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Access resistance of a single conducting membrane channel

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Abstract

We have considered the access resistance (AR) of a single conducting channel placed in a membrane bathed by an electrolyte. The classical expression for AR is due to Hall, who modeled the electrolyte as an ohmic conducting homogeneous medium. This approach is discussed in the present paper and it is shown that it is not valid in all cases, but depends on the ion concentration in solution and the ratio between solution and channel resistivities. To get a new expression for AR, we have combined the use of one-dimensional Nernst–Planck and Poisson (NPP) equations for the mouth of the channel and three-dimensional NPP equations for the outside solution. The influence of ion gradients and the channel itself on AR turns out to be considerable in diluted solutions (and also in the case of small channels in any solution). This influence is weaker in concentrated solutions, for which AR is well described by Hall's expression. © 1998 Elsevier Science B.V.

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1. Introduction

Conductance measurements is one of the tools currently used for studying ion channels. In the common experimental set-up, a membrane containing a number of channels is immersed in an electrolyte solution and the electrodes are placed on the solution chambers on both sides of the membrane. If the permeability of the channel is high enough, in some cases the ion flux may be ultimately limited by the rate at which ions arrive from the bulk to the mouth of the channel [1–3]. So, for a correct interpretation of channel conductance measurements in such a system, it is necessary to take into account that the channel itself is only one part of this complex system. Classically, the effective electric resistance of the total system is considered as the sum of three components: resistance within the channel itself and two contribution to resistance from the current paths converging to the pore [4]. The latter ones have been called access resistance (AR) [5,6].

The exact value of the AR of a conducting membrane channel is important for a correct estimation of the channel conductance itself (for a general review see [4,7,8] and references therein). Moreover, this problem has become a topical question due to the development of measurement methods for a single channel, where AR can play a significant role.

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In the earliest works [5,6,9], the electrolyte solution was modeled as an ohmic conducting homogeneous medium, i.e. it was assumed that the ion current is simply proportional to the electric field. Such a treatment of ion transport in electrolyte is equivalent to ignoring the ion concentration gradients in solution as well as the effect of channel intrinsic resistance on the electric potential profile in solution. The next step was done in the paper by Läuger [1], who presented a model based on the Nernst–Planck formalism, in which ions move radially inward toward the entrance of the channel. He used the a priori simplifying assumption that the net charge density is zero everywhere in solution. Peskoff and Bers [7] extended Läuger's approach and considered the distribution of electric potential near the mouth of the channel by taking into account the ion density gradients arising from the non-zero charge density in solution. They showed that this extension of Läuger's theory leads to a smaller AR. Apart from other conclusions, their work proved that the value of AR depends in a way on the boundary conditions chosen for Nernst–Planck's and Poisson's equations. Peskoff and Bers used, in our opinion, not entirely suitable boundary conditions. In particular, they assumed that the electric field on the hemisphere surface covering the channel is a known constant, and does not depend on the ion fluxes. This boundary condition leads to some paradoxical results (e.g. a non-zero electric field is predicted in the electrolyte solution for zero ion fluxes despite the fact that no other electric field sources except the electric current is taken into account). In this connection, it seems necessary trying to obtain an expression for AR on the basis of different, hopefully more realistic, boundary conditions. This is one of the questions discussed in the present paper.

It is worth noting that in all the above mentioned studies [1,5–7], AR was approximated as the convergence resistance from the bulk solution to a hemisphere of the same radius as the channel, i.e. the contribution of the electrolyte inside the hemisphere itself was assumed to be negligible. But Hall [9] showed that the resistance of the hemisphere is of the same order of magnitude (namely 60%) as the resistance of the solution in the half-space outside the hemisphere. This last statement is now generally accepted [4,8]. Here we will discuss it and will show that it is not valid in all cases, but depends on the channel radius, the solution concentration and the ratio between the solution and channel resistivities. Hall was the only one who evaluated the resistance of the channel mouth. However, he also ignored, as Hille [5,6] did, the ion density gradients. Apparently, the question about the influence of the ion density gradients on the mouth resistance has not been thoroughly discussed yet.

All the above mentioned papers considered mainly the so-called diffusion-limited ion transport across the channel and, as a matter of fact, they ignored the influence of the channel characteristics on the AR. But it is obvious that the electric potential profile in the solution essentially depends on the magnitude of the electric field at the channel entrance which in turn is determined by the channel resistivity. Hence, the latter also influences the AR. This influence will be analyzed here.

