Ionic Flows Through a Single Homogeneous Membrane

A Thermodynamic Analysis

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Summary. The Kedem-Katchalsky equation for the flow of a mono-monovalent salt through a highly charged permselective membrane is given as a first order expansion of a single integral of the Kirkwood-Bearman-Spiegler equations. The integration is performed under the assumption that the partial frictional coefficients ζ_{ij} are concentration independent. Conditions for the validity of the expansion are presented. A close relationship to the Goldman equation is demonstrated. If impermeable salts are present in the bathing solutions, the Kedem-Katchalsky *practical* parameters ω, σ, and τ_1 may be ill-defined. Nevertheless, an ionic flow equation of similar form, but of significant difference, can be derived for this situation. The Kedem-Katchalsky equation for salt flow is a special case of this more general equation.

The *practical* parameters ω, σ, and τ_1, characterizing the flow of a salt through a homogeneous permselective membrane were derived (Kedem & Katchalsky, 1963) for a system having only a single salt in the bathing solution.[1] Because the cation and anion concentrations are equal to each other in either solution, they can be equated to salt concentrations and one can use an osmotic driving force $\Delta \pi_s = 2RT(C_s^I - C_s^{II})$. It would be most unusual to find a biological system where, say, KCl is the only salt present in the solutions on either side of a membrane; one expects to find divalent cations, proteins carrying several ionized groups, etc. In this paper I shall derive ionic flow equations for the flow of the components of a mono-monovalent salt through a charged permselective membrane separating two colloidal solutions, i.e., solutions containing impermeable ions in addition to the two mobile species.

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1 It is assumed that the reader is familiar with the notation of the Kedem-Katchalsky equations.

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The Flow Equations

If the negative gradients of the electrochemical potentials are chosen as the thermodynamic forces in an isothermal diffusion system, the conjugate barycentric flows are given (de Groot & Mazur, 1962) by the linear pheno-menological equations

$$J_i^b = \sum_{j=1}^{n} L_{ij} X_j, \quad i = 1, 2 \ldots n. \tag{1}$$

Since there are, in general, n independent forces and only $n-1$ independent barycentric flows, there must be n conditions on the phenomenological coefficients; and indeed,

$$\sum_{j=1}^{n} L_{ij} = 0, \quad i = 1, 2 \ldots n. \tag{2}$$

The inversion of these flow equations is therefore neither immediate nor trivial and has been discussed in a previous paper (Richardson, 1970). At mechanical equilibrium, it is possible to write

$$X_i = \sum_{j=1}^{n} R_{ij} J_j, \quad i = 1, 2 \ldots n, \tag{3}$$

where $J_i = C_i v_i$ is no longer a relative flow. The conditions on these inverse phenomenological coefficients are

$$\sum_{j=1}^{n} C_j R_{ij} = 0, \quad i = 1, 2 \ldots n. \tag{4}$$

The physical basis of these conditions is that the motion of the barycenter cannot contribute to dissipation (Onsager, 1945).

Bearman and Kirkwood (1958) used statistical mechanical arguments to derive a flow equation in terms of frictional coefficients:

$$X_i = \sum_{j=1}^{n} \zeta_{ij} C_j (v_i - v_j), \quad i = 1, 2 \ldots n. \tag{5}$$

In the same year, Spiegler (1958) proposed the following force equation based upon a consideration of Newtonian frictions:

$$X_i = \sum_{j=1}^{n} f_{ij} (v_i - v_j), \quad i = 1, 2 \ldots n. \tag{6}$$

Eq. (5) can be written (Laity, 1959; Ciani & Gliozzi, 1965)

$$X_i = \frac{\sum_{j \neq i}^{n} \zeta_{ij} C_j}{C_i} J_i - \sum_{j \neq i}^{n} \zeta_{ij} J_j, \quad i = 1, 2 \ldots n, \tag{7}$$

and we see that Eqs. (3) and (7) are mathematically equivalent, with

$$R_{ij} = -\zeta_{ij}, \quad i \neq j \tag{8}$$

and that Eq. (7) includes Eq. (4).

