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Transport of Ions of One Kind through Thin Membranes

I. General and Equilibrium Considerations

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Summary. The general equation for movement of ions of one kind through planar membranes and its equilibrium solutions are reviewed. A simple procedure to obtain exact numerical solutions is presented, and results are displayed as profiles of potential, field and concentration across the membrane. Finally, useful approximations for very low and very high ionic concentrations are given, and the limits of applicability of the constant-field approximation are indicated.

Electrical excitability of membranes has long been associated with ionic transport. The availability of artificial bilayer membranes (Mueller, Rudin, Tien & Wescott, 1962*a*; 1962*b*) has further facilitated experimental study of such transport. By now, several ways are known in which ions can pass lipid membranes. Ions like tetraphenylborate (Liberman & Topaly, 1968; le Blanc, 1969) are membrane-permeable because of their large and hydrophobic exterior, whereas smaller ions can be transported in lipid-compatible molecular wrapping provided by carrier molecules like valinomycin (Lev & Buzhinskii, 1967; Mueller & Rudin, 1967) or pores like gramicidin (Hladky & Haydon, 1970; Urry, 1971).

To describe such transport of ions of one kind in relatively simple mathematical terms, a number of simplifying assumptions will be made. We will consider the presence of only one type of charge carriers inside the membrane, and we will neglect osmotic pressure gradients. Furthermore, we will assume that macroscopic laws can still be applied to rather large ions or ion-molecule aggregates in liquid-crystalline-like films of 50- to 100-Å thickness, so that the problem reduces to that of solving the Nernst-Planck and Poisson equations in the direction perpendicular to the surface of the membrane. Restricting the discussion for the time being to steady-

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state behavior, we have

$$I = nFD\left(\frac{dc}{dx} + \frac{nFc}{RT}\frac{d\psi}{dx}\right) \tag{1}$$

$$\frac{d^2\psi}{dx^2} = -\frac{4\pi nFc}{\varepsilon} \tag{2}$$

where I is the steady-state current density, n the valency of the charge carrier, c its concentration and D its diffusion coefficient. The local potential is denoted here by ψ, and ε is the dielectric constant of the membrane phase. Finally, x is the distance perpendicular to the membrane surfaces (at $x=0$ and $x=d$, respectively) and F, R and T have their usual meanings. We now introduce the dimensionless parameters

$$\varphi \equiv -\frac{nF\psi}{RT}, \quad E \equiv \frac{nFd}{RT}\frac{d\psi}{dx}, \quad s \equiv \frac{x}{d}$$

$$i \equiv -\frac{4\pi nFd^3 I}{D\varepsilon RT}, \quad \gamma \equiv \frac{4\pi n^2F^2d^2c}{\varepsilon RT} \tag{3}$$

whereupon elimination of c between Eqs. (1) and (2) yields

$$i = -\frac{d^3\varphi}{ds^3} + \frac{d^2\varphi}{ds^2}\frac{d\varphi}{ds} \tag{4}$$

or the equivalent expression in terms of the dimensionless field E

$$i = \frac{d^2E}{ds^2} + E\frac{dE}{ds}. \tag{5}$$

The Poisson equation, Eq. (2), now reads in dimensionless form

$$\frac{d^2\varphi}{ds^2} = -\frac{dE}{ds} = \gamma. \tag{6}$$

Integration of Eqs. (4) and (5) yields

$$-\frac{d^2\varphi}{ds^2} + \frac{1}{2}\left(\frac{d\varphi}{ds}\right)^2 = is + A \tag{7}$$

$$\frac{dE}{ds} + \frac{1}{2}E^2 = is + A \tag{8}$$

where the integration constant A is independent of s. Solution of Eqs. (7) or (8) requires three boundary conditions for the general case $i \neq 0$, which will be discussed in Part II of this series (de Levie, Seidah & Moreira, 1972). In the present paper we will focus our attention on the special case $i=0$, for which only two boundary conditions are needed.

Equilibrium Behavior

Under equilibrium conditions, $i=0$ so that Eq. (8) can be rewritten as

$$\frac{dE}{ds}+\frac{1}{2}E^2=A. \tag{9}$$

We now define μ such that

$$E=\frac{2}{\mu}\frac{d\mu}{ds} \tag{10}$$

so that Eq. (9) can be transformed into

$$\frac{d^2\mu}{ds^2}=\frac{1}{2}A\mu \tag{11}$$

with the general solution

$$\mu=C_1\sinh s\sqrt{A/2}+C_2\cosh s\sqrt{A/2} \tag{12}$$

provided $A\neq 0$. Substituting this result for μ back into Eq. (10), and using Eq. (6), we find for the dimensionless potential, electrical field and concentration, respectively,

$$\varphi=-2\ln(C_1\sinh s\sqrt{A/2}+C_2\cosh s\sqrt{A/2})+B \tag{13}$$

$$E=\sqrt{2A}\,\frac{C_1\cosh s\sqrt{A/2}+C_2\sinh s\sqrt{A/2}}{C_1\sinh s\sqrt{A/2}+C_2\cosh s\sqrt{A/2}} \tag{14}$$

$$\gamma=A\left\{\left(\frac{C_1\cosh s\sqrt{A/2}+C_2\sinh s\sqrt{A/2}}{C_1\sinh s\sqrt{A/2}+C_2\cosh s\sqrt{A/2}}\right)^2-1\right\}. \tag{15}$$

To evaluate the integration constants A, B and C_1/C_2 we will define the potential scale such that

$$\varphi_{s=0}\equiv 0 \tag{16a}$$

and we will use the boundary conditions

$$\varphi_{s=1}=v \tag{16b}$$

$$\gamma_{s=0}=\gamma_0. \tag{16c}$$

Substitution of these boundary conditions into Eqs. (13)–(15) yields

$$B=2\ln C_2 \tag{17}$$

$$\varphi=-2\ln\left(\frac{C_1}{C_2}\sinh s\sqrt{A/2}+\cosh s\sqrt{A/2}\right) \tag{18}$$

$$\frac{C_1}{C_2}=\frac{e^{-v/2}-\cosh\sqrt{A/2}}{\sinh\sqrt{A/2}} \tag{19}$$

$$\gamma_0=A\left\{\left(\frac{C_1}{C_2}\right)^2-1\right\}=A\left\{\left(\frac{e^{-v/2}-\cosh\sqrt{A/2}}{\sinh\sqrt{A/2}}\right)^2-1\right\}. \tag{20}$$

For $v \to \infty$, Eq. (20) leads to

$$\gamma_0 = \frac{A}{\sinh^2 \sqrt{A/2}} \tag{21}$$

which requires that A be positive so that $\sqrt{A/2}$ be real. On the other hand, when we consider the case $v=0$, then

$$\gamma_0 = 2A\left(\frac{1-\cosh\sqrt{A/2}}{\sinh^2\sqrt{A/2}}\right) \tag{22}$$

which requires that A be negative so that $\sqrt{A/2}$ be imaginary. Application of the rule of l'Hôpital to Eq. (20) shows that A changes sign when

$$\gamma_0 = 2(e^{-v/2}-1)^2 \tag{23}$$

or

$$e^{-v/2} = 1 \pm \sqrt{\gamma_0/2}. \tag{24}$$

Since it is easier to work with real numbers, evaluation and interpretation of Eqs. (13)–(15) will be simplified by defining

$$2a^2 \equiv A \qquad \text{for } A>0 \tag{25}$$

$$2b^2 \equiv -A \qquad \text{for } A<0. \tag{26}$$

We will thus be able to obtain two sets of mathematically equivalent solutions, which can be transformed into each other through the relation $a = b\sqrt{-1}$, and which will be used in such a way as to avoid imaginary variables. The special case $A=0$ will be considered separately.

