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EFFECTS OF UNSTIRRED LAYERS OR TRANSPORT NUMBER DISCONTINUITIES ON THE TRANSIENT AND STEADY-STATE CURRENT-VOLTAGE RELATIONSHIPS OF MEMBRANES

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SUMMARY

The effects of current-induced electrolyte accumulation and depletion on the electrical properties of a two-layered membrane system have been examined. The membrane consisted of a charged, ion permselective layer and an uncharged, non-selective layer. The model was designed to reveal the properties of membranes possessing long pores with ionic charges at one end or of ion-selective membranes bounded by highly unstirred aqueous layers. Electrolyte concentration profiles in the inert layer and their time-dependent changes were obtained from solutions of the diffusion equation under the condition of constant current. The profiles were then used to calculate the voltage developed across the membrane at various times after the current is switched on. The theoretical results are presented in the form of *i-V* curves with reduced coordinates that can be used to obtain time-current-voltage relationships for membranes of the type considered having any thickness of the non-selective layer and bathed in any concentration of any 1:1 electrolyte. Experimental results on a model composite membrane were in good agreement with calculations that assume that ion transport occurs only under the influence of electrical potential and concentration gradients, suggesting that in such systems, the combined effects of convection, osmosis, electro-osmosis, and concentration-dependence of diffusion coefficients, activity coefficients, and transference numbers are small. Voltage fluctuations in the form of periodic spikes were observed experimentally at the limiting current density (the current density at which the electrolyte concentration at one surface of the selective layer goes to 0). These phenomena were not seen when the current was in the direction leading to accumulation of electrolyte in the non-selective (unstirred) layer. Such composite membranes can exhibit S-shaped and N-shaped *i-V* curves under ramp-voltage and ramp-current clamps, respectively.

INTRODUCTION

There can be little doubt that natural membranes are asymmetric. Asymmetry, if not inherent in the structure itself, is certainly provided by the environment.

Another characteristic which may be ascribed to membranes with almost equal certainty is ion permselectivity.

In addition to the relatively simpler cell membrane, certain tissues such as skin or intestine can be isolated as a structural unit and studied in much the same way as other membranes. These complex structures also exhibit asymmetry, usually as a consequence of there being different types of membranes at the two surfaces.

If the consequences of either structural or environmental asymmetry are that the transference numbers of permeable ions are not constant from one side to the other, then current flow will cause electrolyte concentration changes within or at the surface of such membranes. The result is that these membranes exhibit a time-variant, non-ohmic conductance.

The steady-state behavior of series composite membranes in which transference numbers differ from one layer to the next has been thoroughly treated theoretically by Kedem and Katchalski [10], Katchalski [9], and Richardson [14].

The non-steady-state properties of permselective membranes bounded by unstirred layers have been the subject of analysis by Barry and Hope [4] and by Segal [16]. The object of these papers was to determine the consequences for electroosmosis [4] and capacitance [16] of a difference in tranference number between the membrane and the adjacent solution. Current-dependent concentration changes have long been recognized in excitable tissue [3, 7] and have recently been the subject of detailed theoretical analysis [1, 2]. The major concern of such investigations is the influence of concentration changes on excitability.

The present communication deals with the time-dependent behavior of a particular composite membrane, a two-layered structure, one layer of which is perfectly selective (t^+ or $t^- = 1$) and a second layer which is non-selective (a layer of unstirred electrolyte solution). Since the second layer is simply a convection-free zone, it may be taken to represent a large pore in a thick membrane or an unstirred layer adjacent to a thin membrane. This experimental model is particularly amenable to theoretical analysis.

MATERIALS AND METHODS

(*a*) *Membrane and chamber construction*

The composite membrane consisted of a section of capillary pipet (10 μl microcap, Drummond Sci. Co.) , one end of which was sealed to a piece of commercial anion exchange membrane (A-103, American Machine and Foundry Corp.). An electrically-tight seal between the capillary and the exchange membrane was insured by embedding both in silicone rubber ("silastic" cement, Dow Corning). This composite "membrane" was sealed with stopcock grease to a hole in a partition separating two compartments of a plastic box (Fig. 1). The absence of leak pathways was indicated by the very high resistance of the system (greater than $10^{14}\ \Omega$) when the open end of the capillary tube was plugged with wax.

For all studies reported here, the capillary was cut to a length of 1.0 cm. Since the volume of the intact pipet is accurately known, and its length easily measured, the cross-sectional area is easily calculated. For the tube described this was $2.46 \cdot 10^{-3}$ cm^2. The solution was 0.1 M KCl in all experiments.

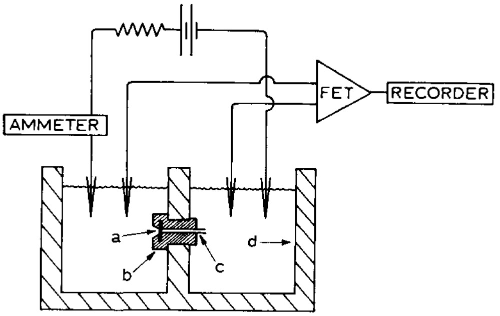

Fig. 1. Experimental layout. (a) Section of ion-exchange membrane which comprises the ion-selective portion of the composite membrane. (b) Molded silicone rubber seal. (c) Capillary tube which comprises the non-selective portion of the composite membrane. (d) Plexiglas chamber.

(*b*) *Electrical measurements*

A standard 4-electrode circuit as shown in Fig. 1 was utilized for all electrical measurements. Current was passed through a pair of Ag-AgCl electrodes of large area (several cm^2) and the potential developed across the membrane detected by a pair of calomel electrodes. Constant current was provided by a battery and a large series resistor. The membrane resistance was less than 1 % of the series resistance with one exception, the experiment of Fig. 8, where it was about 5 %. An ammeter (Hewlett-Packard, model 425A) allowed constant monitoring of the current. The calomel electrodes were connected to a strip chart recorder through a high impedance ($10^{11}\ \Omega$), unity-gain amplifier which insured that the electrodes would not become polarized. The capillary tube was filled with a solution using a blunt, bent needle; the absence of air bubbles was easily verified by inspection.

The results of each experiment were in the form of a time-voltage curve for a given constant current. The process was repeated for a series of constant currents. The duration of an experiment was from a few minutes to about 14 h, depending upon the direction and magnitude of current. The data of a series of experiments was expressed in the form of current-voltage plots consisting of a family of curves, each of which expresses the voltage developed at a particular time after imposition of a given current.

