl}^M}$$

$$= \frac{\ln \xi + \ln(c_{Cl}^{MII}/c_{Cl}^{MI})}{-\ln \xi + \ln(c_{Cl}^{MII}/c_{Cl}^{MI})} \quad (31)$$

Further, because from the equality $a/b = c/d$ it follows the equality $(a+b)/(b-a) = (c+d)/(d-c)$, Eq. (31) becomes:

$$\frac{\begin{array}{c} c_{Na}^{MII} u_{Na}^M + c_K^{MII} u_K^M + c_{Cl}^{MII} u_{Cl}^M - \xi(c_{Na}^{MI} u_{Na}^M \\ + c_K^{MI} u_K^M + c_{Cl}^{MI} u_{Cl}^M) \end{array}}{\begin{array}{c} c_{Cl}^{MII} u_{Cl}^M - c_{Na}^{MII} u_{Na}^M - c_K^{MII} u_K^M - \xi(c_{Cl}^{MI} u_{Cl}^M \\ - c_{Na}^{MI} u_{Na}^M - c_K^{MI} u_K^M) \end{array}} = \frac{\ln(c_{Cl}^{MI}/c_{Cl}^{MII})}{\ln \xi}$$

$$= \frac{\ln(c_{Cl}^{MI} u_{Cl}^M / c_{Cl}^{MII} u_{Cl}^M)}{\ln \xi} \quad (32)$$

Eq. (32) gives implicitly the diffusion potential g_D across the membrane in Planck's conception. To get an explicit expression of g_D, an additional hypothesis is necessary.

2.3. Comparison between the Goldman–Hodkin–Katz formula of the membrane potential and the expression of the diffusion potential across the membrane given by the Planck's theory

In our notations, the formula of Goldman–Hodkin–Katz writes (see [22,23]):

$$g_m = \frac{RT}{F} \ln \frac{c_{Na}^{II} P_{Na} + c_K^{II} P_K + c_{Cl}^I P_{Cl}}{c_{Na}^I P_{Na} + c_K^I P_K + c_{Cl}^{II} P_{Cl}} \quad (33)$$

(coming back to Eq. (32)), let us suppose that the Cl^- ions would be in equilibrium within the membrane, i.e., would have equal electrochemical potentials in the two phases MI

and MII. Then,

$$\mu_{Cl}^{0MI} + RT \ln c_{Cl}^{MI} - F\phi_{MI} = \mu_{Cl}^{0MII} + RT \ln c_{Cl}^{MII} - F\phi_{MII} \tag{34}$$

and, because $\mu_{Cl}^{0MI} = \mu_{Cl}^{0MII}$ (the two ends of the membrane differing only in the concentrations of the ionic species), one gets (see Eq. (28)):

$$fg_D = \ln \xi = \ln \frac{c_{Cl}^{MI}}{c_{Cl}^{MII}} = \ln \frac{c_{Cl}^{MI} u_{Cl}^{M}}{c_{Cl}^{MII} u_{Cl}^{M}} \tag{34'}$$

and thus the quotients in Eq. (32) are equal to unity. Equating the first quotient to unity, and solving the equation thus obtained, one gets:

$$\xi = \frac{c_{Na}^{MII} u_{Na}^{M} + c_{K}^{MII} u_{K}^{M}}{c_{Na}^{MI} u_{Na}^{M} + c_{K}^{MI} u_{K}^{M}} \tag{35}$$

In this mode, have resulted two expressions for ξ, one in function of quantities which refer only to the Cl^- ions, *supposed to be in equilibrium* between the two phases, MI and MII, and the second in function of quantities which refer to both Na^+ and K^+ ions. Of course, these two ionic species may not be in equilibrium within the membrane. Equating, these two expressions of ξ, applying the properties of a sequence of equal quotients, a third expression of ξ results, and taking its logarithm, one finally obtains:

$$g_D = \frac{RT}{F} \ln \frac{c_{Na}^{MII} u_{Na}^{M} + c_{K}^{MII} u_{K}^{M} + c_{Cl}^{MI} u_{Cl}^{M}}{c_{Na}^{MI} u_{Na}^{M} + c_{K}^{MI} u_{K}^{M} + c_{Cl}^{MII} u_{Cl}^{M}} \tag{36}$$