The More Symmetrical Case, $A<0$

When v is small enough so that

$$1-\sqrt{\gamma_0/2} < e^{-v/2} < 1+\sqrt{\gamma_0/2} \tag{27}$$

it is convenient to rewrite Eqs. (13)–(15) as

$$\varphi = -2\ln(p\sin bs + \cos bs) \tag{28}$$

$$E = 2b\left(\frac{p\cos bs - \sin bs}{p\sin bs + \cos bs}\right) \tag{29}$$

$$\gamma = 2b^2\left\{\left(\frac{p\cos bs - \sin bs}{p\sin bs + \cos bs}\right)^2 + 1\right\} = \frac{2b^2(p^2+1)}{(p\sin bs + \cos bs)^2} \tag{30}$$

where p can be evaluated from

$$p = \frac{e^{-v/2} - \cos b}{\sin b} \tag{31}$$

$$\gamma_0 = 2b^2(p^2+1). \tag{32}$$

Combining Eqs. (30)–(32) yields for $s=1$ the expected equilibrium condition

$$\gamma_1=\gamma_0\, e^v \tag{33}$$

which can be substituted back into Eq. (27) to yield the more symmetrical expression

$$|\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}|<1. \tag{34}$$

Note that the condition on the left-hand side of Eq. (27) is always satisfied when $\gamma_0 \geqq 2$, in which case Eq. (34) can be written simply as

$$\sqrt{2/\gamma_1}-\sqrt{2/\gamma_0}<1 \quad \text{for } \gamma_0 \geqq 2 \tag{34a}$$

and an analogous expression pertains when $\gamma_1 \geqq 2$:

$$\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}<1 \quad \text{for } \gamma_1 \geqq 2. \tag{34b}$$

When both γ_0 and γ_1 are 2 or larger, Eq. (34) is always obeyed.

The Less Symmetrical Case, $A>0$

Eqs. (13)–(15) retain their hyperbolic form when

$$e^{-v/2}<1-\sqrt{\gamma_0/2} \quad \text{or} \quad 1+\sqrt{\gamma_0/2}<e^{-v/2} \tag{35}$$

so that

$$\varphi=-2\ln(q\sinh as+\cosh as) \tag{36}$$

$$E=2a\left(\frac{q\cosh as+\sinh as}{q\sinh as+\cosh as}\right) \tag{37}$$

$$\gamma=2a^2\left\{\left(\frac{q\cosh as+\sinh as}{q\sinh as+\cosh as}\right)^2-1\right\}=\frac{2a^2(q^2-1)}{(q\sinh as+\cosh as)^2} \tag{38}$$

where q can now be evaluated from

$$q=\frac{e^{-v/2}-\cosh a}{\sinh a} \tag{39}$$

$$\gamma_0=2a^2(q^2-1). \tag{40}$$

Combining Eqs. (36)–(40) again yields for $s=1$ the equilibrium condition

$$\gamma_1=\gamma_0\, e^v \tag{41}$$

so that Eq. (35) can be reformulated as

$$|\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}|>1 \tag{42}$$

which again can be simplified to

$$\sqrt{2/\gamma_1}-\sqrt{2/\gamma_0}>1 \quad \text{for } \gamma_0 \geqq 2 \tag{42a}$$

$$\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}>1 \quad \text{for } \gamma_1 \geqq 2. \tag{42b}$$

Clearly, Eq. (42) cannot be obeyed when both γ_0 and γ_1 exceed 2.

The Special Case, $A=0$

Substitution of $A=0$ into Eq. (11) yields

$$\mu=C_1 s+C_2 \tag{43}$$

so that Eq. (10) leads to

$$E=\frac{2}{s+r} \tag{44}$$

where we have used $r \equiv C_2/C_1$. Use of Eqs. (6) and (16a) results in

$$\varphi=-2\ln\frac{s+r}{r} \tag{45}$$

$$\gamma=\frac{2}{(s+r)^2} \tag{46}$$

$$\gamma_0=2/r^2 \quad \text{so that} \quad r=\sqrt{2/\gamma_0}. \tag{47}$$

The present case, $A=0$, clearly corresponds to

$$|\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}|=1 \tag{48}$$

or

$$e^{-v/2}=1\pm\sqrt{\gamma_0/2}. \tag{49}$$

Numerical Examples

The mathematical relations summarized above are by no means new. They go back to extensive studies by Max von Laue (1918) on the equilibrium distribution of electrons in vacuum tubes, and were succintly summarized by Skinner (1955) in his work on space charges in insulators. Bruner (1965*a*; 1965*b*) included the adjacent aqueous solutions in the mathematical description which, however, leads to rather untractable results. Among membrane biologists, Cole (1965) briefly mentioned the two most important cases, $A \lesseqgtr 0$. Ciani, Eisenman and Szabo (1969) discussed the totally symmetrical case, and Neumcke and Läuger (1970) attempted to solve the more general situation, but unfortunately used the trigonometric solution throughout. Below we present explicit graphical representations of the pertinent physical parameters: potential, electric field and ionic concentration.

The equations were evaluated numerically for a variety of interfacial concentrations γ_0 and γ_1. Conditions (34), (42) and (48) were used to select the appropriate mathematical formalism, v followed directly from Eqs. (33) or (41), and b or a was calculated from Eqs. (31)–(32) or (39)–(40) by using the Newton-Raphson method. In view of the discontinuities of, e.g., Eq. (31) at $b=0$, π, 2π, etc., the Newton-Raphson method only yields satisfactory results if a reasonably close initial estimate for b is used. Such an estimate can readily be obtained from a graph of γ_0 *vs.* b, using Eqs. (31) and (32). The resulting profiles of potential, electric field and ionic concentrations across the membrane are shown in Fig. 1 for the totally symmetrical case ($\gamma_0=\gamma_1$ so that $v=0$) and in Figs. 2–7 for varying values of γ_1 at fixed γ_0. Corresponding numerical values of A are listed in Table 1. Fig. 8 shows A as a function of $v=\ln \gamma_1/\gamma_0$ over the range $-5 \leqq v \leqq 5$. Another representation of these data is given in Fig. 9, where A is plotted *vs.* v at constant value of the parameter $|\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}|$. All calculations and plots were made on a Hewlett-Packard 9100B–9125A calculator-plotter combination, which gives an indication of the great simplicity of the present approach.