THEORETICAL

The theoretical model corresponding to the experimental membrane of Fig. 1 is shown in Fig. 2. The ion exchange or selective layer extends from $-\Delta x$ to 0 and the unstirred or non-selective layer from 0 to l. The ion exchange layer together with the non-selective layer are referred to as the "composite" membrane. The particular direction of current flow shown in Fig. 2 leads to depletion of electrolyte in the non-selective layer. The non-selective layer is considered to be convection-free. In the experimental part this was insured by using a narrow capillary tube. For this reason the non-selective layer is shown as a tube in Fig. 2, but the actual area is immaterial since current density is used in calculations. The ion selective layer is taken to have a positive ion transference number of 0. The composite membrane is bathed in a solution of 1:1 electrolyte at a concentration of c_0 M, which is assumed

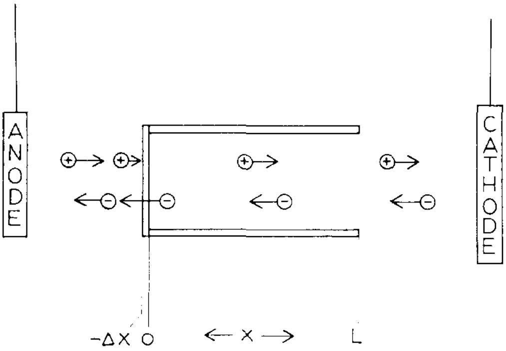

Fig. 2. Ion fluxes and coordinate system for composite membrane. The ion-selective layer extends from 0 to $-\Delta x$. The non-selective layer extends from 0 to l. Current in the direction shown leads to depletion of ions in the non-selective layer.

to be stirred well enough at all times that this concentration extends from left up to $-\Delta x$ and from the right up to l.

Transport of ions in the tube may occur under the influence of both an electric field and a concentration gradient. Constant current will be assumed in the present treatment because it leads to considerable simplification of the mathematics. Given a uni-univalent electrolyte, the ion fluxes (per unit area) in the non-selective layer are expressed by

$$J^+ = -D\frac{\partial c^+}{\partial x} - \frac{t^+ i}{F} \tag{1}$$

$$J^- = -D\frac{\partial c^-}{\partial x} - \frac{t^- i}{F} \tag{2}$$

where c is the electrolyte concentration, D the electrolyte diffusion coefficient, t the transference number, F the Faraday, and i the current density. Equations 1 and 2 assume electroneutrality, i. e., $c^+ = c^-$. Noting that the second terms on the right of Eqns. 1 and 2 are independent of distance within the tube, these equations may be substituted into the continuity equation,

$$\frac{\partial c^\pm}{\partial t} = -\frac{\partial J^\pm}{\partial x} \tag{3}$$

to give:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{4}$$

where the substitution $c^+ = c^- = c$ has been made. This will be recognized as the diffusion equation. The solution under the appropriate conditions will describe the concentration profile in the non-selective layer as a function of time and current.

The steady-state solution of Eqn. 4 is easily obtained by setting $\partial c/\partial t = 0$ and integrating under the following conditions: 1. The whole of the current passing through the ion exchange layer is carried by anions, so that in the region Δx,

$$J^{+} = 0 \tag{5}$$

$$J^{-} = i/F \tag{6}$$

Since the concentrations do not change in the steady state, the fluxes of each ion must be the same in the two layers. Therefore, equating the fluxes of Eqns. 5 and 6 to those of Eqns. 1 and 2, respectively, gives

$$0 = -D\frac{\mathrm{d}c^{+}}{\mathrm{d}x} + t^{+}i/F \tag{7}$$

$$-i/F = -D\frac{\mathrm{d}c^{-}}{\mathrm{d}x} - t^{-}i/F \tag{8}$$

2. $c = c_0$ at $x = l$. The steady-state solution is,

$$c(\infty) = c_0 - \frac{ilt^{+}}{DF} + \frac{ixt^{+}}{DF} \tag{9}$$

It should be noted that the concentration profile in the non-selective layer is linear, the concentration at the right face being c_0 and that at the left face being

$$c(0, \infty) = c_0 - \frac{ilt^{+}}{DF} \tag{10}$$

If the direction of current flow which results when the anode is on the left and the cathode is on the right (Fig. 2) is taken to be positive current, then the latter causes depletion whereas negative current causes accumulation of electrolyte in the non-selective layer. Because the concentration of electrolyte at $x = 0$ cannot be reduced below zero, a limiting positive current is reached when the current density has the value dictated by

$$c_0 - \frac{i'lt^{+}}{DF} = 0 \tag{11}$$

where the prime denotes the limiting current. This result is analogous to the polarographic limiting current. There is no limitation to current in the negative direction, although at some very high current value the solubility product of the salt would be exceeded and precipitation would occur.

The procedure for obtaining the time-dependent solution is lengthy and provides little insight into the physical processes, so will not be given. Instead, the interested reader is referred to the paper by Rosebrugh and Miller [15], in which the analogous equation for a reversible electrode is solved. The time dependence of the electrolyte concentration profile in the non-selective layer is,

$$c(x, t) = c_0 + \frac{ilt^{+}}{DF}\left(-1 + \frac{x}{l} + S\right) \tag{12}$$

Where the time dependence is contained in S, it is given by,

$$S = \sum_{n=1}^{\infty} \frac{2}{(n-\frac{1}{2})^2\pi^2} \exp\left(-\frac{D(n-\frac{1}{2})^2\pi^2 t}{l^2}\right) \cos\left[(n-\tfrac{1}{2})\frac{\pi x}{l}\right] \tag{13}$$

After substituting for lt^+/DF from Eqn. 11, Eqn. 12 may be written as

$$c(x, t) = c_0 \left[1 + \frac{i}{i'}\left(-1 + \frac{x}{l} + S\right)\right] \tag{14}$$

a function of time, thickness of the non-selective layer, reduced layer thickness (x/l) and reduced current density (i/i'). The concentration profiles in the non-selective layer have been calculated from this equation for various times. These are presented in Fig. 3. The numbers on each curve refer to the value of Dt/l^2 chosen for the profile calculation. Since these values are the only condition-dependent parameters of the figure, the curves represent concentration profiles of any 1:1 electrolyte after a particular reduced current has been flowing for the time equal to the product of the number on the curve and D/l^2. The number in parentheses is the time "t" in seconds given by substituting values of D and l^2 used for the experimental part.