Therefore, in the general case, when all three ionic species are not in equilibrium within the membrane, the Planck's formula leads to Eq. (32), which does not permit to get an explicit expression of g_D. In the particular case, when the Cl^- ions are in equilibrium within the membrane, the Planck's formula leads to the expression (36) of g_D; which is of the Goldman–Hodkin–Katz type. In other words, if the Cl^- ions are in equilibrium within the membrane, the membrane potential in the Goldman–Hodkin–Katz theory is in fact a Planck's diffusion potential. However, a few words are necessary concerning the equivalence of formulae (32) and (36).

In the Goldman–Hodkin–Katz theory, the quantities P_{Na}, P_K, P_{Cl} express the *permeabilities* of the membrane to the ionic species Na^+, K^+, Cl^-, and have the expressions [21,22]:

$$P_{Na} = \frac{F}{d} u_{Na}^{M}; \quad P_K = \frac{F}{d} u_K^{M}; \quad P_{Cl} = \frac{F}{d} u_{Cl}^{M} \tag{37}$$

where d is the thickness of the membrane.

To introduce the permeabilities P_{Na}, P_K, P_{Cl} in Eq. (36), suffice to multiply the ionic mobility by the same factor F/d. Thus,

$$g_D = \frac{RT}{F} \ln \frac{c_{Na}^{MII} P_{Na} + c_{K}^{MII} P_K + c_{Cl}^{MI} P_{Cl}}{c_{Na}^{MI} P_{Na} + c_{K}^{MI} P_K + c_{Cl}^{MII} P_{Cl}} \tag{36'}$$

In the deduction of Goldman–Hodkin–Katz formula, it has been supposed that the two potential differences at the two junctions I/membrane and membrane/II compensate each other, and for this reason the membrane potential reduces to the potential difference across the membrane. This supposition holds true if the ionic species *distribute at equilibrium* in between the corresponding phases put into contact at the two liquid junctions. Indeed, according to the developments given in this paper, this supposition implies the equalities:

$$g_{m1} = (\phi_I - \phi_{MI}) = (\phi_I - \phi_{MI})_{Na} = (\phi_I - \phi_{MI})_K$$
$$= (\phi_I - \phi_{MI})_{Cl} \quad \text{and} \quad g_{m2} = (\phi_{II} - \phi_{MII})$$
$$= (\phi_{II} - \phi_{MII})_{Na} = (\phi_{II} - \phi_{MII})_K = (\phi_{II} - \phi_{MII})_{Cl} \tag{38}$$

Then, equating the electrochemical potentials in the phases in contact, say for Na^+ ions, one gets:

$$\mu_{Na}^{I} + RT \ln c_{Na}^{I} + \phi_I = \mu_{Na}^{0MI} + RT \ln c_{Na}^{MI} + \phi_{MI} \tag{39}$$

and

$$\mu_{Na}^{0II} + RT \ln c_{Na}^{II} + \phi_{II} = \mu_{Na}^{0MII} + RT \ln c_{Na}^{MII} + \phi_{MII} \tag{39'}$$

But, $\mu_{Na}^{0I} = \mu_{Na}^{0II}$ and $\mu_{Na}^{0MI} = \mu_{Na}^{0MII}$. Thus, Eqs. (39) and (39') lead to:

$$RT \ln \frac{c_{Na}^{I}}{c_{Na}^{II}} + \phi_I - \phi_{II} = RT \ln \frac{c_{Na}^{MI}}{c_{Na}^{MII}} + \phi_{MI} - \phi_{MII} \tag{40}$$

