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The Biological Membrane Potential: A Thermodynamic Approach

Tormod Førland and Terje Østvold

Norwegian Institute of Technology, Division of Physical Chemistry,
and College of Arts and Science, Chemistry Department, The University
of Trondheim, Trondheim, Norway

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Summary. The emf of the following galvanic cell

$$\mathrm{Ag}\,|\,\mathrm{AgCl}\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\,|\,C_{\mathrm{K}}(1)\,C_{\mathrm{Na}}(1)\,C_{\mathrm{Cl}}(1)\,C_{\mathrm{R}}(1)\,|\text{ Membrane }|$$
$$C_{\mathrm{K}}(2)\,C_{\mathrm{Na}}(2)\,C_{\mathrm{Cl}}(2)\,C_{\mathrm{R}}(2)\,|\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\mathrm{AgCl}\,|\,\mathrm{Ag}$$

is calculated on the basis of classical irreversible thermodynamics. The membrane is permeable to water, K^+, Na^+ and Cl^- ions, but impermeable to the anion R^-. If the membrane consists of separate channels for transport of cations and anions, these channels being charged or neutral, the emf calculated for the present cell can be approximated by the equation

$$E=\frac{RT}{F}\left\{(1-t'_{\mathrm{Cl}})\ln\frac{C_{\mathrm{Na}}(1)+\dfrac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}KC_{\mathrm{K}}(1)}{C_{\mathrm{Na}}(2)+\dfrac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}KC_{\mathrm{K}}(2)}-t'_{\mathrm{Cl}}\ln\frac{C_{\mathrm{Cl}}(1)}{C_{\mathrm{Cl}}(2)}\right\}$$

which for zero transport number of Cl^- ions in the membrane, $t'_{\mathrm{Cl}}=0$, gives

$$E=\frac{RT}{F}\ln\frac{C_{\mathrm{Na}}(1)+\dfrac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}KC_{\mathrm{K}}(1)}{C_{\mathrm{Na}}(2)+\dfrac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}KC_{\mathrm{K}}(2)}.$$

In these equations u' is the mobility of an ion in the membrane and C is the concentration of an ion in solution. K is the equilibrium constant for the equilibrium

$$\mathrm{KCl(aq)}+\mathrm{NaM(membrane)}=\mathrm{NaCl(aq)}+\mathrm{KM(membrane)}.$$

The second equation is recognized as the Goldman-Hodgkin-Katz equation for "the membrane potential" when the membrane is cation conducting. The present equations, however, give the total emf for the galvanic cell including *not negligible* contributions to the cell potential from the KCl salt bridges.

Goldman (1943) has presented a detailed calculation of the potential difference between two solutions separated by a nerve membrane. Goldman considered this to be a solid membrane immersed in a solution containing ions moving under the combined influence of diffusion and electrical forces. The membrane was assumed to be a uniform system in which the ion mobilities and activity coefficients were constant. Hodgkin and Katz (1949) later assumed that the concentration of ions in the membrane at its edges were proportional to those in the electrolyte solutions in contact with it. On the results obtained by Goldman and on the basis of this additional assumption, Hodgkin and Katz presented the well-known Goldman-Hodgkin-Katz (G-H-K) equation for the membrane potential. Having the electrolytes NaCl and KCl with concentration gradients across the membrane, the G-H-K equation is given by

$$E=\frac{RT}{F}\ln\frac{P_{\mathrm{Na}}C_{\mathrm{Na}}(1)+P_{\mathrm{K}}C_{\mathrm{K}}(1)+P_{\mathrm{Cl}}C_{\mathrm{Cl}}(2)}{P_{\mathrm{Na}}C_{\mathrm{Na}}(2)+P_{\mathrm{K}}C_{\mathrm{K}}(2)+P_{\mathrm{Cl}}C_{\mathrm{Cl}}(1)}. \tag{1}$$

In this equation, E is the potential difference between the right-hand-side electrolyte (2), and the left-hand-side electrolyte (1), C with subscript is concentration in solution of the different ions, and P_{Na}, P_{K} and P_{Cl} are permeability coefficients. These coefficients are defined as $u'\beta RT/aF$ where u' is the mobility of an ion in the membrane, β the partition coefficient between membrane and solution, a is the thickness of the membrane, and R, T and F have their usual meanings. The potential given by the G-H-K equation is not a measurable quantity and assumptions which are not possible to control experimentally must be introduced before measured potentials can be compared with Eq. (1). We therefore find it useful to present a calculation of the emf of a concentration cell containing a membrane with transport properties similar to what we may find in biological membranes without introducing assumptions which can not be checked by experiment or which do not rest on well-founded thermodynamic arguments.

Presentation of the Problem

To demonstrate our alternative method for calculating cell potentials we choose the following galvanic cell:

$$\mathrm{Ag}\,|\,\mathrm{AgCl}\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\,|\,C_{\mathrm{K}}(1)\,C_{\mathrm{Na}}(1)\,C_{\mathrm{Cl}}(1)\,C_{\mathrm{R}}(1)\,|\cdot\text{Membrane}$$

$$|\,C_{\mathrm{K}}(2)\,C_{\mathrm{Na}}(2)\,C_{\mathrm{Cl}}(2)\,C_{\mathrm{R}}(2)\,|\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\mathrm{AgCl}\,|\,\mathrm{Ag}.$$

The fundamental equation for calculation of an emf of a reversible galvanic cell is $\Delta G + FE = 0$ where ΔG is the total change in Gibbs energy in the cell per Faraday transferred. This equation is based on the first and second law of thermodynamics. If an irreversible diffusion process takes place in the cell, in addition to the process connected to the charge transfer, the problem can be dealt with within the framework of irreversible thermodynamics.

The Gibbs energy of the cell will change during charge trnasfer due to the irreversible diffusion that takes place and due to the charge transfer itself. It can be shown from the postulates of irreversible thermodynamics (Förland, 1964; Förland, Thulin & Østvold, 1971) that the Gibbs energy change can be separated into two parts, one time-dependent, $\Delta G_{(t)}$, and one dependent on the electric charge transferred, $\Delta G_{(Q)}$, and the last one only is connected to the outer emf, E:

$$\Delta G_{(Q)} + FE = 0. \tag{2}$$

This equation is the same as the above equation for a cell with reversible reactions only. ΔG_Q is given by the following equation (*see* Förland & Thulin, 1968; Förland *et al.*, 1971):

$$\Delta G_Q = \Delta G' - \int_{\substack{\text{over} \\ \text{cell}}} \sum_i \mu_i \, dt_i \tag{3}$$

where $\Delta G'$ is the change in Gibbs energy at and close to the two electrodes. The summation is carried out over all components, in the phase law sense, necessary to describe the system. ΔG_Q can be calculated when the cell reaction is known and when the transport coefficient of neutral components t_i, and the chemical potentials μ_i of the components of the cell have been measured. The transport coefficient t_i simply expresses the result of a Hittorf transport experiment, where it is found by chemical analysis that a quantity t_i of component i has moved from left to right in a Hittorf cell when 1 Faraday of positive charge has passed through the cell in the same direction. Such a transport coefficient for a neutral component will depend on the kind of electrodes used and the frame of reference chosen for the movement of components. We will show that the statement that the electric potential difference over the cell according to Eq. (1) is created over the membrane, leads to a contradiction when compared with the more fundamental Eq. (3).