Two coordinate systems are given in the figure. The first relates to the conditions described in the experimental section. On the abscissa is plotted the distance in the non-selective layer from the ion-exchange layer. The ordinate covers the range from 0 to 0.1 M and represents the range of possible concentrations when the bathing solution is 0.1 M and the current is set at the positive limiting current. As may be seen, the concentration at $x = 0$ diminishes with time until at $t = \infty$, it becomes zero. With a negative current of the same magnitude, the mirror-image (reflected upward) of this set of curves is obtained, the concentration at $x = 0$ in this case increasing from 0.1 M to 0.2 M.

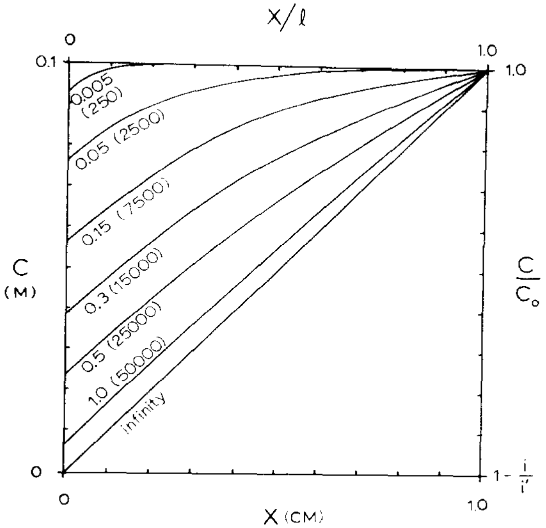

Fig. 3. Concentration profiles in the non-selective portion of the composite membrane. The electrolyte concentration (left axis) and the normalized concentration (right axis) are plotted against distance (lower axis) and normalized distance (upper axis) from the ion-exchange layer. The left and lower axes apply to the experimental conditions when the current is equal to the limiting current (positive).

The second coordinate system (plotted on the upper and right-hand axes) is a normalized one, which allows representation of the concentration gradients for other current values and for other membrane geometries and initial electrolyte concentrations.

Given this information on the time-dependence of the concentration gradients, it is possible to calculate the resistance of the non-selective layer as a function of current density and time. Considering an infinitesimally small column of electrolyte, and assuming concentration-independent mobilities, one can write the differential of the resistance as

$$\mathrm{d}R(t) = \frac{\mathrm{d}x}{(U^+ + U^-)AFc(x, t)}, \tag{15}$$

where A is the cross-sectional area of the membrane and U^+ and U^- are ionic mobilities. The integral from 0 to l of Eqn. 15 is the appropriate expression for the non-selective layer; the concentration as a function of x and t is given by Eqn. 13. It is not the resistance of the tube but rather the voltage developed across it that will be directly accessible experimentally, therefore it is preferable to express the result in terms of voltage. This is easily done using the appropriate form of Ohm's law, namely,

$$V = AiR \tag{16}$$

Combining Eqns. 15 and 16 gives,

$$V(t) = \frac{i}{(U^+ + U^-)F} \int_0^l \frac{\mathrm{d}x}{c(x, t)} = \frac{2t^- RT}{F} \int_0^1 \mathrm{d}(x/l) / \left[1 - \frac{i}{i'}\left(1 + \frac{x}{l} + S\right)\right] \tag{17}$$

where the second equality is obtained from the first using Eqn. 13 and the well-known relationship of Nernst, i.e.,

$$D = \frac{2RTU^+U^-}{(U^+ + U^-)F}. \tag{18}$$

The corresponding expression for the steady-state ($t = \infty$) is easily integrated to give

$$V(\infty) = -\frac{2t^- RT}{F} \ln\left(1 - \frac{i}{i'}\right). \tag{19}$$

The time-dependent expression (Eqn. 17) was evaluated with a combination of graphical and analytical methods using data from Fig. 3. It may be seen from Fig. 3 that the concentration gradient is linear with a slope of $t^+ i/DF$ for some distance (depending upon the time) from $x = 0$. For these linear regions, Eqn. 17 can be integrated directly. The remainder of the tube was divided into segments. The mean concentration in each of these segments was used to calculate the voltage across it and the total voltage across the tube was obtained from the sum of the drops across the individual segments. The results of these calculations are shown in Fig. 4. The units given on the axes have been chosen so that the data of the figure may be used to express the behavior of composite membranes of any geometry

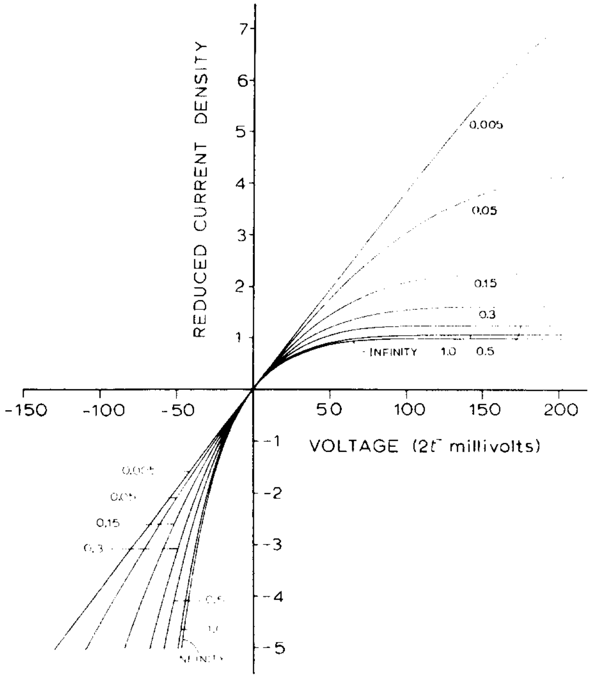

Fig. 4. Potential drop across the non-selective portion of a composite membrane as a function of current and time. Numbers on the curves are values of Dt/l^2. Negative currents lead to accumulation of electrolyte, producing a diminution in voltage with time. Positive currents deplete the membrane of electrolyte and the voltage increases with time. Units are explained in text.

bathed with any 1:1 electrolyte (other electrolytes are amenable to analysis if the theoretical development is made using the product of the stoichiometric number and the Faraday in place of the Faraday as well as the appropriate electroneutrality condition) without the tedium of evaluating the series of Eqn. 14. (For the calculations done here, up to 14 terms had to be included for 1 % accuracy.) The y axis is current density in units of the limiting current, i.e., the reduced current density; current density in normal units is obtained from Eqn. 11. The units given on the abscissa represent millivolts when the electrolyte is KCl, but for other conditions represent $2t^-$ mV. These curves represent the voltage developed when the reduced current (ordinate) has been flowing for the times corresponding to the values of $Dt/1^2$ shown on the curves.