Approximations for Low Ionic Concentrations

When neither γ_0 nor γ_1 exceeds 0.1, we can use the approximation

$$A \approx \tfrac{1}{2} v^2 \tag{50}$$

so that

$$a \approx \tfrac{1}{2} v \tag{50a}$$

$$q \approx -1 \tag{50b}$$

$$\varphi \approx v s \tag{51}$$

$$E \approx -v \tag{52}$$

and use of the Boltzmann equilibrium expression yields

$$\gamma=\gamma_0 e^{\varphi} \approx \gamma_0 \left(\frac{\gamma_1}{\gamma_0}\right)^s = \gamma_0^{1-s} \gamma_1^s . \tag{53}$$

This procedure is chosen to avoid the pitfalls of direct differentiation of the approximation, Eq. (52), which would lead to the erroneous conclusion $\gamma \approx 0$. Eq. (52) is equivalent to the often-used constant-field approximation (Goldman, 1943). The extent to which Eqs. (50) through (53) are obeyed

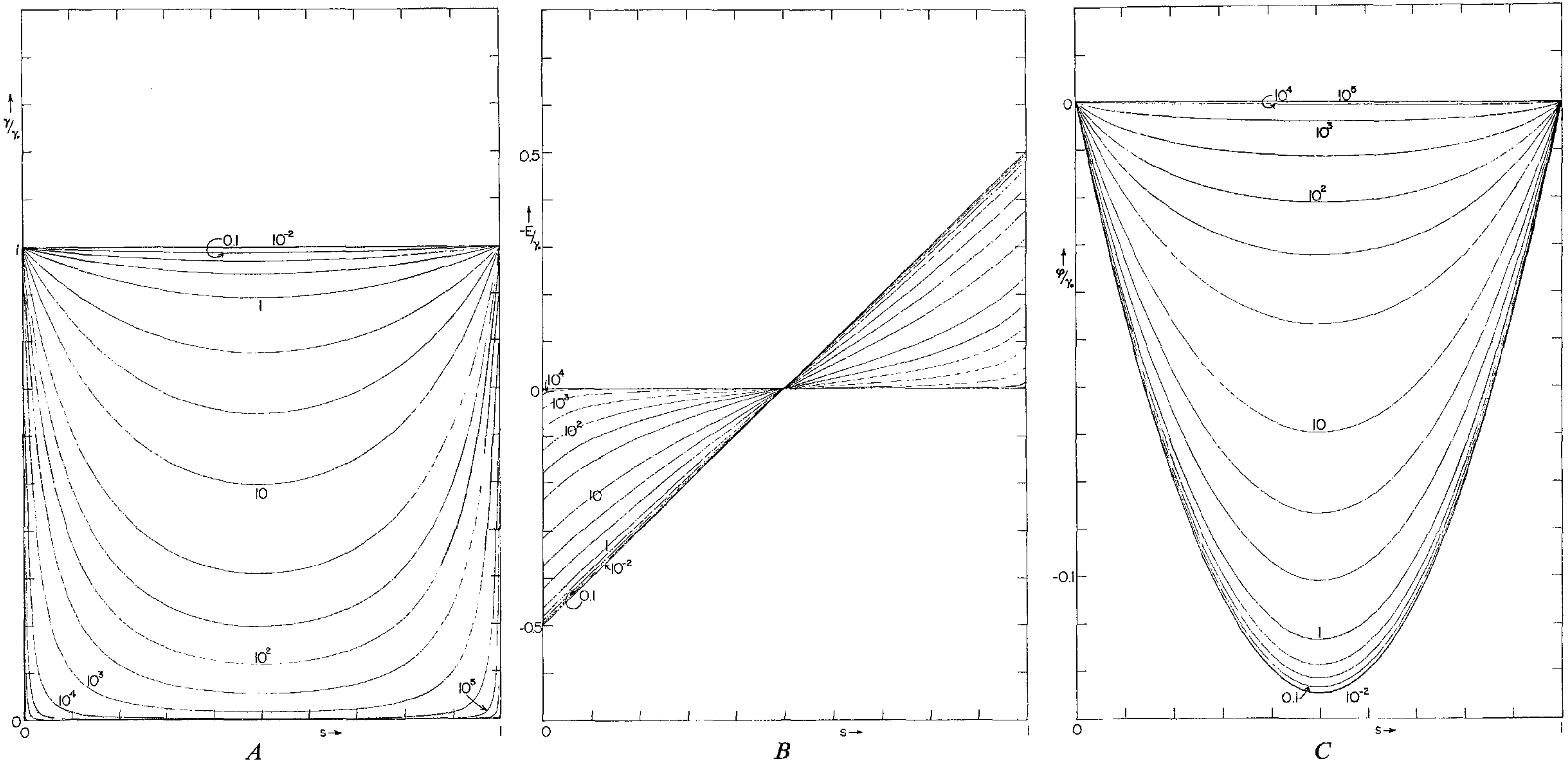

Fig. 1. Profiles of dimensionless concentration (*A*), dimensionless field (*B*) and dimensionless potential (*C*) for the totally symmetrical case, $\gamma_0 = \gamma_1 = 10^{-4}$ to 10^{-2} (identical curves), 0.1, 0.25, 0.5, 1, 2.5, 5, 10, 25, 50, 100, 250, 10^3, 10^4, 10^5, 10^6. Note that γ, E and φ are all scaled through division by γ_0, thus emphasizing the field and potential profiles at low ionic concentrations

