MODEL HYDROPHOBIC
ION EXCHANGE MEMBRANE

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ABSTRACT Two models of hydrophobic ion exchange membranes were examined theoretically with regard to the characteristics of cellulose acetate-nitrate membranes saturated with hydrophobic solvents. The first model, consisting of fixed negative sites dispersed in a homogeneous medium of low dielectric constant, was shown to be invalid for the experimental membranes. The second model, consisting of fixed negative sites in an aqueous channel surrounded by a medium of low dielectric constant, explains many properties of the cellulose acetate-nitrate hydrophobic membranes and was analyzed in some detail. Organic cations can enter the membranes through the hydrophobic phase as well as through the aqueous channels. The mechanism of counterion movement in such a model is assumed to consist of exchange of vacancies and or double-occupied sites positions. The presence of the medium of low dielectric constant around the aqueous channel increases the "self"-energy of the ions in the channel and the electrostatic interaction between a fixed site and a counterion in the membrane. Both these factors can account for the marked dependence of ion mobility in the aqueous channels on the dielectric constant of the surrounding medium. The model predicts membrane preference for monovalent counterions over divalent ones.

INTRODUCTION

Ion exchange membranes are dealt with in many branches of the technological and biological literature. The principal models of such membranes depict ionized groups dispersed homogeneously on a skeleton soaked in aqueous solution (Fig. 1 A) or show ionized groups distributed on the wall of a capillary filled with water and ions (Fig. 1 B) (Teorell, 1953; Schlogl, 1955).

The subject of this article is "model hydrophobic ion exchange membranes." The term "hydrophobic" ion exchange membranes is applied to two types of models which can be considered as a modification of the ordinary ion exchange membrane models as shown in Figs. 1 C and D. The first type consists of ionized groups dispersed on skeleton soaked in a medium of low dielectric constant. The second type consists of an ion exchange aqueous channel bounded by "infinite" hydrophobic media.
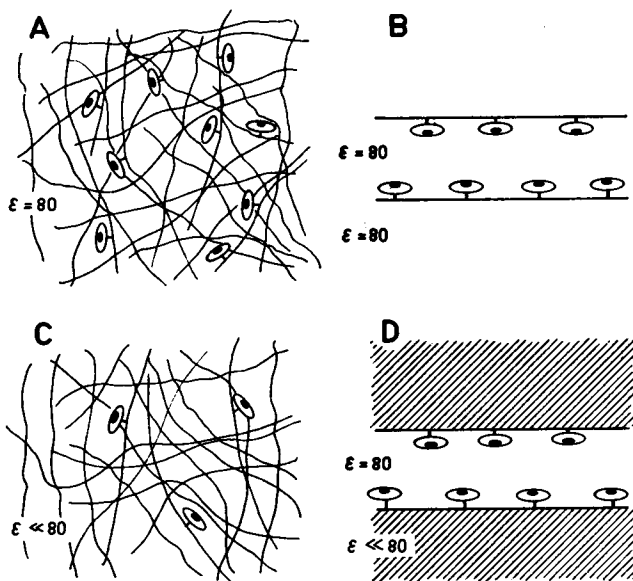
FIGURE 1 Models of ion exchange membranes. (A) Fixed charges attached to skeleton immersed in aqueous solution. (B) Fixed charges on a wall of an aqueous capillary. (C) Same as A except that the fixed sites are soaked in a hydrophobic medium (i.e., dielectric constant ϵ less than 80). (D) The same as B except that "infinite" medium of low dielectric constant surround the aqueous capillary.

Another way of introducing these two types of models is to refer to their uncharged analogues: (a) homogeneous hydrophobic membranes and (b) neutral aqueous capillary embedded in hydrophobic medium. The theoretical analysis of ion distribution between water and homogeneous hydrophobic membranes was dealt with by Verwey and Overbeek (1948) and references to studies on permeability to ions of such membranes can be found in Davies and Rideal (1963). Some features of ionic selectivity of a neutral aqueous capillary immersed in a medium of low dielectric constant are discussed by Parsegian (1969). The analysis of the hydrophobic ion exchange model in this article follows the treatments of the neutral analogues by Verwey and Overbeek (1948) and by Parsegian (1969). As will be evident later the second type of model (D in Fig. 1) will be considered in detail in this presentation.

Models of hydrophobic membranes warrant a special attention because of their possible relevance to the study of biological membranes. It would be advantageous, however, to substantiate the theoretical consequences of the model study on experimental systems. In this presentation the principal theme is the comparison of the models with experimental hydrophobic membranes, which were studied in this laboratory (Ilani, 1965, 1966 a and b, 1968, 1970; Shohami and Ilani, 1973). Chronologically, the experimental system was dealt with first and the model developed

later in order to understand the observed behavior of the hydrophobic membranes. It is therefore beneficial to start by introducing some of the special features of the experimental hydrophobic membranes.

THE EXPERIMENTAL MEMBRANES

Cellulose Ester Filters Soaked in Organic Solvents

Porous disks made of cellulose acetate and nitrate (such as Millipore filters, Millipore Corp., Bedford, Mass.) were immersed in various organic solvents and then interposed between two aqueous solutions. The solvents were retained by the filters even after long (several days) exposure to the aqueous media. In this system it was possible to measure ion fluxes, ion diffusion coefficients, potential differences, and electrical conductance and capacitance. It was also possible to measure ion content within the membrane. The details of methods used can be found in earlier publications (Ilani, 1965, 1966 a, 1968, 1970; Shohami and Ilani, 1973). Some of the prominent features which characterize the membranes are as follows:

(a) The membranes behave like cation exchangers as verified in the following ways: (i) the cation content in the membrane is relatively constant and independent of its concentration in the aqueous solution (Ilani, 1965); (ii) the conductivity of the membrane is within experimental error equal to the conductance due to the cation present (as estimated from flux measurements) (Ilani, 1966 a); (iii) the resistance of the membrane was dependent upon the nature of cation present in the aqueous solution but independent of the nature of anion used (Ilani, 1965; Shohami and Ilani, 1973); (iv) the potential difference in a concentration cell is equal to that of a cation permselective membrane (Ilani, 1966 a; Shohami and Ilani, 1973).

(b) There is significant discrimination between monovalent cations as can be judged from measurement of bi-ionic cell potentials (Shohami and Ilani, 1973).

(c) The discrimination between cations can be resolved into discrimination due to differences in selectivity and in mobility, e.g., the 45-fold potassium-sodium permeability ratio results from a factor of 10–12 in selectivity and a factor of about 4 in mobility ratio (Ilani, 1966 b).