The IR voltage developed across the composite membrane is, of course, not only the voltage drop across the electrolyte of the non-selective layer. In addition, there is a drop across the ion exchange layer given by $V = AiR_e$, as well as a membrane potential across the selective layer and a diffusion potential across the non-selective layer which are produced as a result of the concentration changes at the inner surface of the selective layer. The potential across the ion exchange layer is, according to Teorell [18], assuming activity coefficients are unity,

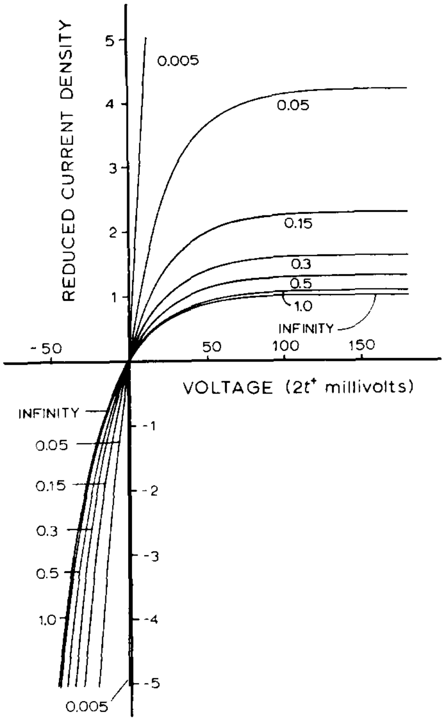

Fig. 5. Total *EMF* developed by a composite membrane as a function of current and time. The numbers on the curves are values of Dt/l^2. Positive current causes the electrolyte concentration on the inner surface of the ion selective layer to decrease while negative currents produce a concentration increase. In both cases, the resulting electrolyte gradients give rise to concentration potentials which increase with time. Units are explained in text.

$$E_e(t) = \frac{RT}{F} \ln \frac{c_0}{c(0,\, t)} \tag{20}$$

There will also arise a diffusion potential in the non-selective layer concomitant with the appearance of a concentration gradient. This potential is given by

$$E_D(t) = (2t^+ - 1)\frac{RT}{F} \ln \frac{c_0}{c(0,\, t)}\,. \tag{21}$$

This equation is valid for all concentration gradients as long as the ionic transference numbers remain constant throughout the gradient. This is approximately true provided c_0 is not too large.

The sum of Eqns. 20 and 21 is

$$E_T(t) = 2t^+ \frac{RT}{F} \ln \frac{c_0}{c(0,\, t)} \tag{22}$$

In terms of the reduced current density (using $c(0, t)$ from Eqn. 13), the sum of the *EMF*'s is given by,

$$E(t) = -\frac{2t^+RT}{F}\ln\left(1 - \frac{i}{i'} + \frac{i}{i'}S\right) \tag{23}$$

where, because $x = 0$, the cosine term of S (Eqn. 12) equals unity.

The steady-state *EMF* is given by

$$E_T(\infty) = -\frac{2RTt^+}{F}\ln\left(1 - \frac{i}{i'}\right) \tag{24}$$

Eqn. 23 represents the total *EMF* developed across the composite membrane during current flow. This equation has been evaluated for a variety of current densities and times of current flow and the results are presented in Fig. 5. As was the case in Fig. 4 these data are also presented in units that can be evaluated for any electrolyte and any geometry. The current units are the same as in Fig. 4. Voltage is given in $2t^+$ mV. When the electrolyte is KCl, these units are simply mV. The curves give the *EMF* developed after the reduced current shown on the ordinate has been flowing for the time corresponding to the value of Dt/l^2 shown on the curves.

It should be noted that the time-dependence of potential development differs considerably from the resistance change in the capillary tube (Fig. 4). This is due to the curvature of the concentration profile at finite times; the concentration at $x = 0$ changes faster than at other positions, and consequently, the exchange layer potential develops faster than does the voltage drop across the capillary tube.

The total voltage across the composite membrane is given by,

$$V_T(t) = AiR_e + \frac{i}{(U^+ + U^-)F}\int_0^1 \frac{dx}{c(x, t)} + \frac{2RTt^+}{F}\ln\frac{c_0}{c(0, t)} \tag{25}$$

Complete current-voltage curves for various times of current flow for any electrolyte and any geometry may be obtained by converting the axes of Figs. 4 and 5 to real voltage and then adding them for corresponding values of Dt/l^2 to the appropriate value of AiR_e. In the steady-state, Eqn. 25 becomes much simpler, namely,

$$V_T(\infty) = AiR_e - \frac{2RT}{F}\ln\left(1 - \frac{i}{i'}\right) \tag{26}$$

Thus, for a given reduced current, the total voltage is independent of transference number. The composite membrane is able to store energy. Thus, if after a long period of current flow, the current is suddenly interrupted, it will behave as a battery, exhibiting a potential (assuming AiR_e to be negligible) of t^+ times that developed across the membrane during passage of current. Obviously, the theoretical steady-state rectification ratio ranges from unity to infinity as the current density is increased from zero to the limiting current density.

If the selective layer allows passage of positive ions instead of negative ions, the behavior of the composite membrane will be indentical to that described here except that it will occur with the current going in the opposite direction.

If the electrolyte concentration is not the same on both sides of the composite membrane, this is easily taken into account by simply adding to Eqn. 25 a term of the form, $E = \pm(RT/F)\ln(c^{\text{left}}/c^{\text{right}})$, where the $+$ is chosen for an anion selective exchange layer and the $-$ is chosen for a cation selective exchange layer. This gives