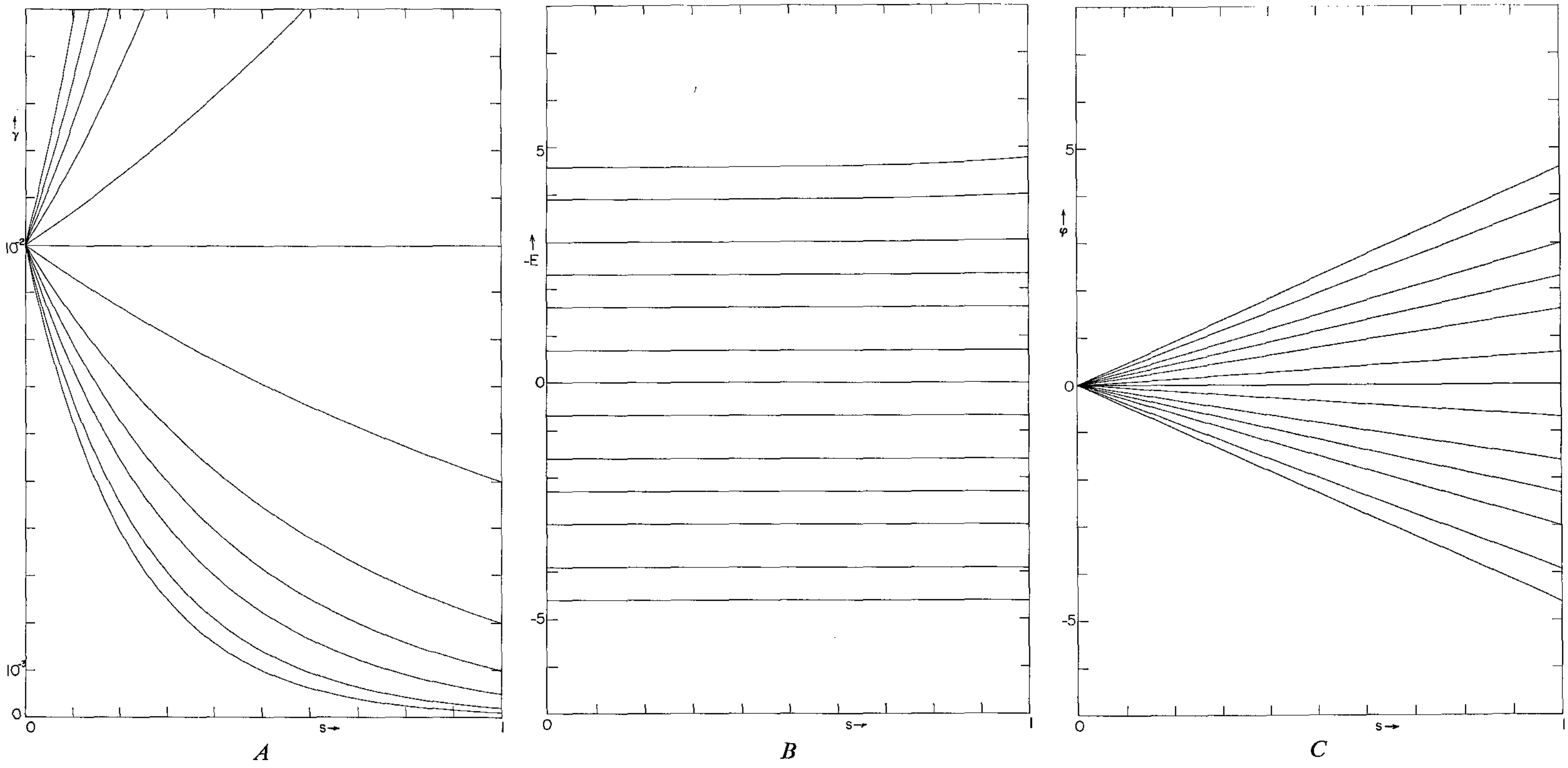

Fig. 2. Profiles of dimensionless concentration (*A*), dimensionless field (*B*) and dimensionless potential (*C*) for (from bottom to top) $\gamma_1/\gamma_0 = 0.01$, 0.02, 0.05, 0.1, 0.2, 0.5, 1, 2, 5, 10, 20, 50, and 100 with $\gamma_0 = 10^{-2}$