(d) There is extreme discrimination between monovalent and divalent cations in these membranes, e.g., the lower limit of the potassium-calcium permeability ratio is above 1,000 (Ilani, 1970).

(e) The electrical conductance of the membranes (or the diffusion constant of a cation in the membrane) is strongly dependent upon the dielectric constant of the saturating organic solvent. In the dielectric constant range of 2.5–10.0 there is about 1,000-fold change in diffusibility of counterions in the membrane. The relation between log diffusibility and the reciprocal value of the dielectric constant is linear (Shohami and Ilani, 1973).

(f) The selectivity of the membranes for some organic cations follows their relative solubility in the pure solvent phase (Shohami and Ilani, 1973).

Basic Theoretical Treatment for Ion Distribution between Membrane and Water Solution

The analysis of the equilibrium state in the membrane water system follows an analysis developed for "ordinary" ion exchange membranes (Mauro, 1962) namely the following Eqs. 1 and 2 must be satisfied: Poisson's equation

$$\nabla^2\psi = (4\pi/\epsilon)\rho, \tag{1}$$

and Boltzmann's equation

$$C^{\pm}(x) = C_w^{\pm}B^{\pm} \exp\left(\mp\psi F/RT\right), \tag{2}$$

where $\nabla^2\psi$ is the laplacian of the electric potential, ϵ is the dielectric constant, ρ is the charge density, $C^{\pm}$ is the concentration of a cation or an anion, subscript w refers to the aqueous phase far from the interface, $B^{\pm}$ is the distribution coefficient of a cation or an anion between the aqueous solution and the relevant phase. The charge density ρ is given by

$$\rho = F(C^+ - C^- - N^-), \tag{3}$$

where F is the Faraday number and N^- is the concentration of fixed negative sites. Eqs. 1–3 are soluble in principle and should yield the ionic concentration and the electric potential profiles in the system, $C^{\pm}(x)$ and $\psi(x)$, respectively.

The parameter $B^{\pm}$ is the important new variable which differentiates the present model from an ordinary water-soaked ion exchange membrane. In the latter the variable $B^{\pm}$ is assumed to be 1.0 while for the present model it is given by

$$B^{\pm} = \exp\left(-\Delta F^{\pm}/RT\right), \tag{4}$$

where $\Delta F^{\pm}$ is the change in free energy per mole associated with the transport of the ion from the aqueous solution into the membrane phase.

For small inorganic ions the change in free energy can be evaluated by the Born principle, namely, one assumes that a neutral sphere of radius a has the same energy in both phases and one calculates the work E required to charge reversibly the sphere to the extent q_0 where q_0 is the charge of the ion, i.e.

$$\Delta E = \int_0^{q_0} \psi^I(a, q) \, dq - \int_0^{q_0} \psi^{II}(a, q) \, dq, \tag{5}$$

where $\psi(a, q)$ is the potential at the surface of the sphere of radius a containing a charge q. The superscripts I and II refer to the respective phases. (It is assumed that the free energy change ΔF is equal to the self-energy change ΔE. Throughout this presentation ΔF and ΔE will be considered to be identical and used interchangeably.)

The Homogeneous Model (Fig. 1 C)

In a homogeneous infinite medium of dielectric constant ϵ the potential is given by

$$\psi(a, q) = q/\epsilon a, \tag{6}$$

therefore Eq. 5 becomes the well-known Born expression

$$\Delta F^{\pm} = (q_0^2/2a)[(1/\epsilon^{\mathrm{I}}) - (1/\epsilon^{\mathrm{II}})]. \tag{7}$$

For ionic radius of 2 Å and $\epsilon^{\mathrm{I}} = 4.0 \ \Delta F$ in Eq. 7 is about 21 kcal/mol and the distribution coefficient at 25°C according to Eq. 4 is about 5×10^{-15}. By introducing Eqs. 3 and 2 into Eq. 1 and by using the appropriate boundary conditions it is possible (Ilani, 1968) to obtain an explicit expression of $d\Psi/dx$. This expression was solved numerically and the results are shown in Fig. 2. The boundary conditions used are: (a) $\psi_{0+} = \psi_{0-}$, i.e. ψ continuous; and (b) overall electroneutrality, i.e. $\int_{-\infty}^{+\infty} \rho \, dx = 0$ (Ilani, 1968).

The resistance of a plate of membrane of thickness dx will be given by

$$dR(x) = \frac{1}{A u_i C_i(x) F} dx, \tag{8}$$

where u_i is the ion mobility and A is membrane area. Therefore the membrane resistance is

$$R_{\mathrm{membrane}} = \frac{1}{A u_i F} \int_0^{\Delta x} \frac{1}{C_i(x)} \, dx, \tag{9}$$

where Δx is membrane thickness. (For the cellulose ester membranes $\Delta x = 0.015$ cm.)

