

ION FLOW THROUGH NARROW MEMBRANE CHANNELS: PART II*

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Abstract. This paper is devoted to the study of the flow of ions through protein channels in physiological membranes. More specifically, it is concerned with the role of the electrical properties of the channel in determining that flow. For the case of long channels, it is shown that, when the channels have a small permittivity (compared to that of the aqueous solution), the potential down the channel is markedly altered. In particular, this potential Φ does not satisfy a one-dimensional Poisson–Boltzmann, but rather is a solution of a new equation, namely,

$$\begin{aligned} & \frac{d^2\Phi}{dz^2} + \frac{2\epsilon}{\alpha^2 \ln\alpha} (\Phi - (1-z)\Delta) \\ & = -\lambda^2 \sum_i Z_i \frac{l_i c_L e^{Z_i \Delta} \int_z^1 e^{Z_i \Phi} d\zeta + r_i c_R \int_0^z e^{Z_i \Phi} d\zeta}{e^{Z_i \Phi} \int_0^1 e^{Z_i \Phi} d\zeta}, \end{aligned}$$

where α is the small aspect ratio and ϵ is the ratio of the permittivity of the channel protein to that of the aqueous solution. The meaning of the other variables are given in the text.

Key words. electrodiffusion, membrane channel

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1. Introduction. Membranes enclosing living cells consist primarily of lipid layers, typically 5×10^{-9} m thick, that provide an effective electrical shield. All the electrical “signalling” that occurs among cells is controlled by protein molecules embedded in the lipid layers. These protein molecules act as channels that permit the selective passage of Ca^{++} , Cl^- , K^+ , and Na^+ ions.

The structure of the lipid membrane as well as the structure of the channel is rather complex. Figure 1 is an artist’s representation of two channel proteins in a planar lipid membrane. The spheres represent the polar head groups of the lipid that make up the impermeable mass of the membrane, the so-called planar lipid bilayer. The channel is a large protein made of a continuous polypeptide chain, illustrated here as a long, thin, bent rod, which, because of random thermal motion, occupies a larger space, shown here by the twisted, larger diameter cylinders. These cylinders pack to form the channel protein. In particular, the cylinders form the wall of the pore through which ions move once the channel is open. No attempt is made to draw a gate of the channel, if one exists. The polypeptide chain is itself made of atoms not shown here. The structure and properties of proteins and channels are described in [1] and [3].

Measurements of the current through a single channel are now being made routinely. A typical set of such measurements is shown in Fig. 2. The current is measured with the patch clamp method using an inside-out excised patch [15]. The channel is the most-studied K^+ channel, the so-called “delayed rectifier,” in the membrane of a neuroblastoma cell, which is a neuron-like cell grown in the laboratory in tissue

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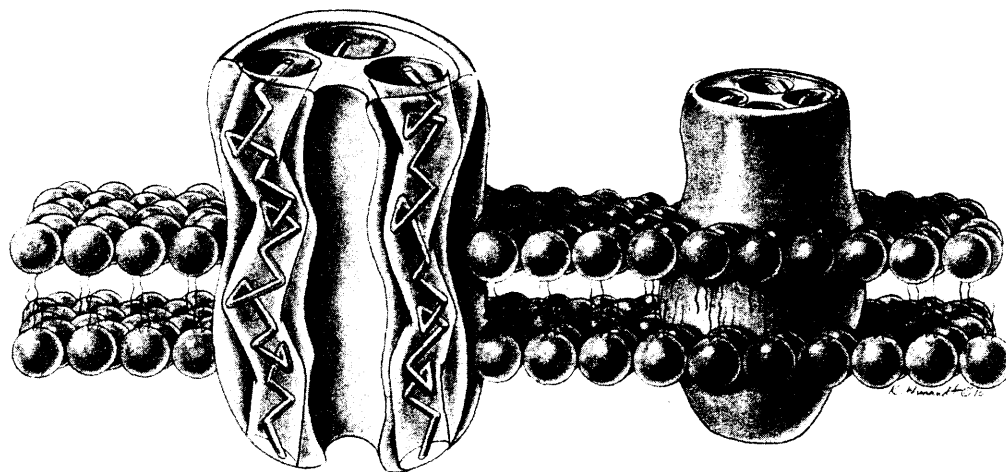


FIG. 1. An artist's representation of a channel embedded in a planar lipid membrane.

