A General Relation between Membrane Potential, Ion Activities, and Pump Fluxes for Nonsymmetric Cells in a Steady State

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ABSTRACT

In a previous paper Jacquez and Schultz [*Math. Biosci.* 20:19 (1974)] derived a set of relations between the membrane potential, ion activities, ion permeabilities, and mediated ion fluxes which held for steady states of cells with plasma membranes that were everywhere the same. In this paper I show that similar relations hold for cells with plasma membranes that are nonuniform. These hold for steady states of polarized cells such as epithelial cells in suspension as well as for cells in epithelial membranes under short circuit conditions when the bathing solutions at the two faces have the same composition.

INTRODUCTION

In a previous paper Jacquez and Schultz [1] derived a set of general relations between the membrane potential, ion activities, ion permeabilities, and mediated ion fluxes which held for steady states of cells with uniform plasma membranes. The derivation depended on the steady state condition for each ion, i.e. that the net flux of each ion is zero. Among the many relations obtained, one of particular interest was the following, which had been derived previously under more restrictive conditions by Mullins and Noda [2]:

$$V_m = \frac{RT}{F}\ln\left\{\frac{c_K^o - \dfrac{J_K^P}{J_{Na}^P}\dfrac{P_{Na}}{P_K}c_{Na}^o}{c_K^i - \dfrac{J_K^P}{J_{Na}^P}\dfrac{P_{Na}}{P_K}c_{Na}^i}\right\}. \tag{1}$$

Here V_m is the membrane potential, J_K^P and J_{Na}^P are the total mediated fluxes of potassium and sodium respectively, and P_K and P_{Na} are the membrane permeabilities for potassium and sodium.

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The purpose of this note is to show that essentially the same relations hold for cells that do not have uniform membranes. The important change that results is that where the permeabilities appear in equations such as (1), there now appear weighted averages of the permeabilities of the different areas of the cell membrane, and similarly for the mediated fluxes.

BASIC ASSUMPTIONS

Consider cells which have a mosaic membrane, i.e. a number of areas with different properties. We assume that the different areas of the surface are in contact with medium of the same composition and that the cells are in a steady state. Assume the interior of the cell is equipotential and the exterior is equipotential, i.e. the internal and external aqueous phases are of negligible resistance compared to the cell membrane. Thus the derivation which follows applies not only to epithelial cells dissociated from a membrane and in suspension in some medium, but also to an epithelial membrane under short circuit conditions when the medium on basal and apical surfaces is of the same composition.

NOTATION

POTENTIALS

ϕ_i, ϕ_o = potentials in inner and outer bulk phases.

$V_m = \phi_i - \phi_o$, the membrane potential.

$\phi_j(x)$ = the potential at point x in the jth area of the membrane which is of thickness a_j. The origin of coordinates is taken at the center of the membrane [3].

$V_{ij} = \phi_i - \phi_j(a_j/2)$, the difference between the potential in the inner bulk phase and the inner membrane surface in the jth area.

$V_{oj} = \phi(-a_j/2) - \phi_o$, the difference between the potential at the outer surface and the outer bulk phase.

$Z_{ij} = \exp(FV_{ij}/RT)$.

$Z_{oj} = \exp(FV_{oj}/RT)$.

FLUXES

J_{jk}^d = the diffusive flux of the kth ion in the jth area of the membrane.

J_{jk}^M = the mediated flux of the kth ion in the jth area. This includes all mechanisms other than simple diffusion, i.e. pumps, facilitated diffusion, cotransport, channels.

By definition fluxes are positive when directed into the cell.

CONCENTRATIONS (ACTIVITIES)

c_k^i, c_k^o = concentrations (activities properly) of the kth ion in inner and outer bulk phases.

THEORY AND RESULTS

The diffusive flux of the kth ion across the jth area of the plasma membrane is obtained by integrating the Nernst-Planck equation across the cell membrane [3]:

$$J_{jk}^d = \frac{-a_j P_{jk}}{\int_{-a_j/2}^{a_j/2} e^{z_k F\phi_j(x)/RT}\,dx} \times \left[c_k^i Z_{ij}^{z_k} e^{z_k FV_j/2RT} - c_k^o Z_{0j}^{-z_k} e^{-z_k FVj/2RT} \right]. \tag{2}$$

We concern ourselves only with ions of valence $z_k = +1$ and consider two such ions, $k = 1,2$. The extension to more species follows the derivation in [1]. Writing the potential function as a sum of odd and even parts, $\phi_j(x) = \sigma_j(x) + \theta_j(x)$, it is easy to show that the integral in the denominator of (2) can be written in the form $g_j\Omega_j$, where $\Omega_j = \int_{-a_j/2}^{a_j/2} e^{F\theta_j/RT}dx$ and g_j is the mean value of $e^{F\sigma_j/RT}$ with respect to the weighting function $e^{F\theta_j/RT}$ [3].