The value of Eq. 9 for the conditions shown in Fig. 2 and $\Delta x = 0.015$ cm is $1/A u_i F \times 3.0 \times 10^{12}$. If u_i equals $\sim 7 \times 10^{-4}$ cm²/V s (mobility of potassium in aqueous solution, see Moore, 1957, p. 446), and membrane area is 3 cm², the value of the above expression is about $10^{10} \ \Omega$. This value is four to five orders of magnitude higher than the experimental value for a membrane saturated with a solvent of dielectric constant 4 (Shohami and Ilani, 1973). This means that even if the mobility of ions in the hydrophobic medium were the same as that in water the measured resistances of the cellulose ester membranes were too low. For solvents of lower dielectric constant which have lower distribution coefficient (e.g., toluene) the difference between the observed and calculated membrane resistances would be even higher. Moreover, if the counterions were separated from the fixed sites by a medium of low dielectric constant they would be expected to form ion pairs and therefore have a low mobility. This factor should also increase the discrepancy between the observed and calculated membrane resistances. These considerations lead
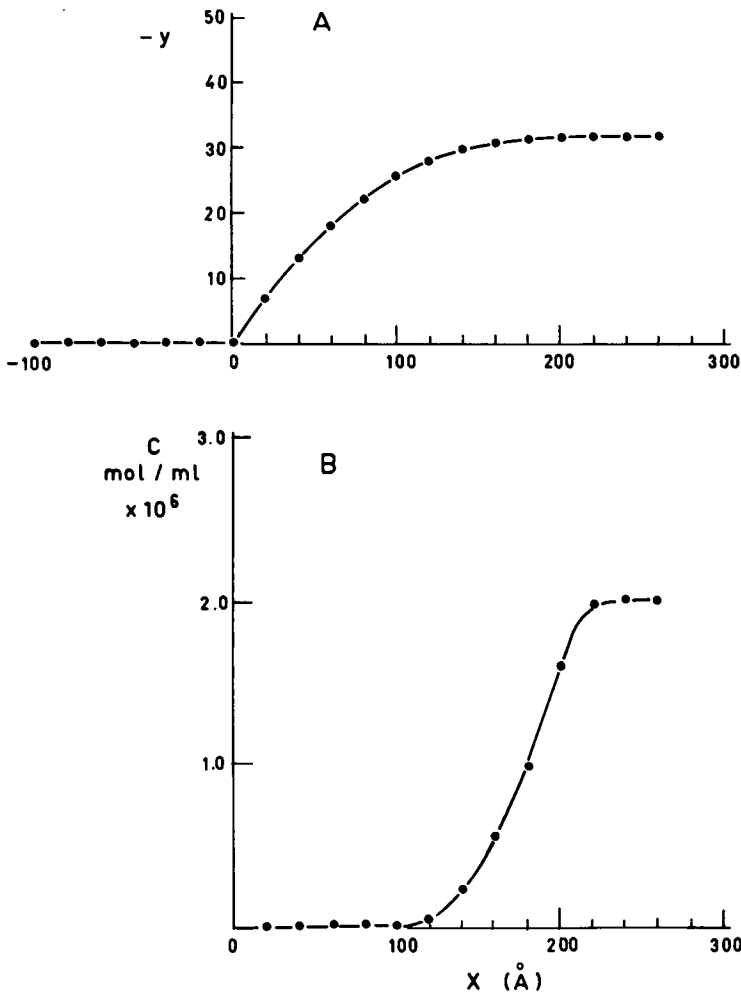
FIGURE 2 (A) The potential profile ($y = F\psi/RT$) across an interface between aqueous solution ($x < 0$) and a homogeneous hydrophobic medium of dielectric constant 4.0 ($x > 0$) containing 2 meq/liter of fixed negative sites. The aqueous solution contains 10 mM of mono-monovalent salt. $B^{\pm}$ is 5×10^{-15} (see text). (B) The concentration profile of the cation in the membranous side of the interface. Note that the concentration of counterions in the interface is extremely low. Electroneutrality is established at a distance greater than 200 Å from the boundary.

therefore to the conclusion that the homogeneous model cannot be valid for the cellulose ester membranes.

Model of an Aqueous Channel Surrounded by Hydrophobic Medium

This model is believed to be valid for the cellulose ester hydrophobic membranes described in the Introduction of this presentation. Such a model is plausible since a

thin film of water can be attached to the surfaces of the pores in the cellulose ester filters in a way analogous to the thin water layer which is purported to be attached to the surface of a paper sheet when exposed to immiscible phases, a situation which occurs in paper chromatography (Block et al., 1952). Also, this model satisfies the conclusion arrived at in the previous paper (Shohami and Ilani, 1973) namely that there must be two routes for ion movement through the membrane.

To facilitate the mathematical treatment of the model the continuous aqueous channel will be assumed to consist of a flat aqueous slab in the hydrophobic medium. The model shown in Fig. 3 consists of a layer of aqueous solution of height $2b$ which is bounded on both sides by semi-infinite media of dielectric constant ϵ_1. In the center of the slab of the aqueous solution there is a uniform distribution of fixed charges at a concentration N moles per unit volume of aqueous film, corresponding to an average separation d between adjacent fixed charge sites. The model shown in Fig. 3 comprises a membrane interposed between two aqueous solutions.

The parameter ΔF which appears in Eq. 4 can be presented qualitatively for this model in the following way: due to medium polarization effects (Born principle) the free energy of the ion is lower in the medium of higher dielectric constant. It is plausible that the free energy will vary in some continuous fashion through the interface (Fig. 4 A; see also Fig. 2 in Gurney, 1962). Figs. 4 B and C, depict, respec-
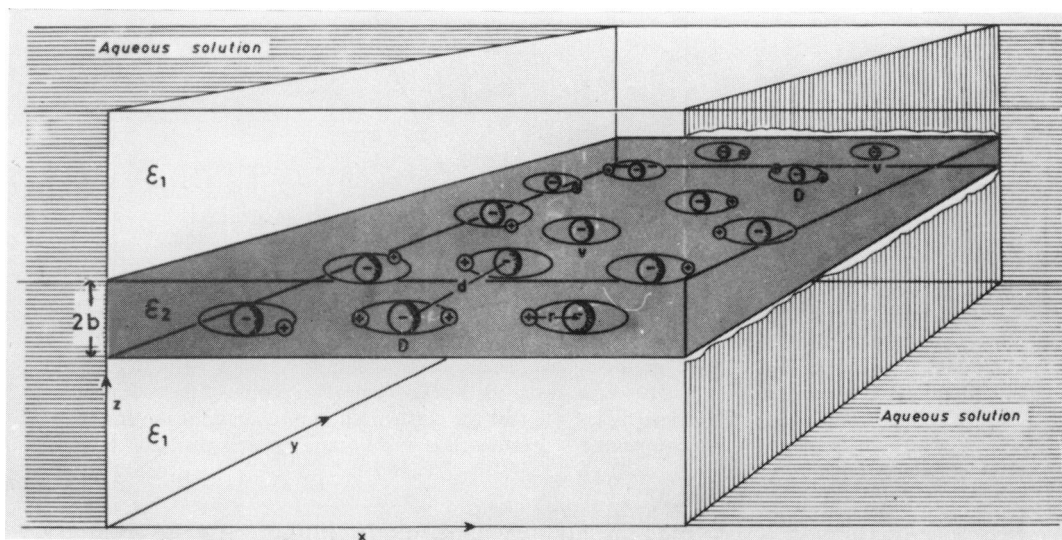

FIGURE 3 A particular model of a continuous aqueous channel present in a medium of low dielectric constant ϵ_1. The negative charges are supposed to be fixed while the cations are mobile. On the average there is one cation per one fixed site. Due to thermal energy of the mobile cations a fraction of the fixed sites can be vacant (v) or doubly occupied (D). d, average distance between fixed sites; $2b$, the thickness of the aqueous slab; r, equilibrium distance between counterion and fixed site.

tively, the ionic free energy profile in a case where thick and thin media of dielectric constant ϵ_2 are entrapped between two ϵ_1 media. ΔE is shown in Fig. 4 C.