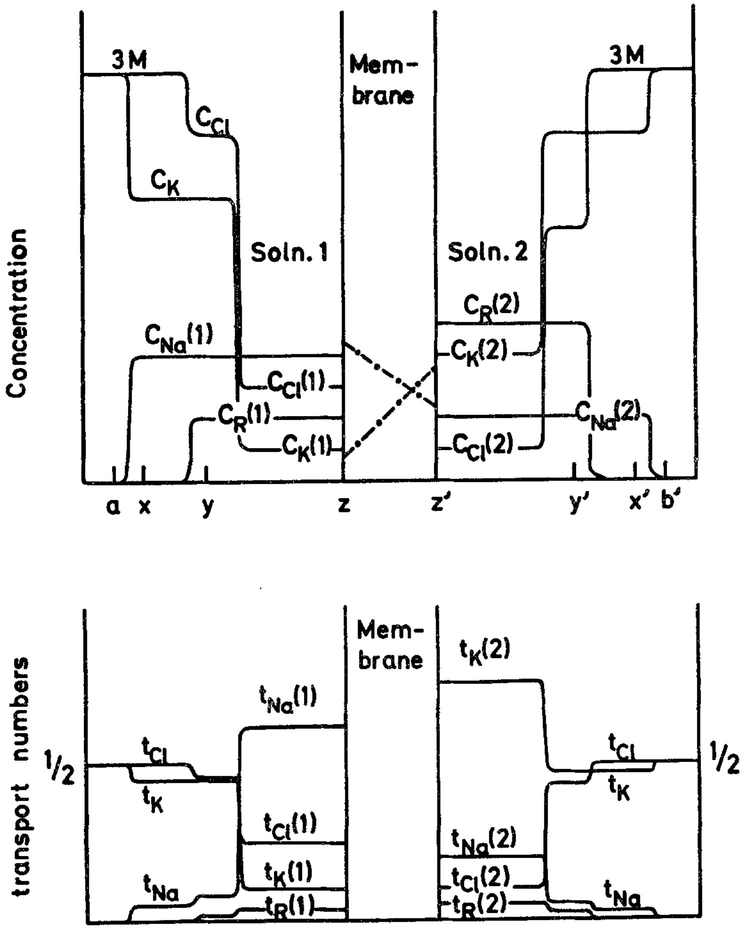

Fig. 1. Schematic diagram of the concentration cell

$$\mathrm{Ag}\,|\,\mathrm{AgCl}\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\,|\,C_{\mathrm{K}}(1)\,C_{\mathrm{Na}}(1)\,C_{\mathrm{Cl}}(1)\,C_{\mathrm{R}}(1)\,|\cdot\text{Membrane}$$

$$|\,C_{\mathrm{K}}(2)\,C_{\mathrm{Na}}(2)\,C_{\mathrm{Cl}}(2)\,C_{\mathrm{R}}(2)\,|\left|\begin{matrix}\mathrm{KCl}\\ 3\,\mathrm{M}\end{matrix}\right|\mathrm{AgCl}\,|\,\mathrm{Ag}$$

showing the variation of concentrations and transport numbers in the aqueous phases along the length of the cell

The cell considered is shown in Fig. 1. In this cell the two electrodes and their close surroundings are identical and $\Delta G' = 0$. The integral $-\int \sum_i \mu_i dt_i$ gives the change in Gibbs energy due to change in composition by charge transfer in the different sections of the cell. In any region where all t_i are constant the change in Gibbs energy is zero. To calculate the total change in composition of the electrolyte over the different sections of the cell, the choice of frame of reference for the movement of all components has no influence on the final result. For the region of concentration gradients in the aqueous phases it is most practical to refer to water as a frame of reference. In the region of the membrane we find it most practical to refer all transport to the membrane as a frame of reference. The solutions contain the four ions K^+, Na^+, Cl^- and R^-. Due to the requirement of electroneutrality, the composition may be described by the content of three components, e.g. KCl, NaCl and KR.

In biological membranes, only transport by K^+, Na^+ and Cl^- ions is considered, and we will therefore in the following discussion assume that the mobility of the R^- anion is negligible in the membrane. It is convenient to split the integrals in Eq. (3) into three parts, one part including the contribution to the Gibbs energy change due to transport in the potassium chloride bridges, ΔG_b, a second part including contributions to ΔG_Q from transport at the interfaces, ΔG_{int}, and the last part which is due to the Gibbs energy change in the membrane, ΔG_m, by the charge transfer.

The Gibbs energy change due to transport in the potassium chloride bridges (*see* Fig. 1), ΔG_b, can be expressed by the equation:

$$\begin{aligned}\Delta G_b = &- \int\limits_{\substack{a\to z\\ \text{over KCl-}\\ \text{gradient}}} \{\mu_{\text{KCl}}\, d t_{\text{KCl}} + \mu_{\text{NaCl}}\, d t_{\text{NaCl}} + \mu_{\text{KR}}\, d t_{\text{KR}}\}\\ &- \int\limits_{\substack{z\to b\\ \text{over KCl-}\\ \text{gradient}}} \{\mu_{\text{KCl}}\, d t_{\text{KCl}} + \mu_{\text{NaCl}}\, d t_{\text{NaCl}} + \mu_{\text{KR}}\, d t_{\text{KR}}\}\end{aligned} \tag{4}$$

where μ_i and t_i denote chemical potential and Hittorf transport coefficient of the neutral component i in solution, respectively.

In the regions $a-z$ and $z'-b'$, water is used as the frame of reference for transport, and the chemical work carried out in these regions during charge transfer is calculated from Eq. (4). In the region of the membrane the membrane matrix will be used as a frame of reference in the present calculation. We therefore have to calculate how this change of coordinate system for the frame of reference will influence our calculation of the total change in Gibbs energy following the cell reaction. In Fig. 2 a schematic diagram of what is happening at the two membrane-electrolyte interfaces, $MEi(1)$ and $MEi(2)$ is shown.

When a small positive charge dQ is passed through the cell from the left- to the right-side electrode at reversible conditions

$$\left(t'_{\text{KM}}(2) - \left(t_{\text{KCl}}(2) + t'_{\text{H}_2\text{O}}(2)\frac{C_{\text{KCl}}(2)}{C_{\text{H}_2\text{O}}(2)}\right)\right)\frac{dQ}{F}$$

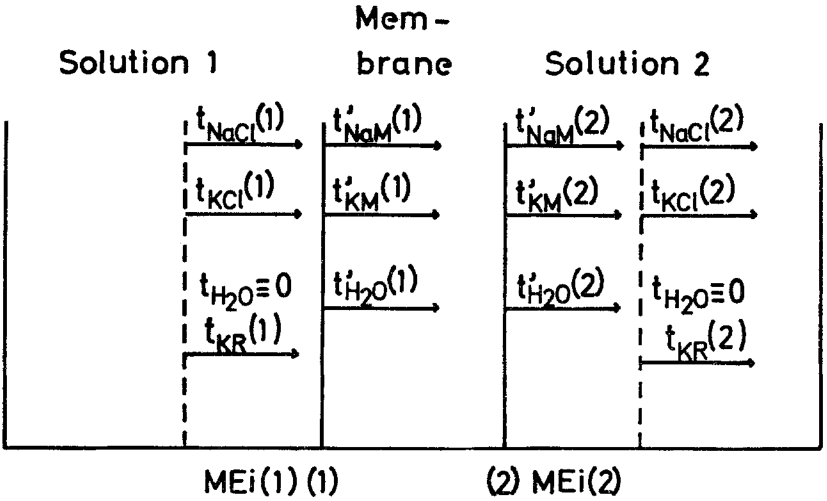

Fig. 2. Transport coefficient in electrolyte (H_2O is chosen as frame of reference) and transport coefficients in membrane (membrane matrix is chosen as frame of reference) at the membrane electrolyte interfaces

moles of KCl are added to the right-hand half-cell at interface *MEi*(2). At the same time