Our main aim is to obtain an expression for the access resistence R_{ac} of a conducting channel accounting for the existence of ion density gradients both in the solution and in the channel mouth as well as for the influence of the channel itself on the electric potential distribution in the solution. We shall show that generally the value of R_{ac} can be essentially larger than that calculated on the basis of earlier expressions [6,9]. As for the fraction of the mouth resistance R_{m} in the total access resistance R_{ac}, it depends to a large extent on the Debye length of the solution (or ionic strength) and the resistivity of the channel. Depending on the experimental conditions, this fraction can vary from 25% to 60%.

2. Results and discussion

Readers primarily interested in using the final results of this theory may prefer to turn directly to Eq. (6). Let us consider a planar charged lipid membrane placed into an aqueous electrolyte solution, with a few different ionic species present. According to Hall [9], the total AR can be split into two parts: (a) the AR in the solution surrounding a hemispherical surface of the same radius as that of the channel and (b) the AR of the hemisphere itself. Let us assume that there is a single open channel with radius A in the membrane, permeable to a few ionic species.

The electrolyte solution is divided into two parts: one extended from the bulk to a hemispherical surface centered on the channel; the other part (''mouth'') is the electrolyte inside the hemisphere itself. Our aim is to determine (by taking into account the ion density gradients) both terms of the AR, namely the convergence resistance of the solution outside and inside the hemispherical surface. We start with the latter, hereafter denoted as mouth resistance.

It is reasonable to assume, as an idealization, that in the steady-state all ion fluxes in the vicinity of the channel entrance are almost perpendicular to the plane of the membrane, i.e. parallel to the channel axis (see Fig. 1). Therefore, in the mouth, both the ionic fluxes and the electric profile are determined by NPP equations in one dimension. In the case of relatively small ion fluxes and not very high channel selectivity, the steady-state electric potential profile with a first order correction on Boltzmann's distribution is determined by the sum of an exponential term and a linear one [10] and can be represented by

$$\psi_{1D}(x) - u = [(\rho_{ch} - \rho_{sl})\exp(-x) - \rho_{sl}x]\,d_{1D} = [\chi\exp(-x) - x]\,i\rho_{sl}/2\pi a^2 \qquad (1)$$

where $\psi_{1D}(x)$ and u denote the dimensionless electric potential profile and the voltage drop in the bulk solution, respectively; the x axis is perpendicular to the membrane plane; d_{1D} is the dimensionless effective density of the electric current in a 1D problem, i is the dimensionless electric current across the channel; a is the dimensionless radius of the channel; $\chi = \rho_{ch}/\rho_{sl} - 1 > 0$. For a 1:1 binary electrolyte of concentration C_o, the dimensionless variables are connected with the real ones (ϕ, I, X, A) in the following manner $\psi(x) = \beta\phi(x)$; $i = I\,k/eC_o(D_+ + D_-)$; $x = kX$; $a = kA$; $D^{\pm}$ denotes the diffusion coefficients, k is the inverse Debye length of the solution; $\beta^{-1} = k_B T/e = 25.7\,\mathrm{mV}$; k_B is Boltzmann's constant, and e is the elementary charge. In Eq. (1), the electric potential profile is given in terms of the dimensionless resistivity of the channel ρ_{ch} and solution ρ_{sl}. The channel resistivity, ρ_{ch} is connected with the value of the dimensionless electric field E_o at the channel entrance as $\rho_{ch} = E_o/d_{1D}$. As for the resistivity of the solution ρ_{sl}, it is introduced in such a way that Eq. (1) would become Ohm's law if the exponential term were neglected, i.e. $\rho_{sl} = R_{sl}[\beta\ eC_o(D_+ + D_-)]$ where R_{sl} is the dimension resistivity. It is easy to see that the resistivity introduced in this manner is equal to the resistivity introduced in the usual way. For the sake of simplicity, we assume Eq. (1) to be valid everywhere inside hemispherical mouth. Electric field lines in the mouth bend gradually towards the channel entrance. However, we assume an ideal picture in which their slope exhibits a discontinuity on the hemisphere and all field lines are assumed parallel inside this hemispherical region (see Fig. 1). Therefore, their density and hence the electric current density d_{1D} everywhere inside the mouth is the same as outside the hemisphere, d_{3D}, i.e. $d_{1D} \approx d_{3D} = i/2\pi a^2$.