It is possible to use the Born principle in order to estimate ΔE for this model, as done in the case of the homogeneous model. However for the present model the energy terms involve polarization of two media. To calculate ψ (a, q) in Eq. 5 one has to take into account the polarization of the media outside the aqueous slab. This is done by method of image charges as shown in Appendix I. Similar calculations were done by Parsegian (1969) for neutral cylindrical pores.

The calculation of ΔE for $a = 1$ and $2b$ equal 6 and 8 Å are shown in Table I. It is based on the Eq. A 7 of Appendix I. The corresponding distribution coefficients $B^{\pm}$ determined by Eq. 4 are also listed. It is obvious that neutral aqueous slabs trapped in a hydrophobic medium excludes ions to an extent which depends upon the size of slabs, the dielectric constant of the medium around the slab and the charge of the ion.
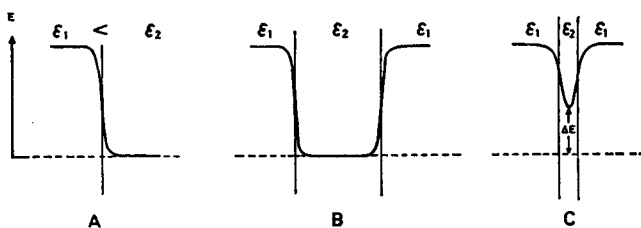

FIGURE 4   (A) The hypothetical free energy of a charged particle in the boundary region between two media of different dielectric constants. (B) The free energy curve when the medium of high dielectric constant is limited on both sides by media of low dielectric constant. If the ϵ_2 region is thick the resulting energy curve is equal to the sum of the two boundary curves. (C) When the ϵ_2 region is thin there is an interaction between the two boundaries. The free energy at the center of the ϵ_2 phase will be different by ΔE from the value of the energy in an infinite ϵ_2 medium.

TABLE I

ΔE AND DISTRIBUTION COEFFICIENT
B FOR IONS OF RADIUS 1 Å PRESENT IN THE
AQUEOUS SLAB OF THE MODEL SHOWN IN FIG. 3

ϵ_1	$b = 3$ Å		$b = 4$ Å	
	ΔE	$B \times 10^3$	ΔE	$B \times 10^3$
	kcal/mol		kcal/mol	
2	4.09	1.09	3.07	5.95
4	3.21	4.73	2.41	17.8
6	2.69	11.3	2.02	34.4
8	2.33	20.5	1.76	53.7
10	2.06	32.4	1.55	75.6

The main concern of this study is to consider the property of the system when the aqueous slab contains fixed charges. Under these conditions a potential difference will develop between the membrane and the surrounding aqueous phases which will affect the concentration of the ions in the membrane water layer as indicated by Eq. 2. In turn, the concentrations of ions determine the charge density (Eq. 3) and therefore affect the potential difference (Eq. 1).

The qualitative nature of the electric potential and ionic concentration profile across the membrane will be similar to that shown in Fig. 2 except that the B^+ is much larger in this case. Far from the interface electroneutrality must prevail and therefore the potential difference must be

$$\psi_\infty = (RT/F) \ln (N^-/C_w B^+), \tag{10}$$

if $B^\pm \ll 1.0$. At the interface the potential varies from its zero level in the bulk aqueous solution to its final value, ψ_∞ in the interior of the membrane. The space charge is positive in the solution side of the interface (where $C^+ > C^-$) and negative in the membraneous side of the interface (where $N^- > C^+$).

Since ΔF is proportional to the second power of the ionic charge content (see Eq. A 7 of Appendix I) while the electric potential energy of an ion is proportional to the first power of the charge content, the model predicts that discrimination between divalent and monovalent counterions will be comparable with discrimination between monovalent cations and anions (see Fig. 5). This is in sharp contrast to the expected "electroselectivity" of ordinary water-soaked ion exchange membranes (Hellferich, 1962) in which preference for the polyvalent counterion is expected and found. The experimental hydrophobic membranes mentioned in the Introduction of this paper are extremely discriminative between mono- and divalent ions and at least part of this is due to preference for the monovalent cations (Ilani, 1970).

As indicated at the end of Appendix I, Eq. A 7 contains a basis for discrimination between ions of different sizes and different valency. According to Eq. A 7 ΔE is an inverse monotonic function of the ion size and is dependent upon ϵ_1. However, the experimental membranes of this study show the following approximate selectivity for the alkali metal ions: Li, Na, K, Rb, Cs: 0.02, 0.1, 1, 1, 1 (Ilani, 1965). Moreover it seems that this pattern is independent of the solvent used (Shohami and Ilani, 1973). At the end of Appendix I we refer to the simplifying assumption which was involved in arriving at Eq. A 7. It is possible that more refined calculations may account for particular selectivity pattern observed in these membranes.

The exact solution of Poisson's equation (Eq. 1) for this model is quite complex because of the inhomogeneity which exists not only in the x axis but also in the z axis (see Fig. 3). This means that in the space charge region, near the interface, the second derivative of the potential will be nonzero in both the x and z directions. The solution shown in Fig. 6 is arrived at by ignoring the variation in the z direction,

AE divalent ions

AE + AE elect.
for monovalent anion
and divalent cation

AE for monovalent ions
AE elect. for monovalent anion

AE + AE elect. for monovalent cation

AE elect. monovalent cation

AE elect. divalent cation
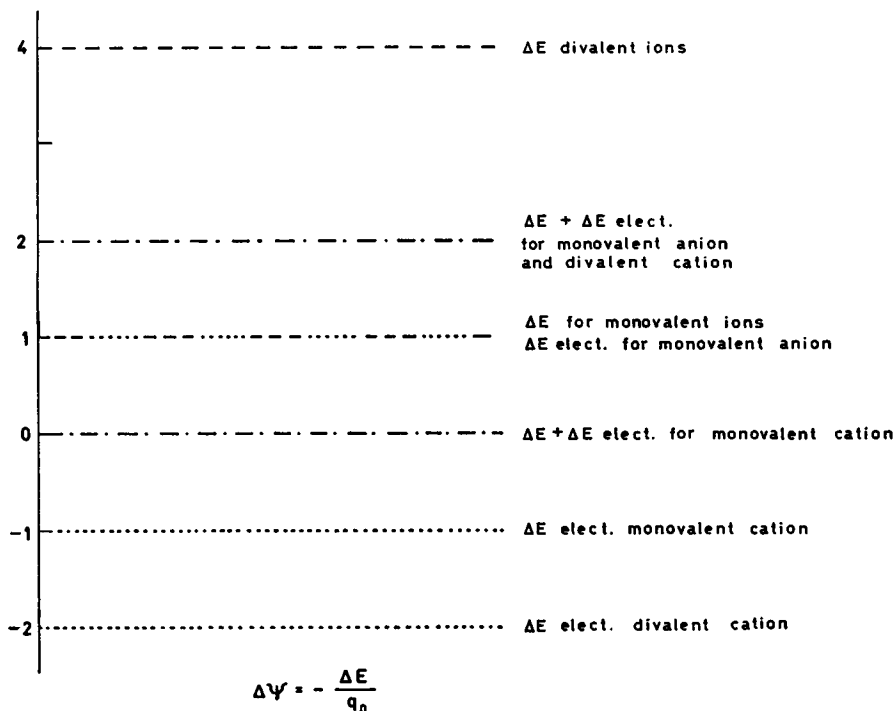
$$\Delta \Psi = - \frac{\Delta E}{q_0}$$