$$\left(t'_{\mathrm{KM}}(1)-\left(t_{\mathrm{KCl}}(1)+t'_{\mathrm{H_2O}}(1)\,\frac{C_{\mathrm{KCl}}(1)}{C_{\mathrm{H_2O}}(1)}\right)\right)\frac{dQ}{F}$$

moles of KCl are taken out of the left-hand side at the interface *MEi*(1). The primed membrane framed transport coefficient t'_{KM} is to be understood as the amount measured in equivalents of KCl which is transferred through the membrane for each equivalent of electric charge in a Hittorf experiment with Cl^- electrodes. Since $t'_{\mathrm{H_2O}}\cdot\frac{C_{\mathrm{salt}}}{C_{\mathrm{H_2O}}}$ normally is very small ($C_{\mathrm{H_2O}}\simeq 500\cdot C_{\mathrm{salt}}$) this term can be neglected in the calculation of ΔG_{int}. Counting potassium chloride, sodium chloride, potassium-R and water transport we get the following equation for the chemical work done at the interfaces per Faraday transferred:

$$\begin{aligned}\Delta G_{\mathrm{int}}={}&(t'_{\mathrm{KM}}(2)-t_{\mathrm{KCl}}(2))\,\mu_{\mathrm{KCl}}(2)+(t'_{\mathrm{NaM}}(2)-t_{\mathrm{NaCl}}(2))\,\mu_{\mathrm{NaCl}}(2)\\&+t'_{\mathrm{H_2O}}(2)\,\mu_{\mathrm{H_2O}}(2)-(t'_{\mathrm{KM}}(1)-t_{\mathrm{KCl}}(1))\,\mu_{\mathrm{KCl}}(1)\\&-(t'_{\mathrm{NaM}}(1)-t_{\mathrm{NaCl}}(1))\,\mu_{\mathrm{NaCl}}(1)-t'_{\mathrm{H_2O}}(1)\,\mu_{\mathrm{H_2O}}(1)\\&+t_{\mathrm{KR}}(1)\,\mu_{\mathrm{KR}}(1)-t_{\mathrm{KR}}(2)\,\mu_{\mathrm{KR}}(2)\end{aligned}\tag{5}$$

where the indexes (1) and (2) on unprimed quantities denote electrolyte 1 and 2, respectively. The primed quantities marked (1) and (2) denote the value of these quantities on the left and right side of membrane, respectively.

The Gibbs energy change in the membrane, ΔG_m, due to the charge transfer can, according to Eq. (3), be expressed by the equation

$$\Delta G_m = - \int\limits_{\substack{z \to z' \\ \text{over} \\ \text{membrane}}} \{\mu'_{\text{KM}}\, d\,t'_{\text{KM}} + \mu'_{\text{NaM}}\, d\,t'_{\text{NaM}} + \mu'_{\text{ClM}}\, d\,t'_{\text{ClM}} + \mu'_{\text{H}_2\text{O}}\, d\,t'_{\text{H}_2\text{O}}\} \tag{6}$$

where μ'_{KM}, μ'_{NaM}, μ'_{ClM} and $\mu'_{\text{H}_2\text{O}}$ indicate chemical potentials of K-membrane, Na-membrane, Cl-membrane and H_2O, respectively in membrane. The primed transport coefficient t'_{ClM} is to be understood as the amount measured in equivalents of ClM (or Cl^-) transported from left to right through the membrane for each equivalent of positive charge passed in the same direction.

In the present discussion we have so far used transport coefficients of neutral components. With electrodes reversible to the Cl^- anion, t_{KCl}, t_{NaCl} and t_{KR} obtained from Hittorf experiments are related to the ionic transport numbers, t_{K}, t_{Na} and t_{R} through the relations $t_{\text{KCl}} = t_{\text{K}} + t_{\text{R}}$, $t_{\text{NaCl}} = t_{\text{Na}}$ and $t_{\text{KR}} = -t_{\text{R}}$. The primed transport coefficients t'_{KM} and t'_{NaM} are equal to the ionic transport numbers t'_{K} and t'_{Na}, respectively, and $t'_{\text{ClM}} = -t'_{\text{Cl}}$.

Introducing ionic transport numbers, Eq. (3) can be written

$$\begin{aligned}
\Delta G_Q &= \Delta G_b + \Delta G_{\text{int}} + \Delta G_m \\
&= - \int\limits_{\substack{a \to z \\ \text{over KCl-} \\ \text{gradient}}} (\mu_{\text{KCl}}(d\,t_{\text{K}} + d\,t_{\text{R}}) + \mu_{\text{NaCl}}\, d\,t_{\text{Na}} - \mu_{\text{KR}}\, d\,t_{\text{R}}) \\
&\quad - \int\limits_{\substack{z' \to b' \\ \text{over KCl-} \\ \text{gradient}}} (\mu_{\text{KCl}}(d\,t_{\text{K}} + d\,t_{\text{R}}) + \mu_{\text{NaCl}}\, d\,t_{\text{Na}} - \mu_{\text{KR}}\, d\,t_{\text{R}}) \\
&\quad + (t'_{\text{K}}(2) - t_{\text{K}}(2) - t_{\text{R}}(2))\,\mu_{\text{KCl}}(2) + (t'_{\text{Na}}(2) - t_{\text{Na}}(2))\,\mu_{\text{NaCl}}(2) \\
&\quad + t'_{\text{H}_2\text{O}}(2)\,\mu_{\text{H}_2\text{O}}(2) - (t'_{\text{K}}(1) - t_{\text{K}}(1) - t_{\text{R}}(1))\,\mu_{\text{KCl}}(1) \\
&\quad - (t'_{\text{Na}}(1) - t_{\text{Na}}(1))\,\mu_{\text{NaCl}}(1) - t'_{\text{H}_2\text{O}}(1)\,\mu_{\text{H}_2\text{O}}(1) \\
&\quad - t_{\text{R}}(1)\,\mu_{\text{KR}}(1) + t_{\text{R}}(2)\,\mu_{\text{KR}}(2) \\
&\quad - \int\limits_{\substack{z \to z' \\ \text{over} \\ \text{membrane}}} \{\mu'_{\text{KM}}\, d\,t'_{\text{K}} + \mu'_{\text{NaM}}\, d\,t'_{\text{Na}} - \mu'_{\text{ClM}}\, d\,t'_{\text{Cl}} + \mu'_{\text{H}_2\text{O}}\, d\,t'_{\text{H}_2\text{O}}\}.
\end{aligned} \tag{7}$$

Calculation of ΔG_B

The transport numbers t_{K}, t_{Na}, t_{R} and t_{Cl} are functions of composition and may change along the length of the galvanic cell in a way similar to what is shown in Fig. 1. Therefore, the salts KCl, NaCl and KR are transported across the salt bridges when current passes through cell. This transport will contribute to ΔG_Q and thus to the observed emf. We will show in the present calculation that this contribution to ΔG_Q is far from being negligible.

It should be mentioned that the KCl salt bridges have been given a Na^+ and R^- content in that part of the bridge which is close to the electrolytes (1) and (2) of the cell. This is done to make the liquid junction reproducible and well defined, and it simplifies the calculation of the integral in Eq. (7), and diffusion data are not needed. It is reasonable to assume that this type of liquid junction will give practically the same potential as the one usually made. Work to check this assumption experimentally is now in progress.

Since the activity coefficients are usually not known as functions of concentration for biological electrolytes found in living cells we may, as a first approximation, operate with low concentration of electrolyte and assume ideal solutions.