Until the physical properties of the partial frictional coefficients (although this use of "partial" may not be precise, it does distinguish between the Bearman-Kirkwood frictions and those of Spiegler) are specified, Eq. (7) is of limited use. Essentially all we can deduce from irreversible thermodynamics is that $\zeta_{ij} = \zeta_{ji}$ and that the ζ_{ij} are independent of the forces and flows. However, the form of Eq. (5) shows us that ζ_{ij} characterizes an interaction per molecule of i and of j. This normalization encourages us to assume that within a given phase the ζ_{ij} are independent of individual concentrations.

A lucid analysis of electrodiffusion in homogeneous membranes based upon the assumption that the partial frictional coefficients ζ_{ij} are concentration independent has been presented by Ciani and Gliozzi (1965, 1966). In a similar vein, but to a different goal, we start from the same differential flow Eq. (7) and analyze the flow of the components of a mono-monovalent salt through a highly charged membrane. In a form similar to the *practical* equation for salt flow, the ionic flow is given as a function of ionic concentrations in the bathing solutions, the water flow and the current. And indeed one can resolve the *practical* parameters from the ionic flow equation under the proper constraints in a system containing ions of only a single salt:

$$\omega = \left(\frac{J_s}{\Delta \pi_s} \right) J_{v, I}, \tag{9}$$

$$(1 - \sigma) = \left(\frac{J_s}{\bar{C}_s J_v} \right) \Delta \pi_s, I, \tag{10}$$

$$\tau_1 = \left(\frac{F J_s}{I} \right) \Delta \pi_s, J_v. \tag{11}$$

The ionic flow equation developed here is applicable to systems where the bathing solutions contain impermeable ions in addition to the univalent permeable cations and anions: we shall call such colloidal systems ionic systems. Kedem and Leaf (1966) have discussed the relationship between salt and ionic transport coefficients in general thermodynamic terms. Here we shall derive the explicit parameters coupling ionic flow to water flow (nearly equal to volume flow in dilute solutions), current, and concentration differences. It is concluded that great care must be exercised in defining and using the *practical* parameters in ionic systems, which, of course, are the

ones most commonly encountered in biology. Before proceeding to the integration of the differential flow equations, let us illustrate this point with an example. Consider the two equations for the flow of KCl through a negatively charged permselective membrane with zero current and no appreciable water flow:

(1) Impermeable ions are in the bathing solutions I and II, and so $C_K^I \neq C_{Cl}^I$ and $C_K^{II} \neq C_{Cl}^{II}$. As will be shown, the salt flow in an ionic system is

$$J_s = \frac{\phi_w^2 K_2}{X \Delta x} (C_K^I C_{Cl}^I - C_K^{II} C_{Cl}^{II}) \tag{12}$$

where K_2 is a generalized diffusion coefficient which includes solute-water, solute-membrane, and solute-solute frictions. Since we have stipulated $I=0$, here we have the flow of a neutral salt (KCl) but we cannot resolve Eq. (12) into a form where $\Delta \pi_s = 2RT(C_K^I - C_K^{II})$ is the driving force.

(2) Suppose that there are no impermeable ions in the bathing solutions, only KCl—i.e., a salt system. We have $C_K^I = C_{Cl}^I = C_s^I$ and $C_K^{II} = C_{Cl}^{II} = C_s^{II}$.

Eq. (12) becomes

$$J_s = \frac{\phi_w^2 K_2}{X \Delta x} (C_s^{I2} - C_s^{II2})$$

$$= \frac{\phi_w^2 K_2 \bar{C}_s}{RTX \Delta x} \Delta \pi_s \tag{13}$$

$$= \omega \Delta \pi_s$$

where

$$\bar{C}_s = \frac{C_s^I + C_s^{II}}{2}. \tag{14}$$

Only in a special case can we define a *practical* parameter ω for neutral salt flow which has $\Delta \pi_s$ as the driving force. There is a similar problem of definition for the reflection coefficient in ionic systems. Eq. (10) defines a reflection coefficient in precise terms but one must also ask: what is the parameter relating J_s and J_v when $\Delta \pi_s \neq 0$? We shall integrate the flow equations with no constraints upon any forces or flows and shall see that the *practical* equation for salt flow,

$$J_s = \omega \Delta \pi_s + \bar{C}_s (1 - \sigma) J_v + \frac{\tau_1}{F} I, \tag{15}$$

is only a special case of a more general ionic flow equation.