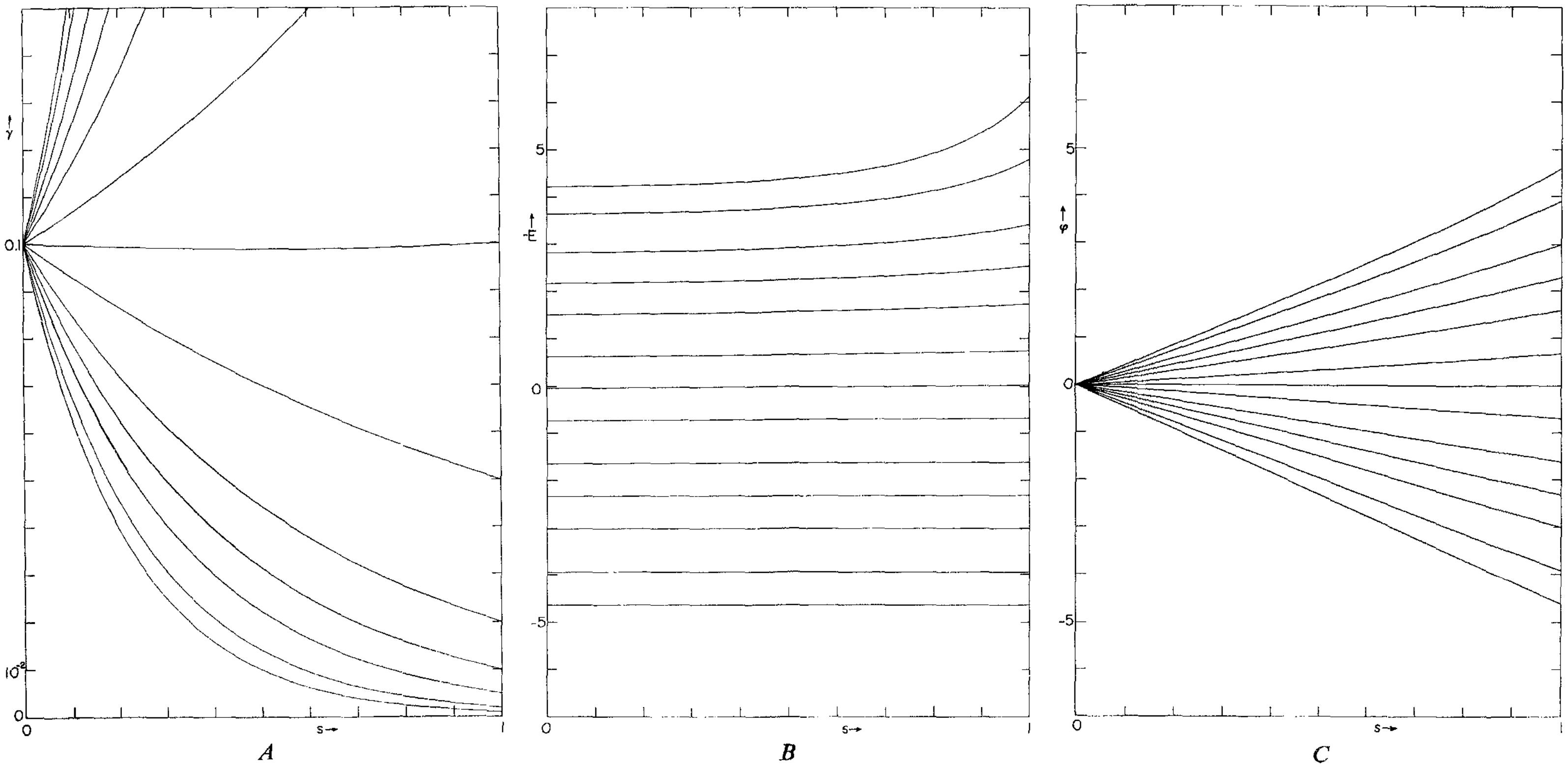

Fig. 3. Same as Fig. 2 except that $\gamma_0 = 10^{-1}$

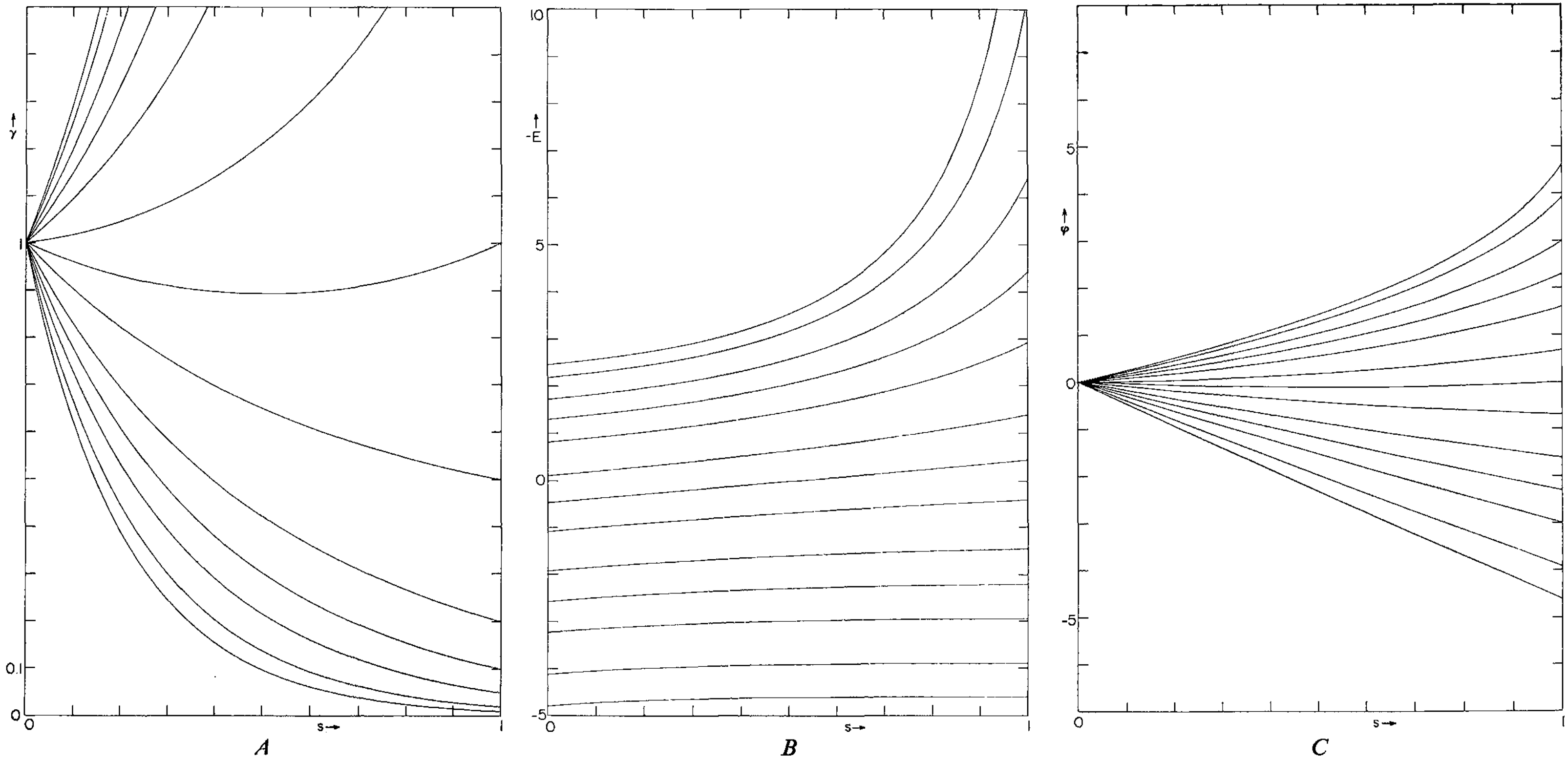

Fig. 4. Same as Fig. 2 except that $\gamma_0 = 1$

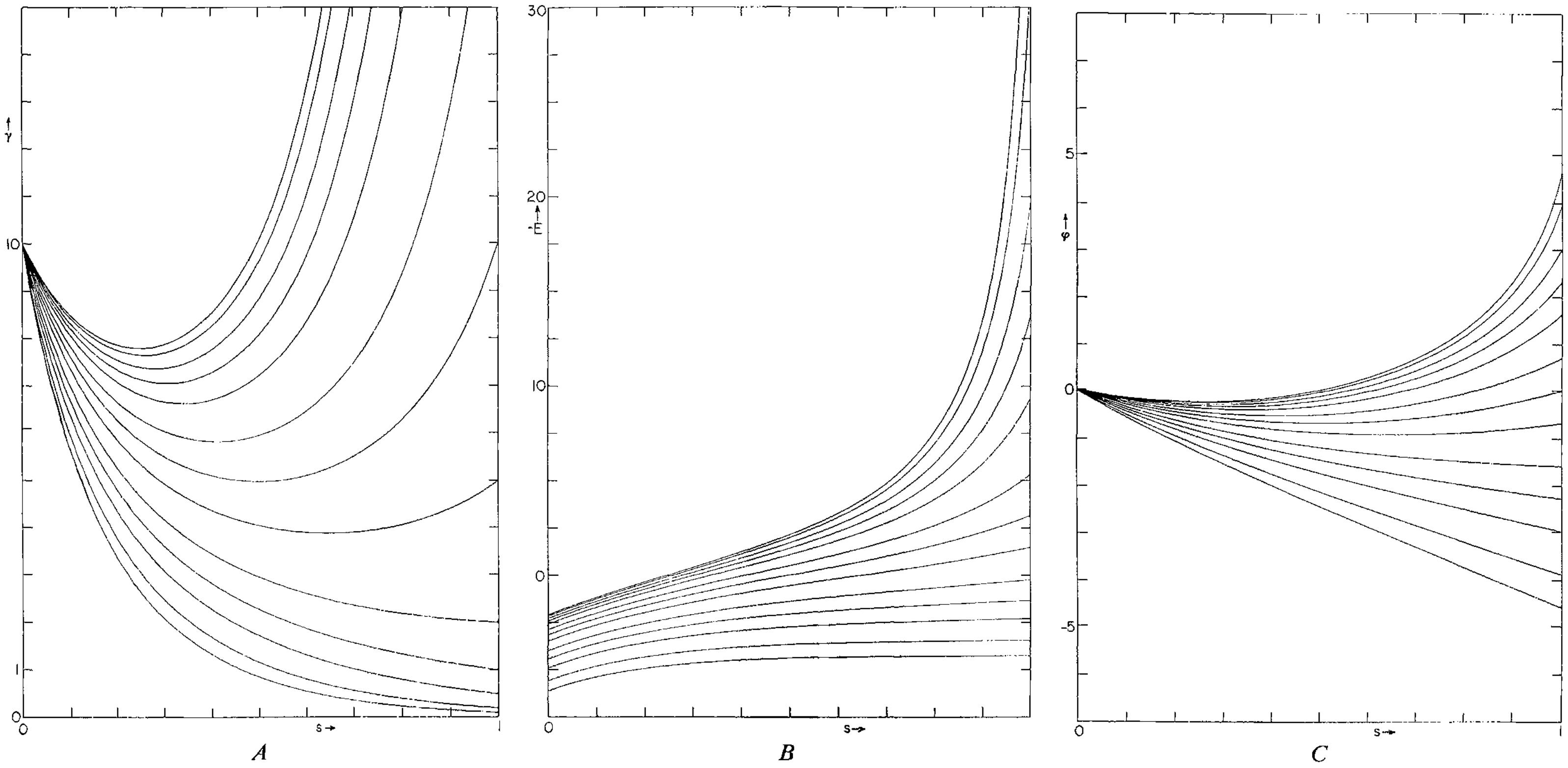

Fig. 5. Same as Fig. 2 except that $\gamma_0 = 10$

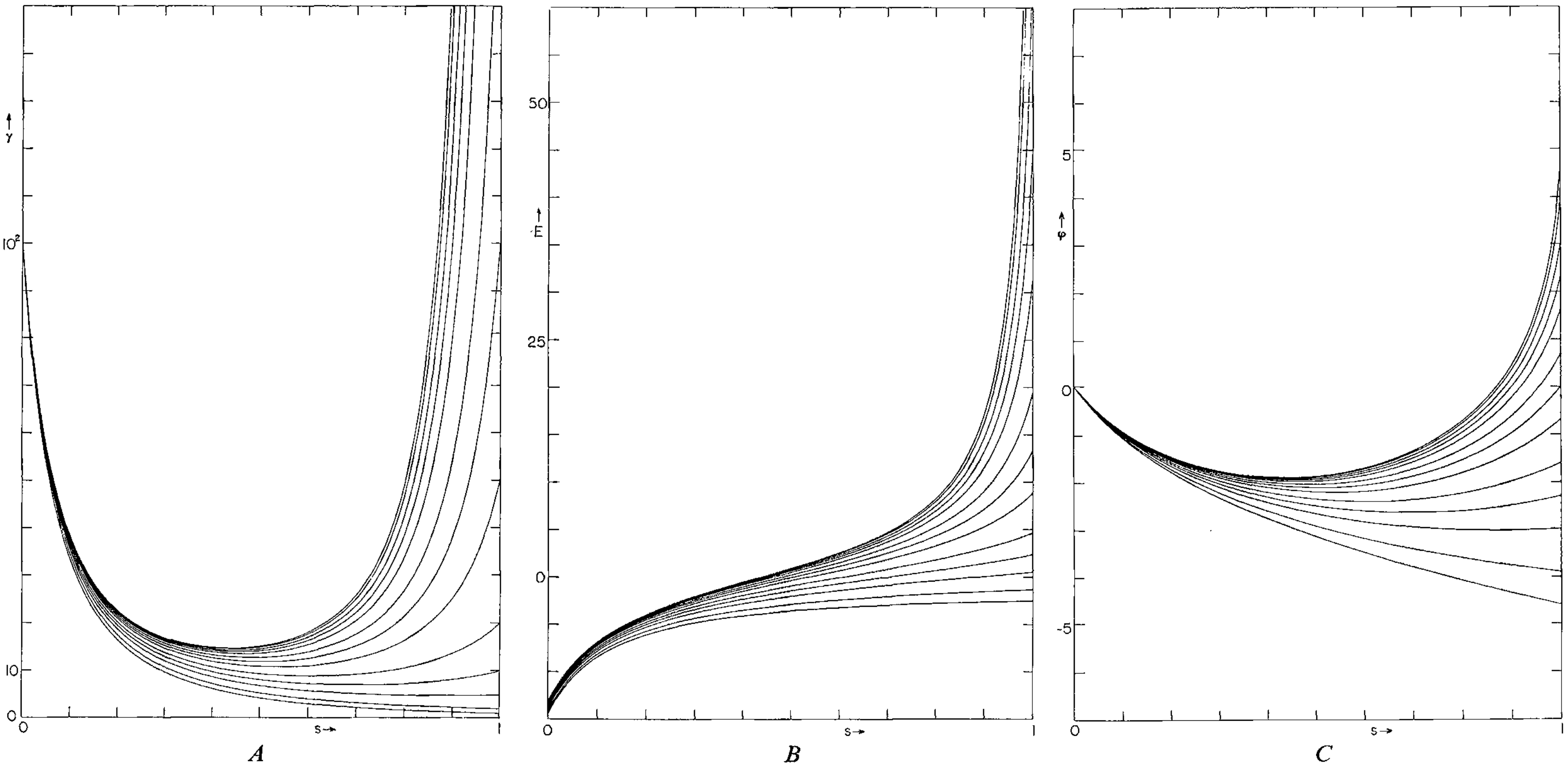

Fig. 6. Same as Fig. 2 except that $\gamma_0 = 10^2$

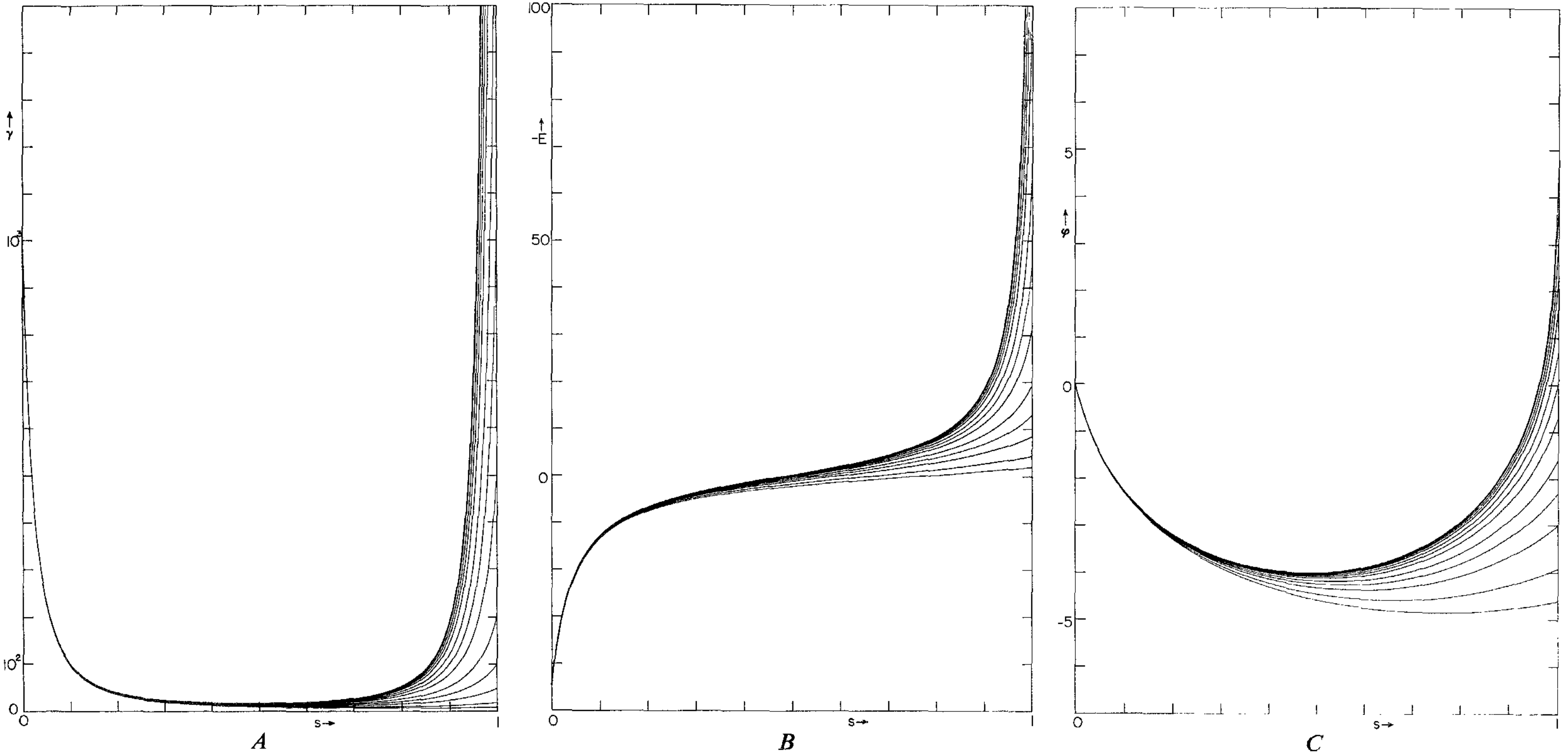

Fig. 7. Same as Fig. 2 except that $\gamma_0 = 10^3$

Table 1. Values of A calculated for constant γ_0 and varying ratio of γ_1/γ_0[a]

γ_1/γ_0	$\gamma_0=10^{-2}$	$\gamma_0=10^{-1}$	$\gamma_0=1$	$\gamma_0=10$	$\gamma_0=10^2$	$\gamma_0=10^3$
0.01	10.6016 4690	10.5823 4262	10.3931 1057	8.8011 7701	2.0647 1068	−7.7831 0287
0.02	7.6494 5754	7.6269 7451	7.4076 1181	5.6254 4419	−1.1877 5064	−10.1198 8748
0.05	4.4840 3585	4.4556 0382	4.1806 1629	2.0786 5793	−4.8029 8499	−12.5467 2195
0.1	2.6470 4216	2.6120 3747	2.2766 8605	−0.1353 3890	−7.0451 4949	−13.9447 7517
0.2	1.2901 7748	1.2457 3234	0.8255 3925	−1.9725 2082	−8.8938 9805	−15.0266 2563
0.5	0.2330 1948	0.1687 2944	−0.4233 7423	−3.8771 9378	−10.7971 9584	−16.0661 6527