In aqueous electrolytes the mobility ratios u_i/u_j of the ions are usually close to being concentration independent and the ionic transport numbers can be expressed as simple functions of concentration and mobility. In the present case

$$t_{\mathrm{K}} = \frac{C_{\mathrm{K}}\, u_{\mathrm{K}}}{C_{\mathrm{K}}\, u_{\mathrm{K}} + C_{\mathrm{Na}}\, u_{\mathrm{Na}} + C_{\mathrm{Cl}}\, u_{\mathrm{Cl}} + C_{\mathrm{R}}\, u_{\mathrm{R}}} \tag{8}$$

and similarly for all the other ionic transport numbers. In this equation u and C mean ionic mobilities and concentrations, respectively. In the different regions of the cell the ionic transport numbers are changing due to the change in concentration of one component (*see* Fig. 1). In the region $a-x$, t_{Na}, t_{K} and t_{Cl} are changing since the concentration of KCl is reduced with the same amount as the concentration of NaCl is increased. Therefore, t_{Cl}, t_{Na} and t_{K} can be expressed as functions of the concentration of Na^+ ions. In the region $x-y$ the ionic transport numbers can be expressed as functions of the concentration of R^- ions and in the region $y-z$ as functions of the concentration of K^+ ions. In the Appendix the calculation is presented. The final result of this calculation is given by the following equation:

$$\begin{aligned} \Delta G_b = {} & (t_{\mathrm{K}}(2) + t_{\mathrm{R}}(2))\, \mu_{\mathrm{KCl}}(2) + t_{\mathrm{Na}}(2)\, \mu_{\mathrm{NaCl}}(2) - t_{\mathrm{R}}(2)\, \mu_{\mathrm{KR}}(2) \\ & - (t_{\mathrm{K}}(1) + t_{\mathrm{R}}(1))\, \mu_{\mathrm{KCl}}(1) - t_{\mathrm{Na}}(1)\, \mu_{\mathrm{NaCl}}(1) + t_{\mathrm{R}}(1)\, \mu_{\mathrm{KR}}(1) \\ & - RT \ln \frac{C_{\mathrm{Cl}}(2)}{C_{\mathrm{Cl}}(1)}. \end{aligned} \tag{9}$$

Calculation of ΔG_m and the Cell Potential, E

After partial integration of the last term in Eq. (6) the Gibbs energy change due to the cell reaction in the membrane, ΔG_m, is given by

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu'_{H_2O}(1) - t'_{H_2O}(2)\,\mu'_{H_2O}(2) \\ & - \int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}} \{\mu'_{KM}\,dt'_K + \mu'_{NaM}\,dt'_{Na} - \mu'_{ClM}\,dt'_{Cl} - t'_{H_2O}\,d\mu'_{H_2O}\}.\end{aligned} \tag{10}$$

In dilute solutions with the same ionic strength, the chemical potential of water does not vary much and we may therefore, in the present calculation, without introducing any serious error, neglect the contribution to ΔG_m from the term $\int t'_{H_2O}\,d\mu'_{H_2O}$.

It is practical in the final result to have an equation that relates the emf of the cell to the concentration of the two electrolytes in half-cells (1) and (2). One cannot integrate the above equation and obtain such a result without introducing further assumptions. We will in the following discussion introduce two methods to calculate ΔG_m, one which is traditional and one which is somewhat different.

Integration through the Membrane Phase

The method which will be discussed resembles the method introduced by Goldman (1943) and Hodgkin and Katz (1949) but deviates from their calculations in the approximations introduced.

Since the chemical potential of water is considered constant through the membrane ($\mu'_{H_2O}(1) = \mu'_{H_2O}(2)$), the above equation can be written

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu'_{H_2O}(1) - t'_{H_2O}(2)\,\mu'_{H_2O}(2) \\ & - \int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}} \{\mu'_{KM}\,dt'_K + \mu'_{NaM}\,dt'_{Na} - \mu'_{ClM}\,dt'_{Cl}\}.\end{aligned} \tag{11}$$

Let us consider a membrane which contains anion as well as cation channels through which anions and cations, respectively, can transport electric charge. These channels may partly consist of dipoles with positive side toward the center of the channel and partly of positively charged molecules close to the channel wall. The excess positive charge of the channel wall may be compensated for by Cl^- ions. These channels will be Cl^--ion conducting. Likewise, cation channels may partly consist of dipoles with negative side toward the center of the channel and partly of negatively charged molecules close to the channel wall. Again the excess negative charge of the channel wall may be compensated for by Na^+ and K^+ cations.

If the ion transport through the membrane takes place through such channels, only (i.e., that there is no free solution shunt), it is reasonable to assume that the Cl^- ion transport number will be constant through the membrane. The value of the constant will depend on what type of cations we have in solution.

To calculate the integrals in Eq. (11) we will introduce the assumptions:

(1) The membrane contains negative and positive sites over which the ions Na^+, K^+ and Cl^- can transport electric charge. There is no solution shunt.

(2) The concentration of negative and positive sites in membrane is constant.

(3) There are constant activity coefficients in membrane of the KM and NaM salts.

(4) Equilibrium is established at the membrane-electrolyte interfaces.

(5) The transport number of chloride ions in membrane is constant.

The calculation is presented in the Appendix, and the final result is given by Eq. (A.21)

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu_{H_2O}(1) - t'_{H_2O}(2)\,\mu_{H_2O}(2) \\ & + t'_K(1)\,\mu_{KCl}(1) + t'_{Na}(1)\,\mu_{NaCl}(1) - t'_K(2)\,\mu_{KCl}(2) - t'_{Na}(2)\,\mu_{NaCl}(2) \\ & - RT(1-t'_{Cl})\left\{\ln\frac{C_{Cl}(1)}{C_{Cl}(2)} + \ln\frac{C_{Na}(1)+\frac{u'_K}{u'_{Na}}K\,C_K(1)}{C_{Na}(2)+\frac{u'_K}{u'_{Na}}K\,C_K(2)}\right\}.\end{aligned} \tag{12}$$

In this equation K is the equilibrium constant for the exchange equilibrium KCl(aq) + NaM(membrane) = KM(membrane) + NaCl(aq).

Introducing the results obtained in Eqs. (5), (9) and (12) in Eq. (7) we obtain the Gibbs energy change, ΔG_Q, for the cell reaction

$$\Delta G_Q = -RT\left\{(1-t'_{Cl})\ln\frac{C_{Na}(1)+\frac{u'_K}{u'_{Na}}K\,C_K(1)}{C_{Na}(2)+\frac{u'_K}{u'_{Na}}K\,C_K(2)} - t'_{Cl}\ln\frac{C_{Cl}(1)}{C_{Cl}(2)}\right\}. \tag{13}$$

The emf of the present cell, E, is thus given by

$$E=\frac{RT}{F}\left\{(1-t'_{\mathrm{Cl}})\ln\frac{C_{\mathrm{Na}}(1)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(1)}{C_{\mathrm{Na}}(2)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(2)}-t'_{\mathrm{Cl}}\ln\frac{C_{\mathrm{Cl}}(1)}{C_{\mathrm{Cl}}(2)}\right\}. \tag{14}$$

This equation deviates significantly from the G-H-K equation when Cl^- mobility in the membrane is considered.

If the membrane is cation-conducting only, $t'_{\mathrm{Cl}}=0$ and the cell potential is given by

$$E=\frac{RT}{F}\ln\frac{C_{\mathrm{Na}}(1)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(1)}{C_{\mathrm{Na}}(2)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(2)} \tag{15}$$

which will be recognized as the classical G-H-K equation.

If two silver-silver chloride electrodes are dipped directly into electrolyte (1) and electrolyte (2), respectively, the emf of the cell obtained, Ag | AgCl | electrolyte (1) | Membrane | electrolyte (2) | AgCl | Ag, is easily calculated.