Integration of the Flow Equations

The membrane system to be considered consists of a permselective membrane with a high concentration of fixed-charge sites separating two

well-stirred reservoirs denoted I and II. The membrane is perdendicular to the x-axis and the membrane-solution interfaces are at $x=0$ and $x=\varDelta x$. The flows are the ionic components of a mono-monovalent salt and water flow. The concentration of the mobile cations in the membrane phase is denoted by C_1 and that of the anions by C_2. These two concentrations are functions of the space variable x. The concentration of the membrane C_m, the concentration of fixed-charge sites X, and the water concentration C_w are assumed to be constant across the membrane. The membrane concentration C_m is related to the microstructure of the membrane and represents an effective concentration of molecules involved in frictional interactions. If the membrane is a uniform network of cross-linked polymer of, say, three species of concentration $\alpha_1 C_m$, $\alpha_2 C_m$, and $\alpha_3 C_m$, each offering different frictions to the i-th mobile species ($\zeta_{i m_1}$, $\zeta_{i m_2}$, $\zeta_{i m_3}$), then the total interaction is characterized by a single term: $C_m \zeta_{im} = C_m(\alpha_1 \zeta_{i m_1} + \alpha_2 \zeta_{i m_2} + \alpha_3 \zeta_{i m_3})$. On the other hand, if the flow is through pores or channels in the membrane, then C_m is not the concentration of molecules in the membrane matrix, but only that fraction along the walls of the pores which partake in frictional interactions.

The flow equations are, assuming that the electrochemical potentials are those of an ideal solution,

$$-\frac{RT}{C_1}\frac{dC_1}{dx}-F\frac{d\psi}{dx}=J_1\frac{C_2\zeta_{12}+C_m\zeta_{1m}+C_w\zeta_{1w}}{C_1}-J_2\zeta_{12}-J_w\zeta_{1w} \qquad (16)$$

and

$$-\frac{RT}{C_2}\frac{dC_2}{dx}+F\frac{d\psi}{dx}=-J_1\zeta_{12}+J_2\frac{C_1\zeta_{12}+C_m\zeta_{2m}+C_w\zeta_{2w}}{C_2}-J_w\zeta_{2w}. \qquad (17)$$

By definition, the flow of current is related to the ionic flows by

$$J_1-J_2=\frac{I}{F}. \qquad (18)$$

A complete specification of the problem requires the addition of Poisson's equation and suitable boundary conditions at the solution-membrane interfaces.

MacGillivray (1968) has, however, provided a sufficient condition for the justification of the familiar electroneutrality assumption which also includes in the criterion justification for the assumption of Donnan equilibrium at the interfaces. The criterion (in the simpler notation of MacGillivray & Hare, 1969) is that the parameter α^2 is small compared to unity, where

$$\alpha^2=\frac{\kappa_0\kappa RT}{F^2 X(\varDelta x)^2}, \qquad (19)$$

κ_0 is the permittivity of free space, and κ is the dielectric constant of the membrane.

For a membrane with a concentration of negative fixed-charge sites X, the condition of electroneutrality is

$$C_1 = C_2 + X. \tag{20}$$

We are interested here in permselective membranes having rather large values of X. To determine the magnitude of α^2, let us assume that $X = 10^{-3}$ moles/cm³:

(1) For an artificial membrane with thickness $\Delta x = 10^{-2}$ cm and dielectric constant κ, we have

$$\alpha^2 = 2.4 \times 10^{-13} \kappa.$$

(2) For a biological membrane with thickness $\Delta x = 70$ A, we have

$$\alpha^2 = 4.9 \times 10^{-5} \kappa.$$

Therefore, the condition is fulfilled for any realistic value of κ. With such small values of α^2, the electroneutrality assumption should be quite good. But the nonlinear flow Eqs. (16) and (17) are most easily integrated under the well-known constant-field assumption (Goldman, 1943). Furthermore, a sufficient condition for the applicability of the constant field assumption is that α^2 be large (MacGillivray & Hare, 1969). That this condition is not necessary and that for certain systems electroneutrality and a constant field are compatible will be shown by the following argument. Since $\alpha^2 \ll 1$, we have the sufficient condition for Eq. (20); we have $dC_1/dx = dC_2/dx$ because X is constant across the membrane. We can combine Eqs. (16) and (17) to obtain

$$-F \frac{d\psi}{dx} = \frac{1}{2C_2 + X} \left\{ J_2 [C_m(\zeta_{1m} - \zeta_{2m}) + C_w(\zeta_{1w} - \zeta_{2w}) - 2X\zeta_{12}] \right.$$
$$\left. + \frac{I}{F}(2C_2\zeta_{12} + C_m\zeta_{1m} + C_w\zeta_{1w}) + J_w[C_2(\zeta_{2w} - \zeta_{1w}) - X\zeta_{1w}] \right\}. \tag{21}$$