1	−0.0099 8752	−0.0987 7044	−0.8925 2241	−4.9711 3805	−11.8844 8548	−16.6234 7817
2	0.2258 2531	0.0984 7814	−0.9929 0106	−5.8139 7141	−12.7205 1992	−17.0328 7066
5	1.2703 6558	1.0537 3577	−0.6538 3214	−6.6180 1694	−13.5189 2470	−17.4077 1017
10	2.6120 3747	2.2766 8605	−0.1353 3890	−7.0451 4949	−13.9447 7517	−17.6010 2311
20	4.4242 1902	3.8933 1077	0.5127 8439	−7.3563 1596	−14.2565 5150	−17.7395 7784
50	7.5282 7297	6.5356 9462	1.4230 1973	−7.6386 6546	−14.5411 9625	−17.8638 5276
100	10.3931 1057	8.8011 7701	2.0647 1068	−7.7831 0287	−14.6876 7660	−17.9269 7190

[a] For $A<0$, Eqs. (28) through (30) apply, whereas Eqs. (36) through (38) should be used when $A>0$. In general, A is bound by $-2\pi^2 \leqq A \leqq \frac{1}{2}v^2$.

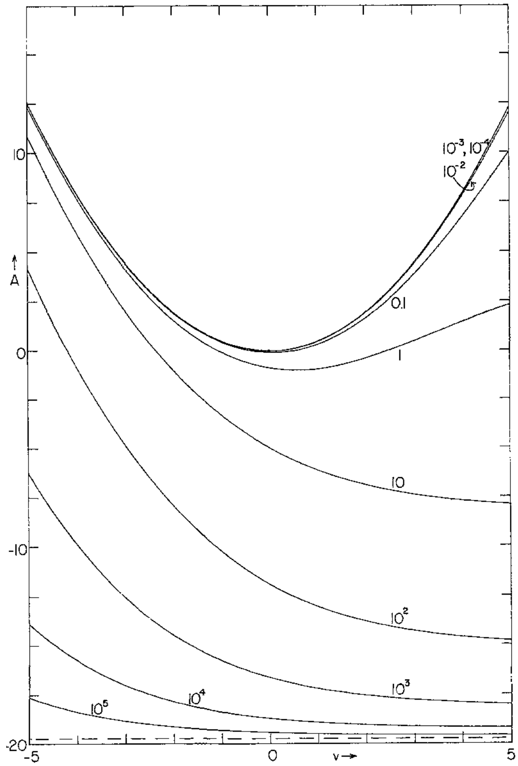

Fig. 8. The parameter A as a function of the dimensionless equilibrium potential $v = \ln \gamma_1/\gamma_0$ for various values of γ_0, as indicated with the curves. The interrupted horizontal line near the bottom of the diagram indicates the lower limit of A, at $-2\pi^2$