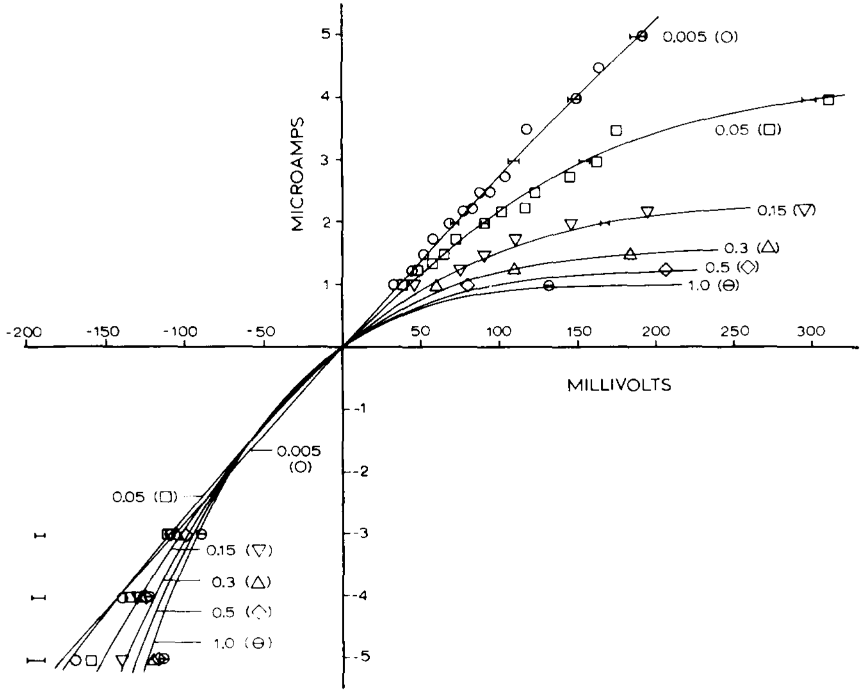

Fig. 6. Comparison of calculated and experimental *i-V* curves. The abscissa represents the total potential developed across the composite membrane when the current shown on the ordinate has been flowing for the time (in units of $5 \cdot 10^4$ s) given by the numbers adjacent to the curves. The symbols are experimental and the lines are calculated.

a "resting potential" which is either augmented or diminished depending upon the direction of current flow.

Finally, it should be noted that since voltages across series elements under constant current are additive, it is a simple matter to describe a selective layer bounded on both sides by non-selective layers (e.g., a membrane with unstirred solutions on both sides). To account for such an additional layer, Eqns. 18 and 23 (with the appropriate value of l) are added to Eqn. 26. If the electrolyte concentration is not the same on both sides, a potential as described in the previous paragraph must also be included.

Because of the different dependence upon transference number, the voltages of Figs. 4 and 5 cannot be combined in a general fashion. Thus, t^+ must be specified before a plot of i against $V_T(t)$ can be made. The curves of Fig. 6 are the total voltage expected for a composite membrane where $t^+ = 0.5$ and the specific resistance of the selective layer is $7.5\,\Omega \cdot \mathrm{cm}^2$. The points will be discussed in Experimental Results, but here we wish to point out some unusual features of the theoretical curves. For all values of current in the positive direction, voltage increases with time, but for negative currents it may decrease (currents more negative than 5 μA), increase (currents between 0 and about 2 μA) or increase and then decrease (currents between about 2 and 3 μA). These phenomena under negative current are due to a different time-dependence for the development of the *iR* drop and the *EMF*; the resistance of the non-selective layer decreases with time due to an accumulation of electrolyte, but this same increase in electrolyte gives rise to an *EMF* that increases in time and the two changes are out of phase. The time-dependent changes of the total potential, for both directions of current flow, are larger, the larger the difference in transference number between the selective and the non-selective layers.

Because of the dependence of voltage on the amount of charge that has flowed, composite membranes exhibit some unusual features under ramp clamps. A ramp current clamp of appropriate slope in the negative direction will give rise to an S-shaped (a maximum followed by a minimum in V as i is increased) i-V curve. This effect follows from the lack of appreciable change of the concentration in the non-selective layer in the early part of the ramp. The membrane will therefore initially behave as an ohmic resistor. Inspection of Fig. 6 reveals that the initial part of the curve would be similar to the curve labelled 0.005. As more charge flows, the tube resistance would fall and the i-V curve would progressively approach the curve marked infinity. Since the voltage continues to rise with current along this curve (albeit with ever-increasing slope), an i-V curve with a minimum in voltage will have been described. In an analogous manner, one predicts that an N-shaped i-V characteristic (a maximum followed by a minimum in i as V is increased) will be traced out by a positive ramp voltage function. Because this latter phenomenon has been verified experimentally, its consideration will be deferred to the Experimental Results section.

EXPERIMENTAL RESULTS

The current-voltage characteristics of the experimental composite membrane are presented in Fig. 6. As described in Materials and Methods, the points at a given current come from one experiment and represent the voltages developed at particular times after switching on the current. For this system, the numbers adjacent to the symbols represent time in units of 50000 s. The curves are plots of Eqn. 25. Error bars are shown because AR_e was given by the manufacturer to be $7.5 \pm 2.5\ \Omega \cdot \text{cm}^2$. Although there are small discrepancies for negative current, the agreement between calculation and measurement is generally quite good.

To determine whether the separate contributions to the composite membrane voltage of the capillary iR drop and the exchange layer potential were as predicted theoretically, another constant current experiment was performed in which the current (positive) was periodically switched off for short intervals. When this is done, AiR_e and $AiR_{\text{capillary}}$ go to zero. The remaining potential is the exchange membrane potential (for KCl, $E_D = 0$), which decays relatively slowly, so that it can be accurately determined. The current was off for only a very small fraction of the total time, hence there was little opportunity for the concentration gradient to relax. The results for a current of 1.37 times the limiting current are shown in Fig. 7. The theoretical curve is calculated assuming 7.5 ohm-cm^2 for the exchange membrane resistance. Except where the voltage went to very high values, the voltage contributions of the two layers of the membrane were in accord with theory.

i-V curves generated by ramp currents or ramp voltages can, for a time-variant resistance, vary widely, depending upon the range and rate of sweep. As alluded to above with respect to ramp functions, ramp voltages may generate N-

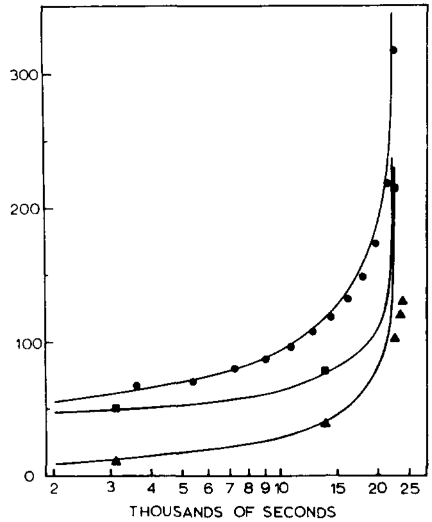

Fig. 7. Comparison of calculated experimental voltage-time curves. The change of the total potential across the membrane under a current of 1.37 times the limiting current (positive) as a function of time is represented by the circles. The contribution to the total potential caused by the resistance change is represented by the squares and the contribution from the *EMF* is represented by the triangles. The lines are calculated as described in the text.