We shall consider steady state flows and therefore J_2, I and J_w are constant across the membrane. Furthermore, we shall consider a membrane having a high concentration of negative fixed charges. In such a membrane, there is a high Donnan exclusion of anions: for example, if $X = 10^{-3}$ moles/cm³ and the water fraction is $\phi_w = \frac{1}{2}$, then

$$\frac{C_2}{X} \cong \frac{\phi_w^2 C_1^I C_2^I}{X^2} \quad \text{(see Eq. 36)} \tag{a}$$

$$\cong 2.5 \times 10^{-3} \text{ if the salt concentration in the bathing solutions is } 10^{-4} \text{ moles/cm}^3.$$

It follows that

$$C_2 |\zeta_{1w} - \zeta_{2w}| \ll X \zeta_{1w}, \tag{b}$$

and since C_m and C_w are also much greater than C_2, we can assume

$$2C_2 \zeta_{12} \ll C_m \zeta_{1m} + C_w \zeta_{1w}. \tag{c}$$

For the sake of this order-of-magnitude argument, we can therefore write Eq. (21) as

$$-F \frac{d\psi}{dx} = \frac{\text{constant}}{2C_2(x) + X}$$

$$\cong \frac{\text{constant}}{X} \left(1 - \frac{2C_2(x)}{X} \right). \tag{22}$$

We see that $-F \dfrac{d\psi}{dx}$ varies from a constant value by the fractional part $2C_2(x)/X$, which in our systems is of the order of magnitude of 10^{-3}. If, however, there were not a high Donnan exclusion in the membrane, then $1/[2C_2(x) + X]$ might be a strong function of x and the field would not be constant. We shall conclude that, for the systems we shall consider, the electric potential gradient across the membrane is constant: that is,

$$-F \frac{d\psi}{dx} = k. \tag{23}$$

The conditions (a), (b) and (c) indicate under what conditions the flow Eqs. (16) and (17), the electroneutrality condition, and the constant field assumption are compatible for a system with $\alpha^2 \ll 1$.

Note that k is a constant which by Eq. (21) depends upon the division of current between the ionic flows J_1 and J_2. The constant k will be evaluated as a function of I, J_w, and the concentrations at the solution-membrane interfaces later in the analysis, but only as an intermediate step. The electric potential difference will not occur in the final equations for the ionic flows.

Returning to Eq. (16) we can now write it as

$$-\frac{dC_1}{dx} = \frac{J_1}{K_1} + a_1 C_1 \tag{24}$$

where

$$K_1 = \frac{RT}{C_m \zeta_{1m} + C_w \zeta_{1w} - X \zeta_{12}} \tag{25}$$

and

$$a_1 = \frac{1}{RT} \left(\frac{I}{F} \zeta_{12} - k - J_w \zeta_{1w} \right)$$

$$= a - \frac{J_w \zeta_{1w}}{RT}, \tag{26}$$

where a is defined by the last two equations.

An integration across the membrane from $x=0$ to $x=\Delta x$ gives

$$J_1(e^{-a_1 \Delta x}-1)=K_1 a_1(C_1''-C_1' e^{-a_1 \Delta x}) \tag{27}$$

where $C_1'=C_1(0)$ and $C_1''=C_1(\Delta x)$. The boundary values of the concentrations are values determined immediately inside the membrane at the solution-membrane interfaces.

To get an equivalent but more symmetric equation, multiply Eq. (27) by $\exp(a_1 \Delta x)$, sum this second equation to Eq. (27), and divide by 2. If the exponent is small compared to unity (see Appendix), this symmetric equation can be expanded to first order terms to give

$$J_1=\frac{K_1}{\Delta x}(\Delta C_1-a_1 \bar{C}_1 \Delta x) \tag{28}$$

where

$$\Delta C_1=C_1'-C_1'' \quad \text{and} \quad \bar{C}_1=\frac{C_1'+C_1''}{2}. \tag{29}$$

Although there are superficial differences, Eq. (27) is essentially the well-known Goldman (1943) equation. However, here the constant a_1 includes not only the electrical potential drop across the inside of the membrane phase but also an ion-ion interaction term and a contribution from water coupling. In our analysis, the constant-field condition is valid only for highly charged membranes and, if the goal of the analysis were Eq. (27), then the Donnan potentials at both of the membrane-solution interfaces would have to be added to the potential drop across the inside of the membrane in order to present an expression in terms of the full measured potential. This type of calculation has been done by Teorell (1953). The next few paragraphs will show the close relationship between the Goldman equation, the *practical* salt flow equation, and the ionic flow equations.