FIGURE 5   Illustration of the energy changes which will accompany ion movement from water into aqueous capillary-containing fixed negative sites and surrounded by medium of low dielectric constant. The self-energy of a monovalent ion ΔE is taken as unity. If a negative potential, $\psi = -\Delta E/q_0$, will develop across the interface the electric energy, ΔE elect., for a cation will be -1 and the net energy difference, $(\Delta E + \Delta E$ elect.$)$, zero. Under the same conditions the net energy difference for the anion will be two units (one for self-energy, and one electric energy) and for a divalent cation the net energy change will be also two (four units of self-energy minus two of electric energy).

i.e., by assuming that $\partial^2 \psi / \partial z^2 = 0$. The main feature of the membrane interfacial region is the presence therein of excess of fixed negative charges, i.e., the presence of relatively low concentration of mobile counterions. Therefore the interfacial region of the membrane has a resistivity which is different from that of the bulk membrane. The consequence of this fact has already been discussed (Ilani, 1968).

The Movement of Ions in the Membrane

In the case where $CB^+/N^- \ll 1$ all the mobile ions in the membrane will be the counterions. In the bulk of the membrane, i.e. far from the interface, there is electroneutrality so that there is on the average one counterion per fixed site. Obviously there will be an electrostatic interaction between a counterion and its nearest fixed site. Such an interaction will hinder ion movement within the membrane.

In first approximation one can assume that the energy required to move a coun-
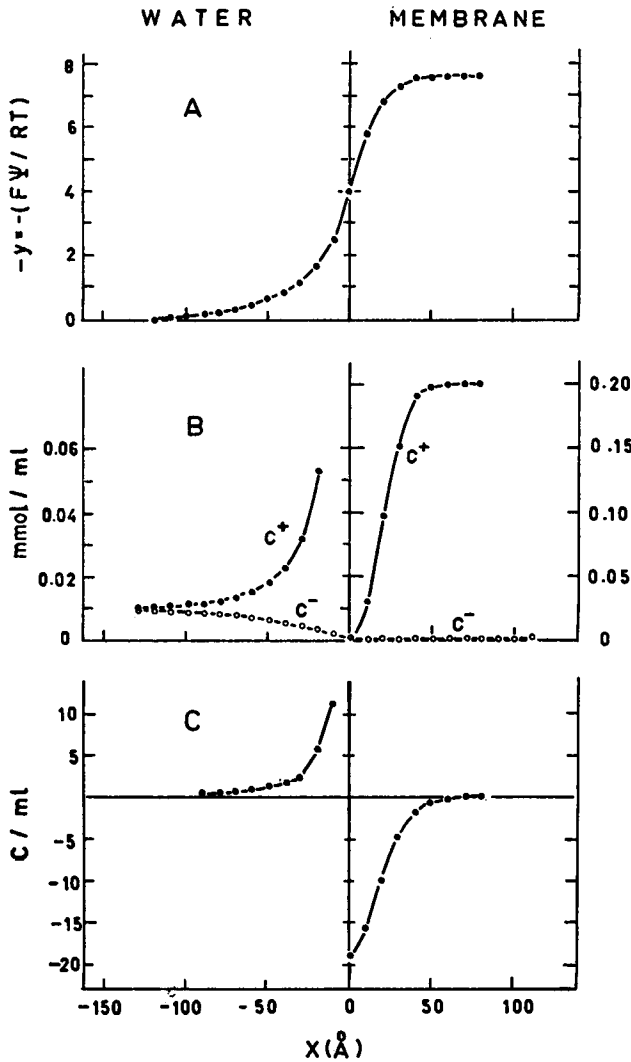
WATER   MEMBRANE

FIGURE 6

FIGURE 7

FIGURE 6   The potential profile (A) at boundary between aqueous solution ($x < 0$) and an aqueous slab surrounded by hydrophobic medium ($x > 0$) as depicted in Fig. 3. This represents a solution of Eqs. 1–3 if it is assumed that $d^2\psi/dz^2 = 0$. The following values are used: $B^{\pm}$ is 10^{-2}, concentration of fixed sites in aqueous slab 200 mM, concentration of salt in water 10 mM and $\epsilon_1 = 6$. The concentration profile of the cation and anion (B) and of space charge (C)·are also shown.
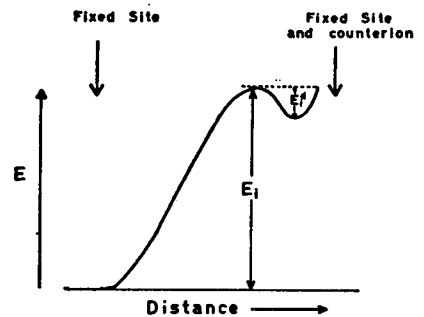
FIGURE 7   The general form of the electrostatic energy curve for a cation moving away from its equilibrium position near a fixed site (see text).

terion from its equilibrium position near a fixed site is determined by the electrostatic interaction of the two charges. This assumption implies that the net electric field caused by the more remote fixed sites and counterions is zero. As the counterion is approaching another fixed site it can polarize it with respect to its counterion so that a shallow energy minimum is expected near the new site. The general form of the energy profile of the counterion in the bulk membrane is shown in Fig. 7.

If Ei (in Fig. 7) $\ll kT$ the movement of counterion in the aqueous slab will be similar to that in a free solution, i.e., it will be limited by friction of the ions with the aqueous medium. At the other extreme, when $Ei \gg kT$ each counterion will reside near a fixed site constituting a fixed ion pair and no movement of ions in the membrane can take place.