The total movement of the kth ion across the jth membrane area is $A_j(J_{jk}^d + J_{jk}^M)$. For a steady state the net movement of each ion is zero:

$$\sum_j A_j\left(J_{jk}^d + J_{jk}^M\right) = 0. \tag{3}$$

Let M_k be the total mediated flux,

$$M_k = \sum_j A_j J_{jk}^M. \tag{4}$$

Consider two ions, $k = 1,2$. For each equation (3) holds. Let m and n be arbitrary multipliers. It follows that

$$m\sum_j A_j J_{j1}^d + n\sum_j A_j J_{j2}^d + mM_1 + nM_2 = 0. \tag{5}$$

Recalling that $z_k = +1$ for $k = 1,2$, we can write Eq. (2) as

$$J_{jk}^d = \frac{-a_j P_{jk} Z_{oj}^{-1} e^{-FV_j/2RT}}{g_j\Omega_j}\left[c_k^i e^{FV_m/RT} - c_k^o \right]. \tag{6}$$

But $Z_{oj}^{-1}e^{-FV_j/2RT}$ can be written in the form

$$Z_{oj}^{-1}e^{-FV_j/2RT} = e^{-FV_m/2RT} e^{F(V_{ij} - V_{oj})/2RT} = e^{-\xi/2}\rho_j. \tag{7}$$

Generally $V_{ij} - V_{oj}$ will be small, so the second term in (7) will be a number close to 1: $\rho_j \simeq 1$.

Substituting in Eq. (5) gives us

$$-m\sum_j \frac{A_j a_j P_{j1} \rho_j e^{-\xi/2}}{g_j \Omega_j}(c_1^i e^{\xi} - c_1^o)$$
$$-n\sum_j \frac{A_j a_j P_{j2} \rho_j e^{-\xi/2}}{g_j \Omega_j}(c_2^i e^{\xi} - c_2^o) + mM_1 + nM_2 = 0. \tag{8}$$

We choose the arbitrary multipliers so that $mM_1 + nM_2 = 0$, i.e. $m/n = -M_2/M_1$. Using this, (8) can be rearranged to give

$$e^{\xi}\left[m\mathcal{P}_1 c_1^i + n\mathcal{P}_2 c_2^i\right] = m\mathcal{P}_1 c_1^o + n\mathcal{P}_2 c_2^o, \tag{9}$$

where

$$\mathcal{P}_k = \frac{\sum_j \left(\frac{A_j a_j \rho_j}{g_j \Omega_j}\right) P_{jk}}{\sum_j \left(\frac{A_j a_j \rho_j}{g_j \Omega_j}\right)}. \tag{10}$$

We note that $\mathcal{P}_k$ is a weighted average of the permeabilities in which the weights take into account not only the relative areas, but also the possibility that the potential profiles differ in the different areas of the plasma membrane. If the thickness and potential profiles are essentially the same in the different areas, then $\mathcal{P}_k$ is simply an area weighted average of the permeabilities to the kth ion.

Equation (9) can now be rearranged to give

$$V_m = \frac{RT}{F}\ln\left\{\frac{c_1^o - \left(\frac{M_1}{M_2}\right)\left(\frac{\mathcal{P}_2}{\mathcal{P}_1}\right)c_2^o}{c_1^i - \left(\frac{M_1}{M_2}\right)\left(\frac{\mathcal{P}_2}{\mathcal{P}_1}\right)c_2^i}\right\}. \tag{11}$$

Note that if $k = 1,2$ are potassium and sodium respectively, then Eq. (11) is the same as Eq. (16) in Ref. [1] with permeabilities replaced by the weighted averages of the permeabilities and the total mediated fluxes replaced by area weighted averages of the mediated fluxes.

Generalization to more than two ions follows the same pattern as in [1].

In conclusion, the relations derived previously for cells with plasma membranes of uniform properties extend to cells with mosaic membranes provided the permeabilities and mediated fluxes are interpreted as averages.

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REFERENCES

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3 J. A. Jacquez, *Math. Biosci.* 12:185 (1971).