We return to the analysis with an integration of Eq. (17) and, after a symmetrical expansion, we obtain

$$J_2=\frac{K_2}{\Delta x}(\Delta C_2+\bar{C}_2 a_2 \Delta x) \tag{30}$$

where

$$K_2=\frac{RT}{C_m \zeta_{2m}+C_w \zeta_{2w}+X \zeta_{12}} \tag{31}$$

and

$$a_2=a+\frac{J_w \zeta_{2w}}{RT}. \tag{32}$$

The two equations for the ionic flows (28 and 30) are put into Eq. (18), and the constant a is evaluated in terms of I, J_w, K_1, K_2, and the boundary

values of the concentrations. This value of a is then put into Eq. (28) to give the flow of the cation, J_1:

$$J_1 = \frac{K_1}{\Delta x} \Delta C_1 - \frac{K_1 \bar{C}_1}{\Delta x} \frac{K_1 \Delta C_1 - K_2 \Delta C_2}{K_1 \bar{C}_1 + K_2 \bar{C}_2}$$
$$+ \frac{K_1 \bar{C}_1 K_2 \bar{C}_2}{RT} \frac{\zeta_{1w} + \zeta_{2w}}{K_1 \bar{C}_1 + K_2 \bar{C}_2} J_w + \frac{K_1 \bar{C}_1}{K_1 \bar{C}_1 + K_2 \bar{C}_2} \frac{I}{F}. \tag{33}$$

To be consistent, this flow equation must be reduced to significant first order terms since we have already used the assumption $C_2 \ll C_1$ in the justification of a constant field. Because of electroneutrality, $\Delta C_1 = \Delta C_2$. The reduction will assume that K_1 and K_2 are of the same order of magnitude. For KCl, $f_{1w} = f_{2w}$ in free solution. The paper of Ginzburg and Katchalsky (1963) shows that f_{sw} is an order of magnitude larger than f_{sm} for sucrose in dialysis tubing; unfortunately this has been used to suggest that solute-membrane frictions can be ignored. But these measurements were done in water-swollen membranes where C_m, in effect, was rather small. If indeed ζ_{sm} is independent of concentration, then $f_{sm} = C_m \zeta_{sm}$ may become significant in tight membranes. If $K_1 = O(K_2)$, then we can write Eq. (33) as

$$J_1 = \frac{K_2}{\Delta x} \Delta C_1 + \frac{K_2 \bar{C}_2}{RT} (\zeta_{1w} + \zeta_{2w}) J_w + \left(1 - \frac{K_2 \bar{C}_2}{K_1 X}\right) \frac{I}{F}. \tag{34}$$

This equation for cation flow is still not complete because the concentrations are given inside the membrane phase at the solution-membrane interfaces, not in the bathing solutions. The condition $\alpha^2 \ll 1$ [see Eq. (19)] is sufficient for the Donnan equilibrium to be valid at the interfaces. That is, the total driving force of either ion must be continuous across the infinitely thin membrane-solution interface. Thus the relationship between concentrations inside and outside the membrane at the interface is

$$C_1^I C_2^I = \frac{C_1'}{\phi_w} \frac{C_2'}{\phi_w}$$
$$= \frac{X + C_2'}{\phi_w} \frac{C_2'}{\phi_w}. \tag{35}$$

The volume fraction of water in the membrane ϕ_w enters the preceding equation because the Donnan condition states that equilibrium exists between the external solution and the solution in the aqueous regions in the membrane. If we refer back to Eq. (7), we see that C_1 and C_2 are the ionic concentrations in the membrane taken as a unit; hence, if ϕ_w is the water fraction in the membrane as a whole, then C_1/ϕ_w is the concentration

in the aqueous regions. In K_1 and K_2, the water concentration C_w is related to the water concentration in the external solution by $C_w^I \cong C_w/\phi_w$.