In the range where $Ei > kT$ a small fraction of the fixed sites in the bulk of the membrane will be vacant or doubly occupied (D and v in Fig. 3). The reaction of formation of a doubly occupied site and a vacancy can be written in the form

$$M + M \leftrightarrows D + v, \tag{11}$$
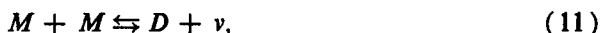
where M is a monooccupied site. The equilibrium constant K for the above reaction is given by

$$K = \frac{[D] \cdot [v]}{[M][M]} \sim X_v \cdot X_D = X_v^2, \tag{12}$$

where X_v and X_D are the fraction of sites present in the form of vacancies and doubly occupied sites, respectively. Since $-RT \ln K = \Delta F^\circ$ it follows that

$$X_D = X_v = \exp(-\Delta F^\circ / 2RT), \tag{13}$$

where ΔF° can be assumed to be given by $N(E_i - E_i^d)$ (see Fig. 7) where N is Avogadro's number.

The mechanism of movement of the counterions in the membrane will then consist of the jumps of counterions from doubly occupied sites to near by monooccupied sites (i.e., exchange of double-occupied sites positions) and by jumps of counterions from monooccupied sites into vacancies (i.e., exchange of vacancies positions). These mechanisms are similar to those suggested for diffusion in crystals (Barrer, 1951). If the exchange of double-occupied sites is the main mechanisms for counterion movement, the diffusion coefficient will depend on the relative abundance of doubly occupied sites and on the energy barrier for the movement from a double-occupied site (E_i^d in Fig. 7). Thus the mobility of the cation will be proportional to products of exponents of $-(E_i - E_i^d)/2kT$ and $-E_i^d/kT$ or

$$\text{ion mobility } \alpha \exp -N[(E_i + E_i^d)/2RT]. \tag{14}$$

The upper curve in Fig. 8 A shows the energy of a monovalent counterion present

at a distance of 2 Å from the center of a monovalent fixed site as function of the reciprocal of the dielectric constant of the outside medium (ϵ_1 in Fig. 3). The lower curve in Fig. 8 A depicts energy of the same counterion at a distance of 28 Å from the fixed site. The middle curve depicts the difference between the above two curves. This difference is closely related to E_i of Fig. 7 (if the distance between fixed sites is around 32–35 Å).

According to Eq. 14 the log of mobility of ion should be proportional to $N(E_i + E_i^d)/2RT$. The middle line in Fig. 8 A has a slope of 2.4 kcal/mol. This should lead to about sevenfold change [i.e., $\exp(-2.4/2RT)$] in mobility per unit change in $1/\epsilon$, as compared with about 10^6-fold change observed in the experimental system (see Fig. 1 in Shohami and Ilani, 1973). One has to assume then that the electrostatic interaction even in a rather narrow slab of water (6 Å thickness) cannot account for the marked dependence of the counterion mobility on the dielectric constant of the saturating solvent.

Fig. 8 B shows the electrostatic interaction between two charges present in an aqueous cylinder surrounded by a medium of low dielectric constant. It is obvious that in such a pore the interactions are much stronger compared with that in an aqueous slab. The slope of the middle curve in Fig. 8 B is about 20 kcal/mol which corresponds to about 10^7-fold change in mobility per unit change in $1/\epsilon$. Thus, if the continuous aqueous channels in the hydrophobic solvent-saturated cellulose ester membranes were cylindrical in form, the effect of the dielectric constant of the solvents on the mobility of counterions could be accounted for.

Another possible cause for the effects of the solvent dielectric constant on the mobility of the counterions in the membrane can be associated with the presence of narrowings in the aqueous channels. It is clear from Table I that the self-energy of ion is dependent upon the thickness of the water slab and therefore the necessity to pass through a narrow zone in the continuous aqueous channel involves passing over an energy barrier. Fig. 9 shows the change in self-energy of cation passing from a 8 to 4 Å water slabs, as function of $1/\epsilon$.

An interesting aspect of the model is that connected with its conductivity when only divalent counterions are present. Under this condition half of the sites will be occupied and half vacant. Thus the movement of a divalent counterion should be faster than that of a monovalent ion. Outwardly, this expectation contradicts the experimental findings in the cellulose ester membranes where it is obvious that the resistance of membranes exposed to solutions containing only divalent cations are higher than that of membranes exposed to monovalent cations (Ilani, 1970). However, it is doubtful whether any of the cations get into the membranes in a divalent form. It is quite likely that only monovalent complexes of divalent ions and monovalent ion contaminants get into the membrane. The clarification of this point is very difficult because of the extremely low membrane permeability to divalent ions (see for instance Fig. 7 in Ilani, 1970).
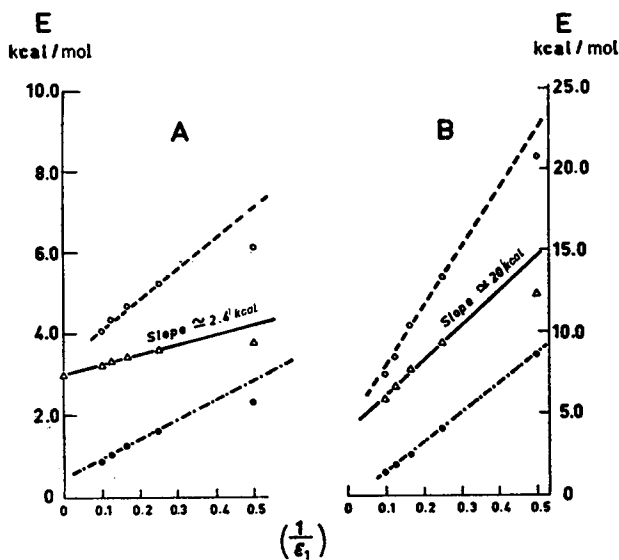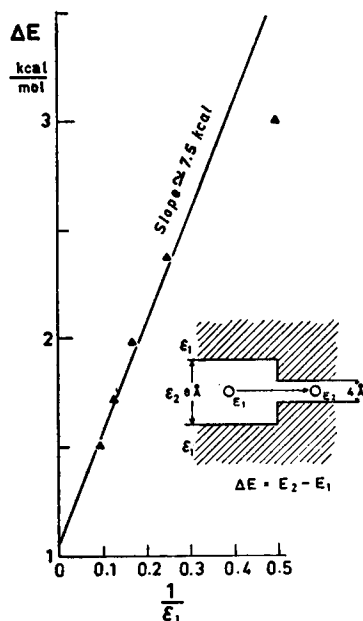
FIGURE 8

FIGURE 9

FIGURE 8   (A) The electrostatic potential energy for a cation present at a distance of 2 Å from a fixed site in an aqueous slab of 6 Å thickness as a function of the dielectric constant of the surrounding medium (upper curve). The way of calculating the values shown by the points is evident from Appendix I. The lower curve represents the energy for the same cation when present at a distance of 28 Å from the fixed site. The middle curve represents the difference between the upper and lower curves. The slope of the middle curve (kilocalories per mole per unit change in reciprocal dielectric constant) is indicated. (B) The same as Fig. 8 except that the aqueous channel is assumed to be a cylinder of 6 Å diameter. The way of calculating this energy is outlined in Appendix II.