Using Eq. (3) and referring movements of components to the membrane matrix as a frame of reference, we obtain

$$\begin{aligned}\Delta G_Q={}&t'_{\mathrm{Na}}(2)\,\mu_{\mathrm{NaCl}}(2)+t'_{\mathrm{K}}(2)\,\mu_{\mathrm{KCl}}(2)-t'_{\mathrm{Na}}(1)\,\mu_{\mathrm{NaCl}}(1)-t'_{\mathrm{K}}(1)\,\mu_{\mathrm{KCl}}(1)\\&+t'_{\mathrm{H_2O}}(2)\,\mu_{\mathrm{H_2O}}(2)-t'_{\mathrm{H_2O}}(1)\,\mu_{\mathrm{H_2O}}(1)+\Delta G_m\ \text{(Eq. (12))}\end{aligned} \tag{16}$$

which gives

$$E=\frac{RT}{F}(1-t'_{\mathrm{Cl}})\left\{\ln\frac{C_{\mathrm{Cl}}(1)}{C_{\mathrm{Cl}}(2)}+\ln\frac{C_{\mathrm{Na}}(1)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(1)}{C_{\mathrm{Na}}(2)+\frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}}K\,C_{\mathrm{K}}(2)}\right\}. \tag{17}$$

Integration over Solutions in Equilibrium with Membrane at any Point Through the Membrane

Instead of integrating Eq. (11) in the way just outlined, an alternative method will be proposed. If we assume that we can split the membrane at any point and introduce a solution containing Na^+, K^+, Cl^- and R^- ions without changing the membrane composition at that point, we can, instead of integrating over the membrane phase, integrate over solutions in equilibrium with it (*see* Förland & Thulin, 1968). *If the transport numbers in the membrane are measured by the Hittorf method and the aqueous chemical potentials are known as functions of concentration, no assumptions, except that of a homogeneous membrane, have to be introduced in the calculation of* ΔG_m. Due to insufficient data, however, we have to introduce the following assumptions:

(1) The membrane is homogeneous.

(2) It is possible at any point of the membrane to make a solution which is in equilibrium with the membrane from mixtures of the two half-cell solutions (Scatchard, 1953).

(3) There are constant activity coefficients of KCl and NaCl.

(4) Equilibrium is established at the membrane-electrolyte interfaces.

(5) The transport number of Cl^- ions in membrane is constant.

Starting with Eq. (11) we obtain

$$\Delta G_m = t'_{H_2O}(1)\,\mu'_{H_2O}(1) - t'_{H_2O}(2)\,\mu'_{H_2O}(2) - \int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}} (\mu'_{KM} - \mu'_{NaM})\,dt'_K. \qquad (18)$$

Along the integration path, assumed chemical equilibrium is established between membrane and solution. When this is introduced in Eq. (18), we get

$$\Delta G_m = t'_{H_2O}(1)\,\mu'_{H_2O}(1) - t'_{H_2O}(2)\,\mu'_{H_2O}(2) - \int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}} \{\mu_{KCl}\,dt'_K + \mu_{NaCl}\,dt'_{Na}\}. \qquad (19)$$

In the Appendix this integration is done and the result is identical with that given in Eq. (A.21). The emf of the cell is again equal to the result given by Eq. (14).

Discussion

Comparison with the Goldman-Hodgkin-Katz Equation

In the calculation of the emf of the above galvanic cell we have used two methods which both are as exact as the laws of irreversible and classical thermodynamics. The weaknesses with the calculations, however, are the approximations introduced. These approximations are such that they in principle can be controlled experimentally. In our first method which is similar to traditional membrane potential-calculations we introduce constant concentration of positive and negative sites across the membrane and constant activity coefficients in membrane assumptions which may not be likely to hold experimentally. The calculation is therefore more meant as an illustration of the approach than as a serious attack on the theoretical problems of membrane potentials. In the second method, however, the approximations introduced seem to us not as restrictive as in the above-mentioned calculation, and some preliminary experimental data seem to indicate that the integration path assumed in the second approach gives good agreement between calculated and measured potentials when the calculation is based on measured transport numbers and activities.

The fundamental difference between the method of emf calculation expressed by the G-H-K equation, Eq. (1), and the method outlined in this paper expressed by Eq. (14) is that in the latter one does not attempt to calculate any quantity that cannot be measured, whereas in the former one operates with unmeasurable quantities. In most cases these unmeasurable quantities will be combined to give measurable quantities in the final result, the calculated emf of the cell, so the two approaches give the same final answer. However, problems may arise when the former method is used, if one wants to bring in physical interpretations during the calculation (e.g., in connection with approximations introduced).

Equations like Eq. (1) give detailed information about where the electric potential difference arises. In the case of the present cell, this is across the membrane, even though this cannot be checked by measurements. Assumptions which are not possible to control experimentally must be introduced before measured potentials can be compared with Eq. (1). Eq. (3), on the other hand, can tell us in an exact way where in the cell the cause of the measured emf is to be found, since contributions to ΔG_Q are well-defined measurable quantities in any section of the cell. When the membrane is cation-conducting the result of the present calculation, based on Eq. (3), is given by Eq. (15) which is identical with the G-H-K equation for the membrane potential. It is evident from the present calculation that the contribution to the cell potential from the KCl salt bridges is considerable. The statement that the electric potential difference over the cell according to Eq. (1) is created over the membrane therefore leads to a contradiction when compared with the results obtained by using the more fundamental Eq. (3).

Comparison with Experimental Results

For galvanic cells with biological membranes it is difficult to give a satisfactory explanation of all experimental results using the classical G-H-K equation.

Baker, Hodgkin and Shaw (1962), Baker, Hodgkin and Meves (1964), Spyropoulos and Teorell (1968), Barry, Diamond and Wright (1971) and Spyropoulos (1972) have reported extensive observations on the electrical properties of biological membranes. Some of their experimental results showed that the cell potential varied linearly with logarithm of concentration of the external electrolyte (one solute only). A ten times reduction in the electrolyte concentration resulted in a change in emf ranging from 42 to 56 mV for potassium chloride to 6 to 21 mV for choline chloride. This is consistent with Eq. (14) and predicts a considerable Cl^- ion transport in membranes when the cation mobility is low.

Concluding Remarks

In the present communication the emf of a concentration cell containing membrane is calculated on the basis of classical irreversible thermodynamics. Instead of making the emphasis on unmeasurable local electric potential differences in the galvanic cell by the calculation of an emf, as is very frequently done, it is demonstrated in this paper that the emphasis should be on the gradients of chemical potential of neutral components of the cell and how the concentration of these components is changed by charge transfer; that means on the coupling between transport of charge and transport of components.

Appendix

Calculations of ΔG_Q

Calculation of the Gibbs energy change following the cell reaction for the galvanic cell

$$\mathrm{Ag}\,|\,\mathrm{AgCl}\left|\begin{array}{c}\mathrm{KCl}\\ 3\,\mathrm{M}\end{array}\right|\,|C_{\mathrm{K}}(1)\;C_{\mathrm{Na}}(1)\;C_{\mathrm{Cl}}(1)\;C_{\mathrm{R}}(1)\,|\;\mathrm{Membrane}\,|$$

$$\cdot\,C_{\mathrm{K}}(2)\;C_{\mathrm{Na}}(2)\;C_{\mathrm{Cl}}(2)\;C_{\mathrm{R}}(2)\,|\left|\begin{array}{c}\mathrm{KCl}\\ 3\,\mathrm{M}\end{array}\right|\mathrm{AgCl}\,|\,\mathrm{Ag}$$

will be presented here together with the assumptions made. As a starting point for the calculation we use Eq. (7) in the preceding text.