For a highly charged negative membrane, a first order solution to the quadratic Eq. (35) is

$$C_2' = \frac{\phi_w^2 C_1^I C_2^I}{X} \tag{36}$$

and so

$$C_1' = X + \frac{\phi_w^2 C_1^I C_2^I}{X}. \tag{37}$$

There are similar expressions for C_1'' and C_2''.

Now we can finally write the ionic flow equation in terms of steady state flows and the ionic concentrations in the bathing solutions. Noting that $\phi_w = \bar{V}_w C_w$, we can write Eq. (34) as

$$
\begin{aligned}
J_1 =& \frac{\phi_w^2 RT}{(f_{2m}+f_{2w}+X\zeta_{12})X\Delta x}(C_1^I C_2^I - C_1^{II} C_2^{II}) \\
&+ \frac{\phi_w(f_{1w}+f_{2w})}{(f_{2m}+f_{2w}+X\zeta_{12})X}\frac{(C_1^I C_2^I + C_1^{II} C_2^{II})}{2}\bar{V}_w J_w \\
&+ \left[1 - \frac{f_{1m}+f_{1w}-X\zeta_{12}}{f_{2m}+f_{2w}+X\zeta_{12}}\frac{\phi_w^2(C_1^I C_2^I + C_1^{II} C_2^{II})}{2X^2}\right]\frac{I}{F}.
\end{aligned}
\tag{38}
$$

The Practical Parameters

The *practical* parameters were defined and derived for a system with only a single salt in the bathing solutions: $C_1^I = C_2^I = C_s^I$ and $C_1^{II} = C_2^{II} = C_s^{II}$ (Kedem & Katchalsky, 1963). For this discussion of the *practical* parameters, we shall assume dilute solutions where the volume flow $J_v \cong \bar{V}_w J_w$.

(1) *Permeability*, ω. In the introductory paragraphs, we anticipated Eq. (38) and showed that ω for a salt is clearly defined only in salt systems. The flow of neutral salt in an ionic system cannot be given with $\Delta\pi_s$ as a driving force.

(2) *Reflection coefficient*, σ. The reflection coefficient for salt can be defined in two ways, and they are not necessarily equivalent.

(a) σ is defined by Eq. (10). Here $C_s^I = C_s^{II} = C_s = \bar{C}_s$; from Eq. (38) we have,

$$
\begin{aligned}
\left(\frac{J_s}{J_v}\right)_{\Delta\pi_s, I} &= \frac{\phi_w(f_{1w}+f_{2w})}{(f_{2m}+f_{2w}+X\zeta_{12})X}C_s^2 \\
&= \bar{C}_s(1-\sigma);
\end{aligned}
\tag{39}
$$

and we deduce that

$$(1-\sigma)=\frac{\phi_w \bar{C}_s(f_{1w}+f_{2w})}{(f_{2m}+f_{2w}+X\zeta_{12})X}. \tag{40}$$

(b) σ is defined by the *practical* Eq. (15). That is, given any values of $\varDelta \pi_s$ and I, the term multiplying J_v is defined as $\bar{C}_s(1-\sigma)$. In this case, $C_s^I \neq C_s^{II}$, and Eq. (38) gives

$$\bar{C}_s(1-\sigma)\equiv\frac{\phi_w(f_{1w}+f_{2w})}{(f_{2m}+f_{2w}+X\zeta_{12})X}\frac{C_s^{I2}+C_s^{II2}}{2}. \tag{41}$$

But this is not a valid definition because the right side of the preceding equation cannot be resolved into $\bar{C}_s$ and a term representing $(1-\sigma)$.

(3) *The transference number for cations*, τ_1. As the reflection coefficient, this parameter can be defined in two ways.