FIGURE 9   The difference in a self-energy ΔE of a particle of 1 Å radius when present in an aqueous slab of 4 and 8 Å thickness as function of the reciprocal of ϵ_1. The difference in self-energies of the ion in the various slabs was determined by Eq. A 7 of Appendix I.

The hindrance of ion mobility due to the presence of narrowings in the aqueous channels is much stronger for the divalent ions since the energy barrier in this case is proportional to the second power of the ion valency. Thus, the effect of narrowings on ion mobility can account for the extreme monodivalent ion mobility ratio as found in studies of the experimental hydrophobic membranes (Ilani, 1970).

Another important aspect of this model is the way in which organic cations can enter and move within the membrane. As implied in the previous paper organic cations may cross the membrane through its hydrophobic region, i.e., through the ϵ_1 media. This conclusion is based on the correlation found between membrane selectivity and ion solubility in the organic solvents. The ability of ions to move

through the organic phase can account for the fact that large organic cations, such as quinine, can cross a membrane containing narrow aqueous channels.

DISCUSSION

The fact that alkali metal ions can move through the cellulose ester filters saturated with organic solvents suggests that continuous aqueous channels must be present in the membrane. The fact that organic cations such as quinine can selectively displace the alkali metal ions from the membrane requires that the hydrophobic phase is present in close proximity to fixed negative charges in the system. Thus, the general outline of the model proposed in Fig. 3 is very plausible for the experimental membranes mentioned in this study.

The model itself is interesting because of its relevance to studies of ion permeability of natural membranes. It is quite likely that the routes for ion movement across cellular membranes involve passing through pores which are lined by a lipid matrix (Davson and Danielli, 1952). Therefore, in principle, the physical factors which were discussed on this paper should be applicable to the aqueous channels in natural membranes. It is also suggested that findings in the experimental "hydrophobic system" should be analyzed in a way which may help elucidate the behavior of natural membranes.

A naïve estimate of the fraction of a cellular membrane which is comprised of aqueous channels can be made in the following way: values of $1,000 \ \Omega \ cm^2$ and $100 \ \text{Å}$ for specific membrane resistance and thickness, respectively, are chosen. If the specific resistivity of the extracellular fluid is $100 \ \Omega \ cm$ and if the aqueous channels have a similar resistivity it follows that each square centimeter of membrane has only $10^{-5} \ cm^2$ of aqueous channels or only 0.001% of the membrane area is comrised of pores. If the pore radius is 3–4 Å this figure may be off by a factor of 3–10 due to "steric" particle exclusion and friction factors (Renkin, 1954; Solomon, 1960). However, ion exclusion by the pores due to medium polarization energy barriers discussed by Parsegian (1969) and in this study is much sharper than exclusion due to steric hindrance. Therefore the estimate of the fraction of membrane surface traversed by pores may be off by several orders of magnitude. This means that from membrane conductance values one cannot arrive at a meaningful estimate of the density of pores in the membranes.

The above considerations apply to a neutral pore. If a cylinder of 100 Å length and a radius of 5 Å contains one charge site on its walls the equivalent concentration of charge sites in the pore is around 300 mM. Thus the presence of a minimal amount of charge on such a pore will endow it with a significant ion-exchange properties. This means that the content of mobile ions in the charged pore may be much higher than that expected for a neutral pore. However, it is clear from this study that the mobility of ions in such a pore can be few orders of magnitude smaller than in a bulk aqueous

solution so that the assumption that the resistivity of the pore is comparable with that of the extracellular fluid may be wrong by a few orders of magnitude.

The qualitative expectation that a pore should be much more permeable to monovalent than to divalent ions seems to be indeed the rule for biological membranes. Estimate of the K-Ca axon-membrane permeability ratio is around 600 (Hodgkin and Keynes, 1957). Recently, it was shown that pores produced in artificial thin lipid membranes by gramicidin are much more permeable to monovalent cations than to divalent cation or monovalent anions (Hladky and Haydon, 1972). The point that was emphasized in this presentation is that the above expectation is true not only for neutral pores but also for charged ones.

According to this study a negatively charged pore can lose its metal cation if an appropriate organic counterion can enter into the lipid phase of the membrane. One expression of such a displacement is a lowered membrane permeability to the particular metal ion. If the organic cation has a low mobility in the lipid phase its presence may also be expressed by decreased membrane conductance. If the single fixed charge site in a pore is located closer to one end of the pore the organic cation may enter the lipid phase only when presented to that side of the membrane. It is possible that these factors underline the mechanism by which tetraethylammonium ions affect the "potassium channel" in the squid axon membrane when applied to the internal side of the axon (Armstrong and Binstock, 1965).

It is important to bear in mind that there may be a significant difference between short or long aqueous pores, i.e. thin or thick membranes, respectively. The term short or long in this case should be used in relation to the measuring stick of the space charge length at the boundary between corresponding two semi-infinite media. In Fig. 6 the space charge region is of the order of 50–80 Å. According to Mauro's study (1962) the space charge region at a junction between aqueous ion exchange membrane and an aqueous solution (at salt concentration of 10 mM) is about 10 Å. Thus it is obvious that in the experimental membranes described in this study (thickness 0.015 cm) the aqueous channels are very long.