Therefore, from the equality $\phi_I - \phi_{II} = \phi_{MI} - \phi_{MII}$, it follows:

$$r_{Na} = \frac{c_{Na}^{MI}}{c_{Na}^{I}} = \frac{c_{Na}^{MII}}{c_{Na}^{II}}; \quad r_K = \frac{c_{K}^{MI}}{c_{K}^{I}} = \frac{c_{K}^{MII}}{c_{K}^{II}}; \quad r_{Cl} = \frac{c_{Cl}^{MI}}{c_{Cl}^{I}} = \frac{c_{Cl}^{MII}}{c_{Cl}^{II}} \tag{40'}$$

Eq. (40') permit to introduce the concentrations c_{Na}^{I}, c_{Na}^{II}, etc. in Eq. (36'), which, because $g_{m1} - g_{m2} = 0$, will give the expression of the membrane potential in Planck's conception, but for the particular case when, the ionic species Na^+, K^+ and Cl^-, distribute at equilibrium in between the corresponding phases put into contact at the two liquid junctions, and, in addition, the Cl^- ions are in equilibrium within the membrane. This expression writes:

$$g_m = g_D = \frac{RT}{F} \ln \frac{c_{Na}^{II} \tilde{P}_{Na} + c_{K}^{II} \tilde{P}_K + c_{Cl}^{I} \tilde{P}_{Cl}}{c_{Na}^{I} \tilde{P}_{Na} + c_{K}^{I} \tilde{P}_K + c_{Cl}^{II} \tilde{P}_{Cl}} \tag{41}$$

where

$$\tilde{P}_{Na} = r_{Na} P_{Na}; \quad \tilde{P}_K = r_K P_K; \quad \tilde{P}_{Cl} = r_{Cl} P_{Cl} \tag{41'}$$

and, as one sees, is equivalent to the expression (33).

3. Conclusions

The rest potential of a biological membrane is the sum of three potential differences, two of them at the liquid junctions between the outside electrolytic solution and the beginning of the membrane, respective the ending of the membrane and the inside electrolytic solution, and the third one across the membrane.

To get the expressions of the first two potential differences, i.e., g_{m1} and g_{m2}, the transport of an ionic species through an ITIES interface has been interpreted as an electrode redox reaction. This has permitted to express proportionally the flux of transport by the current density of "this modeling electrode reaction", and to use the results very recently obtained by Bonciocat et al., concerning a new approach to the theoretical analysis of electrode (and multielectrode) redox reactions, in which the integral equations of Volterra and Abel types play a very important role. The interfaces I/MI and II/MII represent examples of redox three electrodes (because of the three ionic species) and has been analyzed based on this new theoretical approach. In this way have resulted the expressions (19) and (19′) of g_{m1}, respective (26) and (26′) of g_{m2}.

As for the diffusion potential across the membrane, we have chosen to deduce its expression on the basis of the famous Planck's formula, for two reasons: first, because this formula refers to a "constrained diffusion", by which the ionic concentrations remain constant in each section of the diffusion layer, as it happens within a biological membrane due to the action of the hypothetical "Biological Potentiostat"; secondly, because it has been deduced by expressing the velocity of an ion under the simultaneous actions of both concentration and electrical potential gradients, but, unlike the Goldman–Hodkin–Katz deduction, it does not suppose a constant electrical potential gradient within the membrane. It thus results that the Planck's conception is superior to that of Goldman–Hodkin–Katz. To be more clear, it is necessary to use the expressions of the concentration C, and of the gradient $\partial\phi/\partial x$, along the membrane, as they result in the course of the mathematical derivation of the Planck's formula (28)–(29′′′). They are:

$$C_{Mx} = (C_{MII} - C_{MI})\frac{x}{d} + C_{MI} \tag{42}$$

respective

$$\frac{\partial\phi}{\partial x} = \frac{A+B}{2C_{Mx}} = \frac{(A+B)d}{2[(C_{MII} - C_{MI})x + C_{MI}d]} \tag{42′}$$

where Mx is the plane within the membrane at the distance x from the beginning of the membrane, d the thickness of the membrane and A, B, constants. The readers interested in their derivation must consult the cited references.