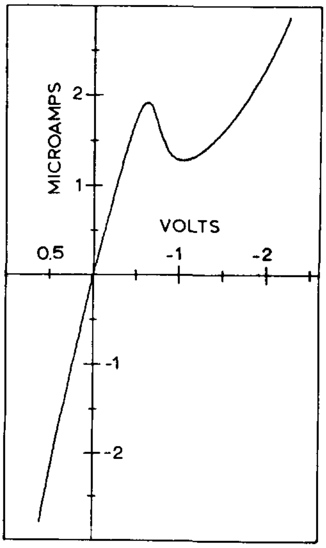

Fig. 8. Response of the composite membrane to a ramp voltage function. The voltage was increased at a rate of 8 mV/s beginning at zero for each polarity. Negative current causes accumulation and positive current depletion of electrolyte.

shaped i-V characteristics when applied in the direction leading to depletion of electrolyte. This follows from the fact that for a while, the current will follow the voltage ohmically, but as the capillary becomes severely depleted, the current must decrease. Eventually, a break-down voltage will be reached where the current will increase again. These qualitative predictions have been verified experimentally. Fig. 8 is a trace of i vs. V as V is increased at a rate of 8 mV/s. The minimum in i is near 1 μA which is close to the theoretical limiting current in this system. Breakdown occurs in the region of 1.25 to 2.0 volts. It should be mentioned that these curves may be demonstrated repeatedly on the same membrane. This means that the breakdown is reversible and therefore unlikely to have occurred in any of the insulation around the membrane. Although water dissociation could account for the current in excess of i', other observations (see below) suggest that failure of the exchange membrane is more likely.

When the membrane is clamped at a relatively high (but below breakdown) voltage, and then this is reduced as a constant function of time, the i-V curve traced is again highly dependent upon the rate of change of the clamp. If the voltage is decreased slowly, the i-V curve drawn is very close to the steady-state curves of Fig. 6 for either polarity. If the voltage is reduced rapidly, the i-V curve bears little resemblance to any of the curves of Fig. 6. The particular curve obtained depends upon whether the holding voltage leads to accumulation or depletion of electrolyte from the intra-membrane space. If the membrane has been depleted of ions and the voltage is rapidly reduced to zero, the current is found to reverse direction. This current is, of course, the current produced by the ion-exchange layer potential which had built up during the voltage clamp. If the voltage is reduced more slowly, the i-V curve describes a loop, which for a positive voltage clamp extends from the holding point in the first quadrant into the fourth quadrant before returning to the origin, and for a negative clamp from the third quadrant into the second quadrant before returning to the origin.

In addition to behavior which was qualitatively or quantitatively predicted,

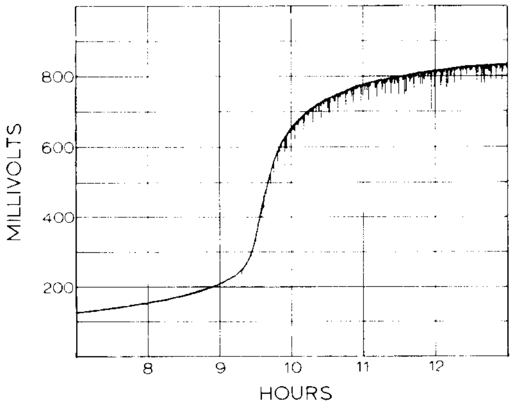

Fig. 9. Voltage-time trace under current in excess of the positive limiting current. The voltage was obtained as a function of time with the current held at 1.11 times the limiting current. Upward curvature at 9.5 h indicates the time at which the electrolyte concentration at the inside surface of the ion-selective layer should theoretically approach zero.

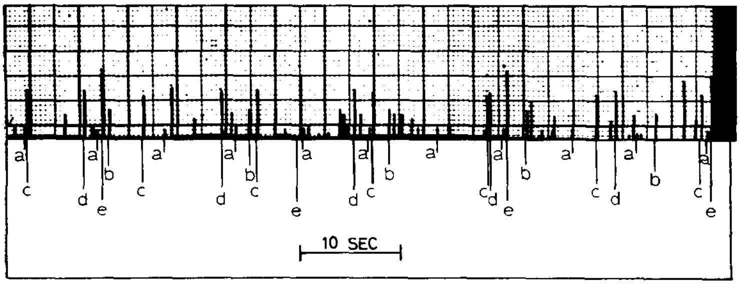

Fig. 10. Detail of plateau region of voltage-time curve. The membrane and current were the same as described for Fig. 9. Both the time and voltage scales are greatly expanded with respect to Fig. 9. The horizontal scale is 10 mV/division.

the composite membrane exhibited an additional, unexpected phenomenon. When positive currents greater than the limiting current were passed through the membrane, the voltage underwent a monotonic increase in time until the time at which the electrolyte concentration should, according to theory, have been reduced to zero at the inside surface of the ion-exchange layer. At this point the voltage began to exhibit rapid, transient transitions to a lower value. This phenomenon is shown in Fig. 9. The curve represents a portion of the voltage-time relationship for a membrane through which a current 11 % greater than the limiting current was passed. The fluctuations, which appear as sharp downward spikes, begin as the voltage is increasing at its most rapid rate. The largest of the fluctuations exhibits a periodicity of about 10 per hour. A section of the plateau region of the voltage-time trace of this membrane under higher voltage and time resolution is shown in Fig. 10 (this trace is inverted with respect to that in Fig. 9). Upon casual inspection this trace appears to be composed of random fluctuations, but closer examination reveals that, in fact, it is the sum of several series of spikes, each of which has a characteristic period and magnitude. In this record, five such series have been identified and are marked with letters "a–e" in the figure. The lines linking each letter with its respective fluctuation are drawn to the same lenghts as the spikes to emphasize that each series has a characteristic magnitude. There remain a number of fluctuations which could not be assigned to a series. It may be that they are random, or, as appears more likely, that they belong to several series with about the same magnitude.

That the fluctuations are a property of the composite membrane and not of the electrodes or the circuit was demonstrated by several methods. If the chamber is physically reversed with respect to the electrodes and current passed through the electrodes in the same direction, the membrane now accumulates salt. In this configuration no fluctuations in voltage are observed even when the current is increased to several times that of the depleting current which had previously generated fluctuations. That the phenomenon is not due to the high impedance of the system when the membrane is depleted of electrolyte was ruled out by replacing the cell with a shallow dish containing distilled water. Despite the fact that the amount of water was chosen to give the same resistance as the membrane when it exhibited fluctuations, the voltage remained constant.