can be judged from Figs. 2, 3, 4 and 8. The difference between Eq. (53) and the curves shown in Fig. 2A cannot be noticed on the scale of that graph.

For small values of v (i.e., for $\gamma_0 \approx \gamma_1$), the approximation represented by Eqs. (50) through (52) is not quite satisfactory. For $v=0$, a more appropriate approximation for low ionic concentrations is

$$A \approx -\gamma_0 \tag{54}$$

$$b \approx \sqrt{\gamma_0/2} \tag{54a}$$

$$p \approx \tfrac{1}{2}\sqrt{\gamma_0/2} \tag{54b}$$

$$\varphi \approx \tfrac{1}{2}\gamma_0\, s(s-1) \tag{55}$$

$$E \approx -\gamma_0(s-\tfrac{1}{2}) \tag{56}$$

$$\gamma \approx \gamma_0 = \gamma_1. \tag{57}$$

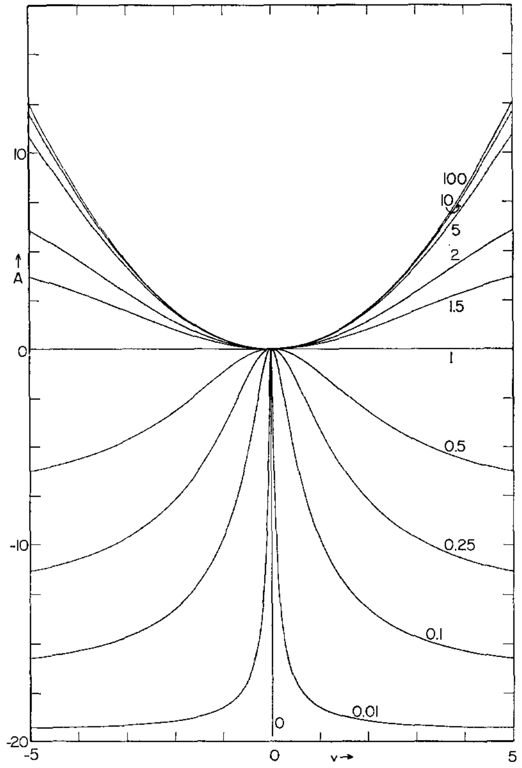

Fig. 9. The parameter A as a function of the dimensionless equilibrium potential $v = \ln \gamma_1/\gamma_0$ for various values of the parameter $|\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}|$ as indicated with the curves

This constant concentration (rather than constant field) behavior, with its corresponding linear field and parabolic potential profiles, is clearly illustrated in Fig. 1*A*, *B* and *C*.