(a) τ_1 is defined by Eq. (11). Here

$$C_s^I=C_s^{II}=C_s,$$

and from Eq. (38) we have

$$\tau_1=1-\frac{f_{1m}+f_{1w}-X\zeta_{12}}{f_{2m}+f_{2w}+X\zeta_{12}}\frac{\phi_w^2 C_s^2}{X^2}. \tag{42}$$

(b) If τ_1 is defined as the term multiplying I/F in Eq. (15), no matter what the values of C_s^I, C_s^{II}, and J_v are, then by Eq. (38)

$$\tau_1=1-\frac{f_{1m}+f_{1w}-X\zeta_{12}}{f_{2m}+f_{2w}+X\zeta_{12}}\frac{(C_s^{I2}+C_s^{II2})\phi_w^2}{2X^2}. \tag{43}$$

Salt Flow in Open-Circuit Systems

The open-circuit system ($I=0$) is of biological interest for several reasons, two being that the resting potential and most passive flows are measured under this condition. Furthermore, it provides an instructive case for illustrating the differences between salt flow in single-salt systems and in ionic systems. Eqs. (12) and (13) show that there is a significant difference in the equations for neutral salt flow in the two types of systems. To make a concrete illustration of this difference, let us pose a question. Given that $I=0$, and, in the language of the neurophysiologist, that $E_K = -\dfrac{RT}{F}\ln C_K^I/C_K^{II}$ is held constant, is the flow of potassium ($J_K=J_{Cl}=J_s$) definitely determined?

If we have only KCl and nonelectrolytes in the bathing solutions, the answer is "yes" because of Eq. (13). But if impermeable chloride salts are

present, the answer is "not at all". In fact, the flow J_K might be positive, negative, or zero! As an example, fix the value of $C_K^I - C_K^{II} > 0$. Set $C_K^I = C_{Cl}^I$ in reservoir I. In reservoir II we put a chloride salt of a large protein in a concentration C_p^{II} and with a degree of ionization v_p. Electroneutrality gives

$$C_K^{II} + v_p C_p^{II} = C_{Cl}^{II}. \tag{44}$$

The ionic flow Eq. (38) gives

$$J_K(=J_s) = \frac{\phi_w^2 K_2}{X \Delta x} (C_K^{I^2} - C_K^{II^2}) - \frac{\phi_w^2 K_2}{X \Delta x} C_K^{II} v_p C_p^{II}. \tag{45}$$

If $C_p^{II} = 0$, we have $J_K > 0$. As protein salts are added to solution II, J_K decreases and reaches zero. Further increase of C_p^{II} finally makes $J_K < 0$. All the while, E_K is held constant and the current is zero.

Let us denote the potassium-chloride salt concentration by C_{s1}. Then $C_K^I = C_{s1}^I$ and $C_K^{II} = C_{s1}^{II}$. Eq. (45) can be written

$$J_K(=J_s) = \omega_{s1} \Delta \pi_{s1} - \frac{\phi_w^2 K_2}{X \Delta x} C_{s1}^{II} v_p C_p^{II}, \tag{46}$$

with

$$\omega_{s1} = \frac{\phi_w^2 K_2 C_{s1}}{RTX \Delta x} \tag{47}$$

and

$$\Delta \pi_{s1} = 2RT(C_{s1}^I - C_{s1}^{II}). \tag{48}$$

We see that in ionic systems there is a colloidal correction term to the *practical* equation for salt flow.

Appendix

The two terms of importance in $a_1 \Delta x$ are

$$\frac{C_w \zeta_{1w}}{RTX} \frac{I}{F} \Delta x \quad \text{and} \quad \frac{J_w \zeta_{1w}}{RT} \Delta x.$$

The following values are reasonable for a wide class of artificial membranes:

$$f_{1w} = C_w \zeta_{1w} = 1.5 \times 10^{15} \text{ dynes-sec/mole-cm}$$
$$\text{(the value for potassium in free solution);}$$
$$\Delta x = 10^{-2} \text{ cm};$$
$$X = 10^{-3} \text{ moles/cm}^3;$$
$$I = 10^{-2} \text{ amps/cm}^2;$$

which gives

$$\frac{C_w \zeta_{1w}}{RTX} \frac{I}{F} \Delta x \cong 0.05.$$

For a membrane of biological dimensions —

$$\Delta x = 70\,\text{A};$$

$$X = 10^{-3}\,\text{moles/cm}^3;$$

$$I = 50\,\text{amps/cm}^2 \text{ of aqueous channel,}$$

we have

$$\frac{C_w \zeta_{1w}}{RTX} \frac{I}{F} \Delta x \cong 0.02.$$

The expansion is certainly valid for any water flows satisfying

$$J_w < \frac{10^{-8}\,\text{cm}}{\Delta x}\ \text{moles/cm}^2\text{-sec.}$$

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