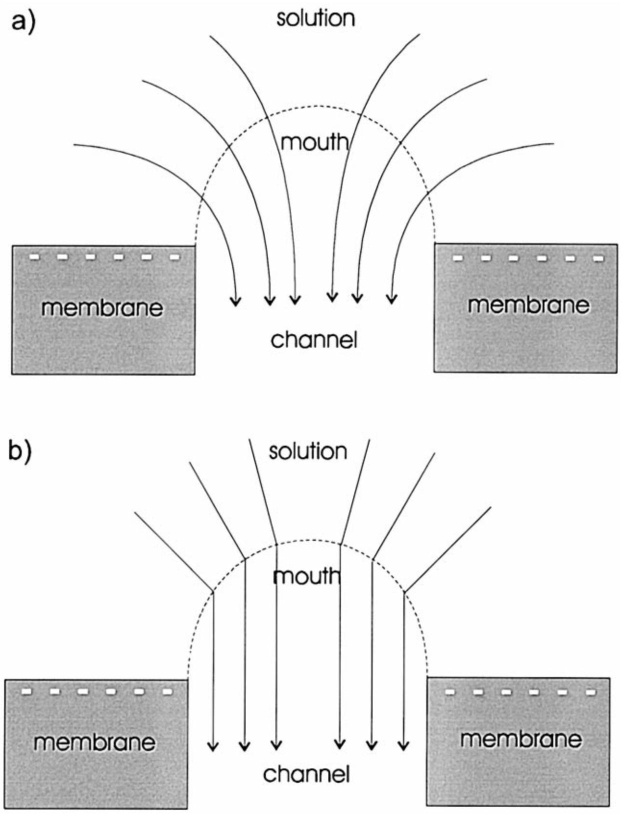

Fig. 1. Sketch of the system under consideration. The hemisphere contains the channel mouth and electric field lines are shown by arrows. Outside the mouth, field lines converge from bulk solution to the hemispherical surface. The real situation, shown in the upper part (a), is modeled in such a way that field lines inside the mouth are assumed to be parallel to the channel axis, as shown in the lower part (b).

Let us discuss shortly the physical origin of the terms in Eq. (1). The first term is pure electrolytic. It takes into account the existence of two kinds of free charge carriers of electrical current in the medium under consideration, i.e. cations and anions, and the mutual screening between them. It becomes significant in systems where channel resistivity differs considerably from that of the solution. The second term in square brackets is the voltage drop in the solution due to the passage of electric current. Only this term can be obtained within the framework of the classical theory of electric current [6,9].

As for the electric potential distribution $\psi_{3D}(x)$ in the solution outside the hemisphere, it can be obtained with the help of NPP equations in 3D and can be represented, in our notation, as

$$\psi_{3D}(\xi)=\frac{\rho_{sl}i}{2\pi\xi}\left[1+B\exp(a-\xi)\right] \tag{2}$$

where ξ is the absolute value of the dimensionless radius-vector. Equation Eq. (2) was firstly obtained (with a different notation) by Peskoff and Bers [7]. In order to determine constant B, they introduced the value of the electric field on the mouth surface as a known fixed parameter. We also use the potential distribution given by Eq. (2), but constant B in our approach follows from the condition that the average value of the electric field on the inner surface of the hemisphere (from Eq. (1)) is equal to the average value of the radial component of the electric field on the outer surface of the hemisphere (from Eq. (2)). Then, constant B is

$$B=\frac{2\chi P}{a(a+1)} \tag{3}$$

where $P = 1-\exp(-a)$. Then, by introducing the convergence resistance of solution $r_{sl}=|[\psi_{3D}(a)-\psi_{3D}(\infty)]/i|$, from (2) and (3) we get

$$r_{sl}=\frac{\rho_{sl}}{2\pi a}\left[1+\frac{2\chi P}{a(1+a)}\right]. \tag{4}$$

As for the mouth resistance r_m, it is reasonable to determine it by averaging the value of the electric potential on the inner surface of the hemisphere:

$$r_m=\left|\frac{\langle\psi_{1D}(0)-\psi_{1D}(R=a)\rangle}{i}\right| =\frac{\rho_{sl}}{\pi^2 a}\left[1+\frac{\pi\chi}{2a^2}(a-P)\right]. \tag{5}$$