Approximation for High Ionic Concentrations

When both γ_0 and γ_1 are larger than about 10^3, a useful approximation is

$$A \approx -2\pi^2 + 4\pi^2(1+e^{-v/2})\sqrt{2/\gamma_0} = -2\pi^2(1-\sqrt{8/\gamma_0}-\sqrt{8/\gamma_1}) \tag{58}$$

$$b \approx \pi - \pi(1+e^{-v/2})\sqrt{2/\gamma_0} = \pi(1-\sqrt{2/\gamma_0}-\sqrt{2/\gamma_1}) \tag{59}$$

$$p \approx \frac{1}{\pi}\sqrt{\frac{\gamma_0}{2}} \tag{60}$$

which can be substituted into Eqs. (28) through (30).

Discussion

In the foregoing we have presented a fairly detailed equilibrium description of membranes with charge carriers of one kind, both because it serves as a stepping stone for the discussion of the steady-state nonequilibrium behavior, and also because useful approximations for the latter case can be based on equilibrium properties (*see* Part II). We have seen that the exact equilibrium solutions use either trigonometric or hyperbolic functions of real arguments, moving from the former to the latter as the interfacial concentrations become less and less similar. At very low ionic concentrations, the hyperbolic solutions apply in all but the most symmetrical cases, whereas the trigonometric solutions must be used when the symmetry, or the ionic concentrations or both are high. The transition from trigonometric to hyperbolic functions and vice versa is perfectly smooth and unnoticeable in Figs. 2–7. The oscillatory character of trigonometric functions need not bother us, since all pertinent values of the parameter b are confined to the interval $|b| \leqq \pi$, which corresponds to

$$A \geqq -2\pi^2. \tag{61}$$

Sometimes, values of b outside the above-indicated range can be found to satisfy the boundary conditions, Eq. (16). However, such solutions lead to infinite, and hence unacceptable, values for γ, E and φ within the interval $0 \leqq s \leqq 1$ by making $(p \sin bs + \cos bs)$ pass through zero within that interval. The upper limit of A is given by Eq. (50).

The above calculations are valid for any type of charge carrier: electrons, ions, holes, etc. In view of the overwhelming evidence for predominantly ionic conduction in biomembranes, the word "ion" has been used in both title and text. It could, of course, be replaced everywhere by "charge carrier" if one would so desire. Likewise, the discussion so far has not implied any restrictions on the thickness of the "thin" membrane mentioned in the title.

To obtain some "feel" for the useful ranges of the dimensionless parameters defined in Eq. (3), Table 2 lists the potential, field and concentration

Table 2. Approximate conversion factors for some dimensionless parameters defined in Eq. (3), and most useful ranges of those parameters for practical biomembranes[a]

Approximate equivalence	Most useful range
$\psi \approx -25\ \varphi$ mV	$-5 \lesssim \varphi \lesssim +5$
$d\psi/dx \approx 50\ E$ kV/cm	$-10 \lesssim E \lesssim +10$
$c \approx 0.2\ \gamma$ mM/liter	$0 \lesssim \gamma \lesssim +10^2$

[a] In these estimates, the following values have been assumed: $n=1$, $T=300$ °K, $d=50$ Å, $\varepsilon_{\mathrm{rel}}=2$.

equivalent to unity value of the corresponding dimensionless parameters, as well as the estimated range of general applicability of these parameters for biomembranes. The usefulness of the constant-field approximation, Eq. (52), is clearly limited to $\gamma \lesssim 0.1$ and consequently to ionic concentrations below about 10^{-5} M.

There is always a certain amount of arbitrariness in the choice of dimensionless parameters. For instance, the present definition of γ gives the Poisson equation a very simple form [*see* Eq. (6)]. However, some of the final results would have assumed a somewhat more compact form if one were to define γ a factor of 2 smaller.

The symmetrical concentration profiles on Fig. 1*A* clearly reveal one of the characteristic aspects of the equilibrium behavior. At low concentrations ($\gamma \ll 1$), the ions are distributed homogeneously throughout the membrane, whereas they avoid the interior of the membrane and form separate space-charge layers at the membrane surfaces for $\gamma \gg 1$. Such behavior can be understood most readily by comparison of the corresponding characteristic thickness $1/\kappa$ of the Gouy-Chapman diffuse double-layer theory with the definition of γ:

$$\kappa^2 \equiv \frac{8\pi n^2 F^2 c^*}{\varepsilon RT} \tag{62}$$

$$\gamma \equiv \frac{4\pi n^2 F^2 d^2 c}{\varepsilon RT} = \frac{\kappa^2 d^2 c}{2c^*}. \tag{63}$$

Taking $c/2c^*$ to be of the order of unity, we see that isolated double layers are obtained when $\kappa^2 d^2 \gg 1$ or $d \gg 1/\kappa$, whereas the double layers overlap when $\kappa^2 d^2 \ll 1$ or $d \ll 1/\kappa$. In the less symmetrical cases depicted in Figs. 2–7 the same general trend is apparent.

In aqueous solutions, the Gouy-Chapman diffuse double-layer theory breaks down when its thickness $1/\kappa$ becomes comparable to the dimensions of the ions forming it; i.e., at about unit ionic strength ($1/\kappa \approx 3$ Å). Similarly, one would expect the present continuum model to become inadequate when the equivalent characteristic thickness $d/\sqrt{2\gamma}$ becomes comparable to the size of the membrane-soluble ions or ion-carrier complexes. For $d = 50$ Å, this would correspond to an upper limit of about 10^2 for γ (*cf.* Fig. 6*A*).

At high ionic concentrations, the electrical field generated by the ionic space charge itself approaches the dielectric breakdown value (*see* Figs. 6*B* and 7*B*). This should restrict the maximum value of γ in a bilayer membrane to about 10^2. Thus, it appears that the present description is adequate for essentially the whole range of ionic concentrations which one can anticipate in biomembranes. The same cannot be said for the constant-field approximation.

Experimentally, one can only control γ_0 and γ_1 when mass transfer in the adjacent aqueous solutions, and transfer across the phase boundaries, are both very fast processes. The question of more generally applicable boundary conditions will be taken up in Part III[1] of this series.

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[1] To be published in a future issue.

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