A. Calculation of ΔG_b.

$$\begin{aligned}\Delta G_b = &-\int\limits_{\substack{a\to z\\ \text{over KCl}\\ \text{gradient}}} \left(\mu_{\mathrm{KCl}}(d t_{\mathrm{K}} + d t_{\mathrm{R}}) + \mu_{\mathrm{NaCl}}\, d t_{\mathrm{Na}} - \mu_{\mathrm{KR}}\, d t_{\mathrm{R}}\right)\\ &-\int\limits_{\substack{z'\to b'\\ \text{over KCl-}\\ \text{gradient}}} \left(\mu_{\mathrm{KCl}}(d t_{\mathrm{K}} + d t_{\mathrm{R}}) + \mu_{\mathrm{NaCl}}\, d t_{\mathrm{Na}} - \mu_{\mathrm{KR}}\, d t_{\mathrm{R}}\right).\end{aligned} \tag{A.1}$$

Let us first calculate the first term, $\Delta G_{b(1)}$ in this equation.

$$\Delta G_{b(1)} = -\int_{a\to z} \left(\mu_{\mathrm{KCl}}(d t_{\mathrm{K}} + d t_{\mathrm{R}}) + \mu_{\mathrm{NaCl}}\, d t_{\mathrm{Na}} - \mu_{\mathrm{KR}}\, d t_{\mathrm{R}}\right)$$

$$\begin{aligned}\Delta G_{b(1)} = &-\Big|_{a\to z} \left(\mu_{\mathrm{KCl}}(t_{\mathrm{K}} + t_{\mathrm{R}}) + \mu_{\mathrm{NaCl}}\, t_{\mathrm{Na}} - \mu_{\mathrm{KR}}\, t_{\mathrm{R}}\right)\\ &+ \int_{a\to z} \left\{(t_{\mathrm{K}} + t_{\mathrm{R}})\, d\mu_{\mathrm{KCl}} + t_{\mathrm{Na}}\, d\mu_{\mathrm{NaCl}} - t_{\mathrm{R}}\, d\mu_{\mathrm{KR}}\right\}.\end{aligned} \tag{A.2}$$

The first term of this equation is equal to

$$t_{\mathrm{K}(3\,\mathrm{M})}\, \mu_{\mathrm{KCl}(3\,\mathrm{M})} - \left(t_{\mathrm{K}}(1) + t_{\mathrm{R}}(1)\right) \mu_{\mathrm{KCl}}(1) - t_{\mathrm{Na}}(1)\, \mu_{\mathrm{NaCl}}(1) + t_{\mathrm{R}}(1)\, \mu_{\mathrm{KR}}(1).$$

To calculate the integral in this equation one has to know the variables in each region where the composition changes in the bridge: In the region $a-x$,

$$C_{\mathrm{Na}} = C \text{ (variable)};\quad C_{\mathrm{K}} = C_{\mathrm{K}}(3\,\mathrm{M}) - C;\quad C_{\mathrm{Cl}} = C_{\mathrm{Cl}}(3\,\mathrm{M}) = \text{constant};$$

$$C_{\mathrm{R}} = 0$$

thus giving

$$t_{\mathrm{K}} = \frac{u_{\mathrm{K}}\, C_{\mathrm{K}}}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C} \tag{A.3}$$

$$t_{\mathrm{Na}} = \frac{u_{\mathrm{Na}}\, C}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C}; \tag{A.4}$$

In the region $x-y$,

$$C_{\mathrm{R}} = C \text{ (variable)};\quad C_{\mathrm{K}} = C_{\mathrm{K}}(3\,\mathrm{M}) - C_{\mathrm{Na}}(1) = \text{constant};$$

$$C_{\mathrm{Cl}} = C_{\mathrm{Cl}}(3\,\mathrm{M}) - C;\quad C_{\mathrm{Na}} = C_{\mathrm{Na}}(1) = \text{constant}$$

thus giving

$$t_{\mathrm{R}} = \frac{u_{\mathrm{R}}\, C}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) + (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C} \tag{A.5}$$

$$t_{\mathrm{Cl}} = \frac{u_{\mathrm{Cl}}\, C_{\mathrm{Cl}}}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) + (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C}; \tag{A.6}$$

In the region $y-z$,

$$C_{\mathrm{K}} = C \text{ (variable)};\qquad C_{\mathrm{Na}} = C_{\mathrm{Na}}(1) = \text{constant};$$

$$C_{\mathrm{R}} = C_{\mathrm{R}}(1) = \text{constant};\quad C_{\mathrm{Cl}} = C + C_{\mathrm{Na}}(1) - C_{\mathrm{R}}(1)$$

thus giving

$$t_{\mathrm{K}} = \frac{u_{\mathrm{K}}\, C}{\sum_i u_i C_i} \tag{A.7}$$

$$t_{\mathrm{Cl}} = \frac{u_{\mathrm{Cl}}\, C_{\mathrm{Cl}}}{\sum_i u_i C_i}. \tag{A.8}$$

Further, the chemical potential of a component will be expressed by the product of concentrations, e.g. $\mu_{\mathrm{KCl}} - \mu^0_{\mathrm{KCl}} = RT \ln C_{\mathrm{K}} \cdot C_{\mathrm{Cl}}$ corresponding to the ideal solution approximation. The integral in Eq. (A.2) then will be equal to:

$$\begin{aligned}
\text{Integral} = RT \Big\{ & \int_{a\to x} (t_{\mathrm{K}}\, d\ln C_{\mathrm{K}} + t_{\mathrm{Na}}\, d\ln C_{\mathrm{Na}}) \\
& + \int_{x\to y} \big((t_{\mathrm{K}} + t_{\mathrm{Na}} + t_{\mathrm{R}})\, d\ln C_{\mathrm{Cl}} - t_{\mathrm{R}}\, d\ln C\big) \\
& + \int_{y\to z} \big((t_{\mathrm{K}} + t_{\mathrm{R}})(d\ln C + d\ln C_{\mathrm{Cl}}) + t_{\mathrm{Na}}\, d\ln C_{\mathrm{Cl}} - t_{\mathrm{R}}\, d\ln C\big)\Big\} \\
= RT \Bigg\{ & \int_{a\to x} \frac{u_{\mathrm{Na}} - u_{\mathrm{K}}}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C}\, dC \\
& + \int_{x\to y} \Bigg(\bigg(1 - \frac{u_{\mathrm{Cl}}\, C_{\mathrm{Cl}}}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) + (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C}\bigg) \frac{(-dC)}{C_{\mathrm{Cl}}} \\
& - \frac{u_{\mathrm{R}}\, C}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) + (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C} \frac{dC}{C}\Bigg) \\
& + \int_{y\to z} \bigg(\frac{u_{\mathrm{K}}\, C}{\sum_i u_i C_i} \frac{dC}{C} + \frac{dC}{C_{\mathrm{Cl}}} - \frac{u_{\mathrm{Cl}}\, C_{\mathrm{Cl}}}{\sum_i u_i C_i} \frac{dC}{C_{\mathrm{Cl}}}\bigg)\Bigg\};
\end{aligned} \tag{A.9}$$

$$\begin{aligned}
\text{Integral} = RT \Bigg\{ & \ln \bigg(1 + \frac{(u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1)}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M})}\bigg) \\
& - \ln \bigg(1 + \frac{(u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C_{\mathrm{R}}(1)}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M}) + (u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1)}\bigg) + \ln \frac{C_{\mathrm{Cl}}(1)}{C_{\mathrm{Cl}}(3\,\mathrm{M})}\Bigg\}
\end{aligned} \tag{A.10}$$

where $u_{\mathrm{K}} = u_{\mathrm{Cl}}$ has been introduced since the mobility of potassium and chloride ions are almost equal in aqueous solutions. The two first terms of Eq. (A.10) are usually very small, and they may be expressed approximately by

$$RT \ln \bigg(1 + \frac{(u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) - (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C_{\mathrm{R}}(1)}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M})}\bigg).$$