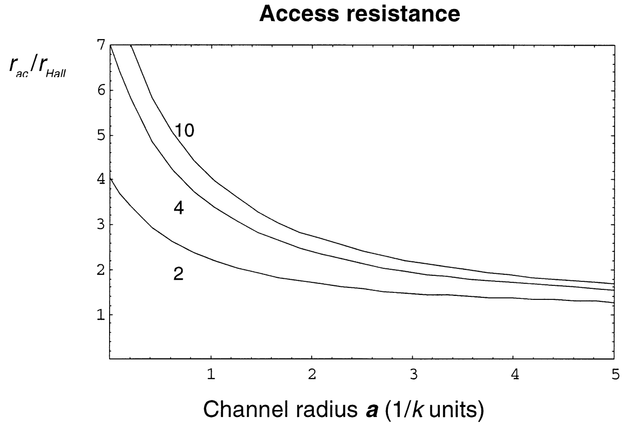

Fig. 2. The dimensionless access resistance r_{ac} (in units $r_{Hall}=\rho_{sl}/4a$) as a function of the dimensionless channel radius a for three different ratios between channel resistivity and solution resistivity is ρ_{ch}/ρ_{sl}: 2, 4 and 10.

Finally, we obtain from (4) and (5) the total access resistance, $r_{ac} = r_{sl} + r_m$ of a single channel:

$$r_{ac}\cong r_{Hall}\left[1+\frac{\pi}{\pi+2}\frac{\chi}{a}\left(1+\frac{P}{a}\frac{a-1}{a+1}\right)\right] \tag{6}$$

where $r_{Hall} = \rho_{sl}/4a$ is the classic Hall's expression for AR [9].

Fig. 2 displays the influence of the channel radius on the ratio of r_{ac}:r_{Hall} for three different values of the channel resistivity ρ_{ch}. It is shown that r_{ac} depends significantly both on channel radius and channel resistivity. But as the radius increases, r_{ac} approaches Hall's value.

It is necessary to note that mouth resistance introduced above depends on the mouth geometry. In the case considered here, Eqs. (4)–(6) correspond to a hemispherical one. For another geometry, the results could be different. However, the ratio of mouth resistance to solution resistance, η, obtained for the same geometry, does not depend on the mouth geometry chosen

$$\eta=\frac{r_m}{r_{sl}}=\frac{2}{\pi}\frac{1+\pi\chi(a-P)/2a^2}{1+2\chi P/a(1+a)}. \tag{7}$$

There are two limit cases, when relatively simple expressions are obtained. In the limit case of diluted solutions ($a \ll 1$), Eqs. (6) and (7) become

$$r_{ac}=r_{Hall}[1+3\chi/2]\approx 3\rho_{ch}/8a \tag{8a}$$

$$\eta=\frac{2}{\pi}\frac{1+\pi\chi/4}{1+2\chi}\cong 0.25 \tag{8b}$$

As we can see in this case, the AR is determined by the channel resistivity ρ_{ch} and the channel radius a. But it is necessary to underline that the fraction of r_{ac} in the total resistance of the whole membrane-channel system decreases when the channel resistivity ρ_{ch} increases. The mouth fraction of the total AR is ca. 25%.

In the limit case of a concentrated solution ($a \gg 1$) and not very big ρ_{ch}, then $r_{ac} = r_{Hall}$ and $\eta = 2/\pi$, i.e. in this case, Hall's expression [9] is valid. However, if besides the condition $a \gg 1$, we have also $\rho_{ch} \gg \rho_{sl}$, then

$$r_{ac} = \frac{\rho_{ch}}{4a^2} \frac{\pi}{\pi + 2} \qquad (9)$$

and hence AR is again determined by the channel resistivity ρ_{ch}.

Finally, let us compare our results with Peskoff and Bers' [7]. They estimated only r_{sl} and obtained $r_{sl} = \rho_{sl}/2\pi(1+a)$. As it follows from Eq. (4) their result corresponds to a big channel with high resistivity $\rho_{ch} \approx \rho_{sl}\, a^2/2 \gg 1$.

Summarizing, we can say that the influence of the channel itself on AR is considerable in diluted solutions (and also in the case of small channels in any solution). In a concentrated solution and large channels [8,11] this influence is weaker and AR is described by Hall's expression [9].

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