The fluctuations were examined on an expanded time scale with a storage

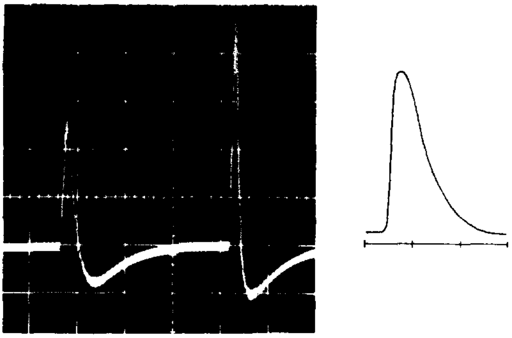

Fig. 11. Detail of fluctuation in voltage. On the left is a tracing obtained from an A-C coupled oscilloscope of two of the smallest set of the fluctuations shown in Fig. 10. The voltage scale is 2 mV/division and the time scale is 20 ms/division. A graphical integration of the larger fluctuation is on the right for which the voltage scale is arbitrary.

oscilloscope. A tracing which includes two fluctuations is presented in Fig. 11. Because the oscilloscope was A-C coupled, the record is that of the derivative of the pulses. By graphical integration an approximation of one of the fluctuations was reconstructed and is shown next to the tracing. Although the fluctuations shown here were relatively fast, they were also quite small. The larger fluctuations had a very similar shape and were consequently proportionately slower.

It should be emphasized that the approach to constant voltage of the voltage-time trace as shown in Fig. 9 is a feature which was not predicted by the theory in the form presented above. A perfectly permselective ion-exchange layer was assumed, and this leads to the expectation that the voltage will go to infinity for all positive currents greater than the limiting current. Real ion-exchange membranes allow finite co-ion currents, and the voltage consequently remains at some finite value. The resistance of the composite membrane after the voltage has become constant may be used to calculate the co-ion transference number. This was between 0.01 and 0.001. Because of this non-ideal behavior, theory and experiment as shown for positive currents in Figs. 7 and 8 will begin to diverge under extended conditions (higher current, longer times) which allow development of voltage in excess of a few volts.

DISCUSSION

Assumptions

To begin this section it is appropriate to examine the assumptions which have gone into the theory presented above. The first assumption was that K^+ and Cl^- mobilities are equal. This is true to better than 1 % at room temperature and is unlikely to result in appreciable error. Although not explicit, a more tenuous assumption was made early in the development, namely that the electrolyte diffusion coefficient is concentration independent. In fact, that of KCl changes by about 7 % between 0 and 0.1 M. The value used for the calculation of the data presented in Figs. 3, 4 and 5 was that for infinite dilution. For positive currents, the most critical stage is when the concentration near the exchange layer approaches zero, so that this is an appropriate choice for calculations of membrane behavior under depleting currents. For negative currents this choice of D might be expected to produce greater error, i.e. the values of Dt/l^2 would be larger than appropriate for the actual concentrations found in the non-selective layer. In fact, however, because the *EMF* and the iR drop for positive currents go in opposite directions, and except for very high currents, by about the same magnitude, most of the potential error is cancelled in the total potential. The individual potential contributions would, however, still be calculated to develop more rapidly by a choice of D that is too large, and this may be the reason for the lag of the experimental data behind the theoretical curves in Fig. 7.

The solution in the non-selective layer has been presumed to be convection free. How good an assumption this is will clearly depend upon the stituation. In the case of the capillary tube used in the experiments presented below, given its small diameter, this is almost certainly true for thermal and concentration convection. A larger effect is expected from electro-osmosis. This will depend upon the nature of the ion selective layer, but for the commercial ion exchange membrane used in the experimental part, it can be estimated. The transference number of water through commercial ion exchange membranes has been determined [11] and a figure of roughly 10 water molecules per ion was obtained. Since the salt concentration is near 0.1 M for the present experiments and the water concentration is about 55 M, the water transport due to electro-osmosis should be approximately 1/55 that of the salt transport. This 2 % effect on concentration profiles would cause an enormous underestimation of the voltage produced by currents very close to the positive limiting current density, but only because the voltage is extremely sensitive to small changes in current under such conditions. The effect on predicted current densities for a given voltage would, on the other hand, be in error by less than 2 %. Since osmotic pressure differences do not become appreciable unless very large negative currents are used, local osmosis should be negligible unless the selective layer has a very high water permeability. For a polystyrene sulfonate membrane [12] the effect of osmosis on gradients in the capillary should be less than 1 % per hour.

It thus appears that the consequences of the assumptions necessary for the analysis of the electrical behavior of composite membranes by simple diffusion theory are relatively minor and, as corroborated by experiment, most predictions should be accurate to within about 10 % in the worst case.

Comparisons with theoretical analysis of bipolar membranes

Katchalsky [9] and Richardson [14] have analyzed the steady-state electrical properties of bipolar membranes, that is, membranes consisting of two layers with different ion selectivities; both give expressions in which the voltage developed across such a membrane depends upon the transference numbers of the ions in each of the layers. Under the conditions that one of their layers has $t^- = 1$ and the other, $t^- = \frac{1}{2}$, and that the electrolyte concentration on both sides of the membrane is the same, i.e., conditions corresponding to those we have dealt with experimentally, their expressions for the steady-state voltage become

$$V_T(\infty) = AiR_e + AiR_a - \frac{RT}{F}\ln\left(1 - \frac{i}{i'}\right) \tag{27}$$

where R_a is the resistance of the aqueous layer.

The difference between this expression and Eqn. 25 is that the former contains the *EMF* term contained in the latter, but has the apparent constant, AiR_a, in place of the variable term given by Eqn. 18.

This comparison with previous treatments of bipolar membranes brings to light the fact that although such analyses provide an accurate expression for the sum of the *EMF*'s that develop across these membranes, they ignore the contribution to the potential drop that comes from depletion or accumulation in one or both of the layers. Depletion and accumulation are referred to in such treatments, but they are assumed to occur in an infinitely thin layer between the two selective portions of the bipolar membrane. In fact, it is easy to show by setting t^+ of Eqn. 18 to unity, which results in a bipolar membrane composed of a perfect anion exchanger back to back with a perfect cation exchanger, that for "depleting current" (but not for current in the other direction), there is actually no depletion; the resistance to current flow comes about only from space charge effects, that is, a strong potential opposes the displacement of the counter-ions relative to the fixed charges in both layers. Electroneutrality is not strictly obeyed, so there would be a small current flow before the resistance goes to infinity, but this would be essentially only a capacitance current.