The change in Gibbs energy over the KCl-bridge $(a - z)$ will thus be

$$\begin{aligned}
\Delta G_b(1) = {} & t_{\mathrm{K}}(3\,\mathrm{M})\, \mu_{\mathrm{KCl}}(3\,\mathrm{M}) - \big(t_{\mathrm{K}}(1) + t_{\mathrm{R}}(1)\big)\, \mu_{\mathrm{KCl}}(1) - t_{\mathrm{Na}}(1)\, \mu_{\mathrm{NaCl}}(1) \\
& + t_{\mathrm{R}}(1)\, \mu_{\mathrm{KR}}(1) + RT \ln \bigg(1 + \frac{(u_{\mathrm{Na}} - u_{\mathrm{K}})\, C_{\mathrm{Na}}(1) - (u_{\mathrm{R}} - u_{\mathrm{Cl}})\, C_{\mathrm{R}}(1)}{(u_{\mathrm{K}} + u_{\mathrm{Cl}})\, C_{\mathrm{K}}(3\,\mathrm{M})}\bigg) \\
& + RT \ln \frac{C_{\mathrm{Cl}}(1)}{C_{\mathrm{Cl}}(3\,\mathrm{M})}.
\end{aligned} \tag{A.11}$$

An analogous change in Gibbs energy $\Delta G_b(2)$ will take place in the right-side KCl-bridge, and the total change in Gibbs energy ΔG_b for both sides will be

$$\begin{aligned}\Delta G_b = {} & (t_K(2)+t_R(2))\,\mu_{KCl}(2)+t_{Na}(2)\,\mu_{NaCl}(2)-t_R(2)\,\mu_{KR}(2)\\ & -(t_K(1)+t_R(1))\,\mu_{KCl}(1)-t_{Na}(1)\,\mu_{NaCl}(1)+t_R(1)\,\mu_{KR}(1)\\ & -RT\ln\left(1+\frac{(u_{Na}-u_K)(C_{Na}(2)-C_{Na}(1))-(u_R-u_{Cl})(C_R(2)-C_R(1))}{(u_K+u_{Cl})\,C_K(3\,\mathrm{M})}\right)\\ & -RT\ln\frac{C_{Cl}(2)}{C_{Cl}(1)} \qquad \text{(A.12)}\end{aligned}$$

where the term

$$-RT\ln\left(1+\frac{(u_{Na}-u_K)(C_{Na}(2)-C_{Na}(1))-(u_R-u_{Cl})(C_K(2)-C_K(1))}{(u_K+u_{Cl})\,C_K(3\,\mathrm{M})}\right)$$

will generally be very small and may be omitted.

B. Calculation of ΔG_m; Integration Through the Membrane Phase. According to Eq. (11) the Gibbs energy change for the cell reaction in the membrane, ΔG_m, is given by

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu'_{H_2O}(1)-t'_{H_2O}(2)\,\mu'_{H_2O}(2)\\ & -\int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}}\{\mu'_{KM}\,dt'_K+\mu'_{NaM}\,dt'_{Na}-\mu'_{ClM}\,dt'_{Cl}\}. \qquad \text{(A.13)}\end{aligned}$$

We have assumed that the membrane has a constant number of positive sites and dipoles with positive side to Cl^- channel over which Cl^- ions can carry charge, and a constant number of negative sites and dipoles with negative side to cation channel over which Na^+ and K^+ ions can transport electric charge. We further assumed that the transport number of the Cl^- ion is a constant when the electrolyte composition on both sides of the membrane is given.

At the membrane-electrolyte interfaces the following exchange equilibria are assumed to be established

$$\mathrm{KCl(aq)}+\mathrm{NaM}(m)=\mathrm{KM}(m)+\mathrm{NaCl(aq)}. \qquad \text{(A.14)}$$

We therefore have at both interfaces

$$\mu_{KCl}-\mu_{NaCl}=\mu'_{KM}-\mu'_{NaM}. \qquad \text{(A.15)}$$

The equilibrium constant, K, for this exchange equilibrium may for dilute solutions be expressed by

$$K=\frac{C_{\mathrm{Na}}\,C'_{\mathrm{K}}}{C_{\mathrm{K}}\,C'_{\mathrm{Na}}}. \tag{A.16}$$

After partial integration of Eq. (A.13) we introduce the assumption of local equilibrium at the two interfaces. We then obtain

$$\begin{aligned}\Delta G_m = {} & t'_{\mathrm{H_2O}}(1)\,\mu_{\mathrm{H_2O}}(1)-t'_{\mathrm{H_2O}}(2)\,\mu_{\mathrm{H_2O}}(2)\\ & +t'_{\mathrm{K}}(1)\left(\mu_{\mathrm{KCl}}(1)-\mu_{\mathrm{NaCl}}(1)\right)-t'_{\mathrm{K}}(2)\left(\mu_{\mathrm{KCl}}(2)-\mu_{\mathrm{NaCl}}(2)\right)\\ & +\mu'_{\mathrm{NaM}}(1)-\mu'_{\mathrm{NaM}}(2)+t'_{\mathrm{Cl}}(2)\,\mu'_{\mathrm{NaM}}(2)-t'_{\mathrm{Cl}}(1)\,\mu'_{\mathrm{NaM}}(1)\\ & +\int\limits_{\substack{z\to z'\\ \text{over}\\ \text{membrane}}}\left\{t'_{\mathrm{K}}\,d\mu'_{\mathrm{KM}}+t'_{\mathrm{Na}}\,d\mu'_{\mathrm{NaM}}\right\}.\end{aligned} \tag{A.17}$$

In this expression, however, $t'_{\mathrm{Na}}+t'_{\mathrm{K}}\neq 1$ since $t'_{\mathrm{Cl}}\neq 0$ and ΔG_m cannot be calculated without knowing the value of the chloride ion transport number. When we assume that t'_{Cl} is constant through the membrane, the transport numbers for $\mathrm{K^+}$ and $\mathrm{Na^+}$ ions in the membrane may be expressed by

$$t'_{\mathrm{K}}=(1-t'_{\mathrm{Cl}})\frac{u'_{\mathrm{K}}\,C'_{\mathrm{K}}}{u'_{\mathrm{K}}\,C'_{\mathrm{K}}+u'_{\mathrm{Na}}\,C'_{\mathrm{Na}}}\qquad t'_{\mathrm{Na}}=(1-t'_{\mathrm{Cl}})\frac{u'_{\mathrm{Na}}\,C'_{\mathrm{Na}}}{u'_{\mathrm{K}}\,C'_{\mathrm{K}}+u'_{\mathrm{Na}}\,C'_{\mathrm{Na}}}. \tag{A.18}$$

We will now introduce a new variable, x, such that

$$C'_{\mathrm{Na}}=C'_{\mathrm{Na}}(1)+\left(C'_{\mathrm{Na}}(2)-C'_{\mathrm{Na}}(1)\right)x=C'_{\mathrm{Na}}(1)+\Delta C'_{\mathrm{Na}}x$$

$$C'_{\mathrm{K}}=C'_{\mathrm{K}}(1)+\left(C'_{\mathrm{K}}(2)-C'_{\mathrm{K}}(1)\right)x=C'_{\mathrm{K}}(1)+\Delta C'_{\mathrm{K}}x.$$