Eq. (42′) shows that, from the point of view of the Planck's conception, the supposition used by Goldman–Hodkin–Katz, i.e., $\partial\phi/\partial x$ = constant, implies $C_{MI} = C_{MII}$, which means:

$$c_{Cl}^{MI} = c_{Cl}^{MII}, \text{ as well as } c_{Na}^{MI} + c_{K}^{MI} = c_{Na}^{MII} + c_{K}^{MII} \tag{43}$$

conditions, however, very restrictive.

Further, let us integrate Eq. (42′) from $x = 0$, to $x = x$, and let us take into account Eq. (42) too. Then,

$$\phi_{Mx} - \phi_{MI} = -\frac{(A+B)d}{2(C_{MII} - C_{MI})} \ln\frac{C_{MI}}{C_{Mx}} \tag{44}$$

Coming back to the hypothesis used to derive Eq. (36) as a particular case of the Planck's formula, i.e., the Cl^{-} ions are in equilibrium within the membrane, let us write it in the general form:

$$\mu_{Cl}^{0MI} + RT \ln c_{Cl}^{MI} - F\phi_{MI} = \mu_{Cl}^{0Mx} + RT \ln c_{Cl}^{Mx} - F\phi_{Mx} \tag{45}$$

From Eqs. (44) and (45) results:

$$\ln\frac{c_{Cl}^{MI}}{c_{Cl}^{Mx}} = f(\phi_{MI} - \phi_{Mx}) = \frac{f(A+B)}{2(C^{MII} - C^{MI})} \ln\frac{c_{Cl}^{MI}}{c_{Cl}^{Mx}} \tag{46}$$

which implies,

$$\frac{f(A+B)d}{2(C^{MII} - C^{MI})} = 1 \tag{46′}$$

and therefore,

$$C^{MII} - C^{MI} = \frac{f(A+B)d}{2} \tag{47}$$

It thus results:

$$c_{Cl}^{MII} = c_{Cl}^{MI} + \frac{f(A+B)d}{2} \tag{47′}$$

and

$$c_{Na}^{MII} + c_{K}^{MII} = c_{Na}^{MI} + c_{K}^{MI} + \frac{f(A+B)d}{2} \tag{47′′}$$

conditions, of course, less restrictive than those given by Eq. (43). Consequently, to get the Goldman–Hodkin–Katz formula by particularizing the Planck's formula, the additional hypothesis expressed by Eq. (45) is much more indicated than the hypothesis of a constant electrical potential gradient ($\partial\phi/\partial x$ = constant) along the membrane.

Concerning the distribution at equilibrium of the ionic species in between the phases put into contact, as a condition, which permits to neglect the contribution of the difference $g_{m1} - g_{m2}$ to the membrane potential g_m, one may consider that it is implicitly supposed in the Goldman–Hodkin–Katz approach too.

Finally, one may conclude:

- the correct membrane potential is the sum of all three contributions, g_{m1}, $-g_{m2}$ and g_D;
- the approach used in this paper to get the expressions of g_{m1} and g_{m2}, represents a novelty, which proves the importance

of the integral equations of Volterra type and Abel type, in the future development of the theoretical electrochemistry;
- to get the expression of the diffusion potential difference across the membrane, the Planck's approach is superior to the Goldman–Hodkin–Katz approach, but has the disadvantage of not giving an explicit expression of g_D;
- by using a less restrictive hypothesis (i.e., the Cl^- ions are in equilibrium within the membrane) than that used by Goldman–Hodkin–Katz approach (i.e., $\partial\phi/\partial x = $ constant across the membrane), the Planck's formula particularizes into the Goldman–Hodkin–Katz formula.

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