It might be suggested that layer-depletion or accumulation terms do not appear in the Katchalsky-Richardson equations because they were not designed to deal with layers (aside from the junction layer) in which concentration changes are possible. This appears to be the case, but if it is, one must inquire into how severely this limits the applicability of these equations. The equations of Katchalsky [9] and of Richardson [14] contain the transference number for one of the ions in each of the layers and the implication is that such transference numbers can be assigned any value from 0 to 1. In fact, the Katchalsky-Richardson equations are valid for layers that are not perfectly permselective only in some rather unusual cases, namely, if layers are a mosaic of highly charged anion and cation exchangers (the area of each determining the overall selectivity), liquid exchangers containing mobile uncharged sites for both anions and cations (the proportions of each determining the selectivity), or, if the layers are infinitely thin (selectivity could depend upon either chemical, electrostatic, or steric discrimination). If the layers were fixed-charge exchangers, they could be partially selective only because the charge density were low. In that case the layer must contain some bulk electrolyte which would be susceptible to depletion or augmentation upon passage of current. Hence current-dependent layer resistances would need to be considered. Although these considerations reveal serious limitations of the Katchalsky-Richardson equations with respect to predicting *i-V* characteristics, they do not affect the validity of their predictions of potentials across bipolar membranes caused by concentration differences.

The present treatment, it should be emphasized, is unable to cope with a composite membrane unless one layer is perfectly permselective (except for the trivial conditions mentioned above where one layer is a liquid exchanger, a mosaic of fixed charges, or very thin) and the selectivity of the other layer depends only upon ionic mobilities. It is hence most likely to be of use in predicting electrical effects of unstirred layers adjacent to plasma membranes.

Voltage fluctuations

The major deviation of the experimental results from the theoretically predicted behavior was the rapid fluctuation of the membrane resistance when, under positive current, the voltage reached relatively high values. This kind of behavior is reminiscent of breakdown phenomena, and since it occurred coincidentally with severe electrolyte depletion in the region next to the exchange membrane, it appears reasonable to suggest that the inner surface of that membrane is partially depleted of counter-ions and, perhaps as a result of fixed charge repulsion, becomes mechanically unstable. If this were the case, one would expect breakdown at the thinnest or weakest areas. The consequences of breakdown in a few small regions of the ion-exchange membrane would be that these areas would become co-ion permeable, and the salt concentration would then locally increase. As this occurred, the condition for breakdown would no longer obtain, and the condition for depletion would be re-established. Since the salt which had been injected during the breakdown would be removed during a well defined length of time, voltage spikes could occur in a periodic manner. This would be in accord with the observations that the fluctuations appear in discrete sets, that the largest fluctuations generally have the longest period, and that the number of sets increases with an increase in current. On this basis, the breakdown of the membrane as a whole would depend upon the cumulative effect of more and more areas undergoing break-down.

Other membranes that exhibit resistance fluctuations

Shashoua [17] has described a composite membrane formed by polymerizing a polybase on the surface of a polyacid which also exhibits sharp fluctuations in resistance within a certain range of voltages. In some, but not all of the situations described [17], such fluctuations are observed under depleting current, and it may be that these are related to those we have observed.

Another artificial membrane system which exhibits fluctuations similar to those described here is the oxidized linseed oil membrane of Monnier et al. [13]. This membrane, prepared by oxidizing a layer of oil floating on the surface of an aqueous solution, exhibits sharp, periodic current transitions when held under voltage clamp. The membrane is cation selective due to the presence of carboxylate groups formed during oxidation and is therefore potentially a system in which depletion phenomena may occur. If this membrane has a breakdown voltage near that at which the fluctuations occur, the periodicity of the latter could again be explained as the time necessary for depletion of a salt-permeable layer. This layer could be either the unstirred water layer or a deep irregularity in the surface of the membrane. Given the rather small currents necessary to elicit fluctuations, and the fact that only certain spots on the membrane surface exhibit this property, the latter possibility appears quite plausible. The i-V curve of this membrane has the current plateau that would be expected for a system in which depletion can occur. Kamo et al. [8] have investigated the electrical properties of a model membrane (cation selective) consisting of a dioleylphosphate-impregnated millipore filter that also exhibits resistance fluctuations. There are indications that tranference number differences between membrane and unstirred layers play a role in this system. They describe, for example (their Fig. 7b) an increase in voltage across a membrane when current is passed from a dilute to a more concentrated KCl solution which occurs in about

1 s. One can easily calculate that if the unstirred layer has a typical thickness of 100 microns, nearly complete electrolyte depletion should occur at the membrane surface under a current of 0.2 mA. This is very close to the value of 0.13 mA that they used. The unstirred layers in this system are symmetrical, so the concentration of salt on the other side of the membrane would increase, and since their membrane loses selectivity in fairly low electrolyte concentrations, some complex and long-lasting effects, as they observed, would be expected.

Do unstirred layers account for resistive "action potentials" of frog skin?

Tissues which contain multi-layered structures provide a relatively large space for convection-free diffusion, and it is here that one may expect accumulation and depletion phenomena to be particularly evident. One such biological system which exhibits many of the properties found or predicted for the composite membrane studied here is frog skin. When frog skin is subjected to a constant current of a critical magnitude, the potential across the skin goes through a transient maximum. This phenomenon was first studied by Finkelstein [5] and more recently in considerable detail by Fishman and Macey [6]. A change in tissue resistance is the basis of the change in voltage, and for this to occur, the current must be maintained throughout the voltage peak. A latency period exists during which application of the current stimulus fails to elicit a response. If the skin is subjected to a critical ramp voltage clamp, an N-shaped curve is observed. Ramp clamps which are more rapid than the optimum produce *i-V* curves which reveal a low, almost ohmic resistance. Clamps which are slower than the optimum reveal an *i-V* curve with a plateau in current which rises rapidly in the position of the last leg of the N-shaped curve. With only slight reservation, all of these phenomena find a ready explanation in terms of electrolyte depletion in composite membranes. The threshold current could correspond to the limiting current. A maximum in the voltage under current clamp would be a property of any depleting system which has a relatively sharp breakdown voltage. The refractory period could be the time for diffusion to replenish the electrolyte in the inert layer. Some characteristics of frog skin, such as the requirement for a particular ionic composition of the bathing solution are not easily explained on the basis of the simple model; however, the other similarities are sufficiently striking that the model should be given serious consideration.

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