With constant activity coefficients and $C'_{\mathrm{M}}=\text{constant}$, Eq. (A.17) becomes

$$\begin{aligned}\Delta G_m = {} & t'_{\mathrm{H_2O}}(1)\,\mu_{\mathrm{H_2O}}(1)-t'_{\mathrm{H_2O}}(2)\,\mu_{\mathrm{H_2O}}(2)\\ & +t'_{\mathrm{K}}(1)\left(\mu_{\mathrm{KCl}}(1)-\mu_{\mathrm{NaCl}}(1)\right)-t'_{\mathrm{K}}(2)\left(\mu_{\mathrm{KCl}}(2)-\mu_{\mathrm{NaCl}}(2)\right)+(1-t'_{\mathrm{Cl}})\\ & \cdot\left\{\mu'_{\mathrm{NaM}}(1)-\mu'_{\mathrm{NaM}}(2)+RT\left\{\int_{x=0}^{1}\frac{u'_{\mathrm{K}}\,\Delta C'_{\mathrm{K}}}{\sum\limits_i u'_i\,C'_i(1)+\sum\limits_i u'_i\,\Delta C'_i x}\,dx\right.\right.\\ & \left.\left.+\int_{x=0}^{1}\frac{u'_{\mathrm{Na}}\,\Delta C'_{\mathrm{Na}}}{\sum\limits_i u'_i\,C'_i(1)+\sum\limits_i u'_i\,\Delta C'_i x}\,dx\right\}\right\}\end{aligned} \tag{A.19}$$

where $\sum\limits_i$ means the summation over $\mathrm{K^+}$ and $\mathrm{Na^+}$ ions.

Integrating Eq. (A.19) we obtain

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu_{H_2O}(1) - t'_{H_2O}(2)\,\mu_{H_2O}(2) \\ & + t'_K(1)\left(\mu_{KCl}(1) - \mu_{NaCl}(1)\right) - t'_K(2)\left(\mu_{KCl}(2) - \mu_{NaCl}(2)\right) + (1 - t'_{Cl}) \\ & \cdot \left\{\mu'_{NaM}(1) - \mu'_{NaM}(2) + RT \ln \frac{C'_{Na}(2) + \dfrac{u'_K}{u'_{Na}}\, C'_K(2)}{C'_{Na}(1) + \dfrac{u'_K}{u'_{Na}}\, C'_K(1)}\right\}.\end{aligned} \tag{A.20}$$

When the equilibrium constant for the above exchange equilibrium is introduced in this equation we get

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu_{H_2O}(1) - t'_{H_2O}(2)\,\mu_{H_2O}(2) \\ & + t'_K(1)\,\mu_{KCl}(1) + t'_{Na}(1)\,\mu_{NaCl}(1) - t'_K(2)\,\mu_{KCl}(2) - t'_{Na}(2)\,\mu_{NaCl}(2) \\ & + RT(1 - t'_{Cl})\left\{\ln \frac{C_{Cl}(2)}{C_{Cl}(1)} + \ln \frac{C_{Na}(2) + \dfrac{u'_K}{u'_{Na}}\, K C_K(2)}{C_{Na}(1) + \dfrac{u'_K}{u'_{Na}}\, K C_K(1)}\right\}.\end{aligned} \tag{A.21}$$

C. Calculation of ΔG_m; Integration Over Solutions in Equilibrium with Membrane at Any Point Through the Membrane. According to Eq. (19) the Gibbs energy change for the cell reaction in the membrane, ΔG_m, is given by

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu'_{H_2O}(1) - t'_{H_2O}(2)\,\mu'_{H_2O}(2) \\ & - \int_{z \to z'} \{\mu_{NaCl}\, d t'_{Na} + \mu_{KCl}\, d t'_K\}.\end{aligned} \tag{A.22}$$

By integrating this equation by parts remembering the equilibrium at the interfaces ($\mu'_{H_2O} = \mu_{H_2O}$), we get

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu_{H_2O}(1) - t'_{H_2O}(2)\,\mu_{H_2O}(2) \\ & + t'_{Na}(1)\,\mu_{NaCl}(1) + t'_K(1)\,\mu_{KCl}(1) - t'_{Na}(2)\,\mu_{NaCl}(2) - t'_K(2)\,\mu_{KCl}(2) \\ & + \int_{z \to z'} (t'_{Na}\, d\mu_{NaCl} + t'_K\, d\mu_{KCl}).\end{aligned} \tag{A.23}$$

Introducing the assumption of constant activity coefficients the Gibbs energy change in the membrane is given by

$$\begin{aligned}\Delta G_m = {} & t'_{H_2O}(1)\,\mu_{H_2O}(1) - t'_{H_2O}(2)\,\mu_{H_2O}(2) \\ & + t'_K(1)\,\mu_{KCl}(1) + t'_{Na}(1)\,\mu_{NaCl}(1) - t'_K(2)\,\mu_{KCl}(2) - t'_{Na}(2)\,\mu_{NaCl}(2) \\ & + RT\{\int_{z \to z'} (t'_K\, d \ln X_K C_t C_{Cl} + t'_{Na}\, d \ln X_{Na} C_t C_{Cl})\}.\end{aligned} \tag{A.24}$$

In this equation X_{Na} and X_K are ionic fractions $X_{Na} + X_K = 1$ and $C_t = C_{Na} + C_K = C_{Cl} + C_R$ is the total salt concentration. Since t'_{Cl} is assumed constant the integral of Eq. (A.24) can be written

$$\begin{aligned}\text{Integral} &= RT\left\{(1-t'_{\mathrm{Cl}})\left\{\int_{C_{\mathrm{Cl}}(1)}^{C_{\mathrm{Cl}}(2)} d\ln C_{\mathrm{Cl}} + \int_{C_t(1)}^{C_t(2)} d\ln C\right\}\right. \\ &\quad \left. + \int_{z\to z'} (t'_{\mathrm{K}}\, d\ln X_{\mathrm{K}} + t'_{\mathrm{Na}}\, d\ln X_{\mathrm{Na}})\right\} \qquad \text{(A.25)} \\ &= RT(1-t'_{\mathrm{Cl}})\left\{\ln\frac{C_{\mathrm{Cl}}(2)}{C_{\mathrm{Cl}}(1)} + \ln\frac{C_t(2)}{C_t(1)} + \int_{X_{\mathrm{Na}}(1)}^{X_{\mathrm{Na}}(2)} \frac{u'_{\mathrm{Na}} - u'_{\mathrm{K}} K}{u'_{\mathrm{Na}} X_{\mathrm{Na}} + u'_{\mathrm{K}} X_{\mathrm{K}} K}\, dX_{\mathrm{Na}}\right\}\end{aligned}$$

where the equilibrium constant, *K*, for the above exchange equilibrium is introduced. When the integration is performed and the result introduced in Eq. (A.24) the change in Gibbs energy in the membrane becomes:

$$\begin{aligned}\Delta G_m &= t'_{\mathrm{H_2O}}(1)\,\mu_{\mathrm{H_2O}}(1) - t'_{\mathrm{H_2O}}(2)\,\mu_{\mathrm{H_2O}}(2) \\ &\quad + t'_{\mathrm{K}}(1)\,\mu_{\mathrm{KCl}}(1) + t'_{\mathrm{Na}}(1)\,\mu_{\mathrm{NaCl}}(1) - t'_{\mathrm{K}}(2)\,\mu_{\mathrm{KCl}}(2) - t'_{\mathrm{Na}}(2)\,\mu_{\mathrm{NaCl}}(2) \\ &\quad + RT(1-t'_{\mathrm{Cl}})\left\{\ln\frac{C_{\mathrm{Cl}}(2)}{C_{\mathrm{Cl}}(1)} + \ln\frac{C_{\mathrm{Na}}(2) + \frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}} K C_{\mathrm{K}}(2)}{C_{\mathrm{Na}}(1) + \frac{u'_{\mathrm{K}}}{u'_{\mathrm{Na}}} K C_{\mathrm{K}}(1)}\right\}. \qquad \text{(A.26)}\end{aligned}$$

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