If the pores in biological membranes were wide enough so that they resemble more closely the ordinary aqueous ion exchange membranes which have a space charge region of only few angstroms a pore of 100 Å length is still a long pore. On the other hand, if the 100-Å long pores resemble the aqueous channels discussed in this study they should be considered short. Qualitatively it can be concluded that the fact that charged pores are short implies that a significant fraction of the fixed charges will be "vacant," like the fixed sites near an interface of a thick membrane (Fig. 6). Thus, a study of the characteristics of neutral and charged short pores may be relevant to biology if the pores in biological membranes are narrow enough so that they exclude ions due to medium polarization effects.
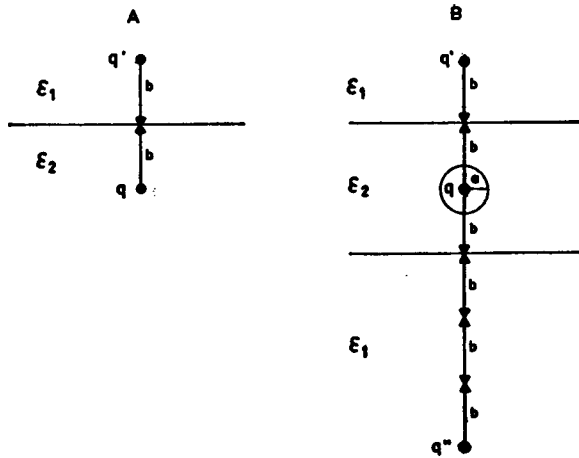
FIGURE 10   Illustration of image charges as discussed in Appendix I.

APPENDIX I

Determination of Self-Energy of Ion Present in an Aqueous Slab Interposed between Hydrophobic Media

When a charge q is present in a medium of dielectric constant ϵ_2 at a distant b from a surface boundary with a medium of dielectric constant ϵ_1, the potential at any point in the first medium can be calculated by assuming that in addition to the charge q there is an image charge q' present at distance $2b$ from the charge q (see Fig. 10 A). The relation between the charge and its image is

$$q' = Kq, \qquad (A\,1)$$

where

$$K = (\epsilon_2 - \epsilon_1)/(\epsilon_2 + \epsilon_1). \qquad (A\,2)$$

If media of dielectric constant ϵ_1 are present on both sides of ϵ_2 medium (Fig. 10 B), it is necessary to take into account image charge of the image, e.g. in Fig. 10 B q' is the image of q on the upper boundary, q'' is the image of q' on the lower boundary and so on. Similarly an image q' will be present below the lower boundary, q'' above the upper boundary, etc. (these images are now shown in Fig. 10 B).

If we denote the coordinate perpendicular to the boundary as z axis and the coordinate parallel to the boundaries as the x axis and if the charge q is present at the point $(0, 0)$ the potential at a point $(0, x)$ will be given by

$$\psi(0, x) = \frac{q}{\epsilon_2 x} + \frac{q}{\epsilon_2}\left(\frac{2K}{[(2b)^2 + x^2]^{0.5}} + \frac{2K^2}{[(2\cdot2\cdot b)^2 + x^2]^{0.5}} + \cdots\right). \quad (A\,3)$$

The first term in Eq. A 3 is the potential that would occur if the charge q were present in

an infinite medium of dielectric constant ϵ_2. The second term is the potential due to the presence of the dielectrics ϵ_1 on both sides of the slab.

The self-energy of a charged particle with a radius a present in a medium of dielectric constant ϵ_2 interposed between media of dielectric constant ϵ_1 is determined by calculating the work necessary to bring successively small amounts of charge dq to the point $(0, a)$ (Fig. 10 B). Therefore the self-energy of the ion (i, a) will be

$$E = \int_0^{q_0} (q/\epsilon_2)\, dq\, [(1/a) + F(a, b, \epsilon_1)], \qquad (A\,4)$$

where $F(a, b, \epsilon_1)$ is the sum of the parenthesized expression on the right-hand side of Eq. A 3, and q_0 is charge of the ion. Integration of Eq. A 4 leads to

$$E = (q_0^2/2\epsilon_2 a) + (q_0^2/\epsilon_2)F(a, b, \epsilon_1). \qquad (A\,5)$$

Since the first expression in Eq. A 5 is the self-energy of the ion in an infinite medium of dielectric constant ϵ_2 the second term in Eq. A 5 expresses the difference ΔE between the self-energy of an ion present in the center of slab of Fig. 10 B, and energy of an ion present in an infinite medium of dielectric constant ϵ_2.

Thus

$$\Delta E = \frac{q_0^2}{\epsilon_2} \left(\frac{2K}{[(2b)^2 + a^2]^{0.5}} + \frac{2K^2}{[(2\cdot2\cdot b)^2 + a^2]^{0.5}} + \cdots \right), \qquad (A\,6)$$

or

$$\Delta E = \frac{q_0^2}{\epsilon_2} \left(\sum_{i=1}^{\infty} \frac{2K^i}{[(i\cdot2\cdot b)^2 + a^2]^{0.5}} \right). \qquad (A\,7)$$

It should be noted that Eq. A 7 contains the basis for discrimination between ions of various valences (q_0) and sizes (a). The discrimination on the basis of size is monotonic, i.e. the larger the ion the smaller is ΔE. For instance, for the alkali metal ions ΔE should increase in the order Cs < Rb < K < Na < Li. However, it should be noted that Eq. A 7 is based upon the simplified assumption that in the charging process the element of charge dq is brought to middle portion of the ion. It is clear from Fig. 4 C that bringing the charge to a more eccentric position $(z \neq 0)$ involves larger energies. This factor would tend to increase the self-energy of the larger ion. Thus, it is possible that discrimination between ions of various radii will not be monotonic.

APPENDIX II

The potential near a charge site present in an aqueous cylinder $(\epsilon = \epsilon_2)$ surrounded by an outside medium of low dielectric constant $(\epsilon = \epsilon_1)$. If a point charge q is present on the axis of the cylinder the potential along the central axis at a distance x from the charge is given by (see Smythe, 1968, pp. 204–206)

$$\psi(x) = \frac{q}{\epsilon_2} \left[\frac{1}{x} + \frac{2}{\pi} \int_0^{\infty} \frac{kb\,(R - 1\,K_0\,(kb)\,K_0'\,(kb)}{1 - kb\,(R - 1)\,I_0\,(kb)\,K_0\,(kb)} \cos\,(kx)\, dk \right] \qquad (A\,8)$$

where K_0, K_0', and I_0 are modified Bessel functions of imaginary argument, R is the ratio ϵ_1/ϵ_2, and b is the radius of the cylinder.

The value of the integral term in Eq. A 8, $\alpha(x)$, was computed numerically on a digital computer (CDC 6400) and introduced into Eq. A 8 to obtain the following expression

$$\psi(x) = \frac{q}{\epsilon_2} \left[\frac{1}{x} + \frac{2\alpha(x)}{\pi} \right]. \qquad (A\,9)$$

The electrostatic energy of a charged particle present at distance x from the point charge will be therefore given by

$$E(x) = \psi(x)\,q_0, \qquad (A\,10)$$

where q_0 is the charge of the particle. The values of E shown by the points in Fig. 8 B were calculated by Eq. A 10.

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