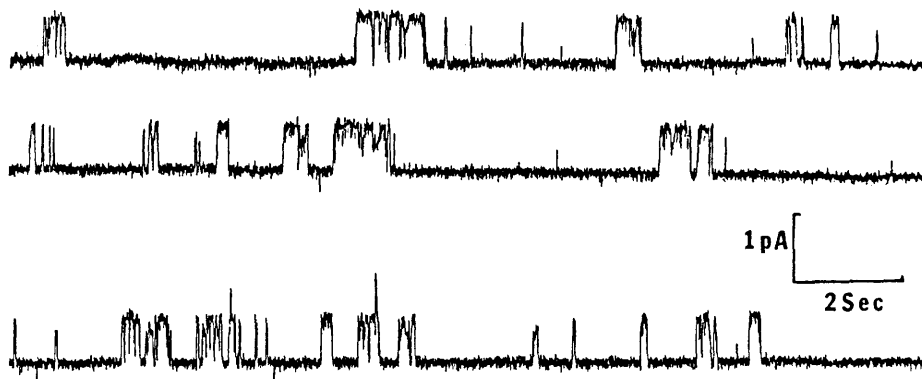


FIG. 2. A continuous recording of current from a single K^+ channel of neuroblastoma cell. The external solution is mostly 150 mM NaCl and 5.5 mM KCl, 1.8 mM $CaCl_2$, 0.8 mM $MgCl_2$ held at pH 7.2 by 10 HEPES (N-2-hydroxyethyl piperazine-N'-2-ethane sulfonic acid). The internal solution is 150 mM K glutamate along with 10 HEPES and 5 EGTA (ethene glycol-bis-(β -aminoethyl ether) N,N,N',N'-tetraacetic acid) to keep free calcium very low, around 3 μ M.

culture [12]. The potential across the channel is maintained at -20 mV. The external solution is mostly 150 mM NaCl and 5.5 mM KCl, where M stands for moles per liter of solution. The internal solution is mostly 150 mM K glutamate. Current through this channel is carried chiefly by K^+ : the channel is "selective" for K^+ for unknown reasons. The movement of K^+ is driven by both concentration and electric potential gradients. The other ions in the solution prevent water movement (Na^+) or maintain the channel in a normal condition, i.e., prevent slow irreversible changes in

observed currents.

The experimental record represents a continuous reading of current through the channel. Closed periods alternate with open periods. The amount of time spent in each state is widely variable, depending on the experimental and biological conditions. The channel shown in Fig. 2 is closed most of the time, and the lower level of current in each of the horizontal segments is a baseline, which has zero mean. The deviations from zero represent instrumentation noise. Channel openings appear as sudden, upward deflections of the current record to a new level, characteristic of the channel type, concentration gradient, and potential gradient. The time course of channel opening has not been resolved: it is faster than $20 \mu\text{s}$. The processes controlling the opening and duration of opening are called gating. They are thought to represent conformation changes in the channel protein and depend sensitively on experimental conditions.

The mean current through the channel is quite reproducible and is thought to represent the movement of ions similar to that of ions in solution. Current through many types of open channels shows random fluctuations very different from those of the baseline. These fluctuations are of at least two types, one representing zero-mean noise processes, the other representing rapid closings too brief to resolve with our instrumentation.

In this paper, we consider a single aspect of the complex problem of ion permeation through biological membranes; namely, we restrict our attention to the case of the open channel exclusively. In other words, we do not analyze the gating process. Rather, we set the stage for a theory that predicts the magnitude of the ion current through the channel as a function of the ion concentration across the membrane as well as the potential difference *once the channel is open*.

We model the lipid layer and channel wall as a dielectric slab, and the pore in the channel as a cylindrical hole. This perforated barrier separates two distinct domains of an electrolyte solution. Keeping the schematic diagram shown in Fig. 1 in mind, we discuss the left and right half-spaces as the left and right baths. We assume that the concentration of ions in these two baths is uniform such as to be electrically neutral. As this model indicates, we are focusing on a single channel, tacitly assuming that, in so doing, nearby channels do not interact with it.

The plan of the paper is as follows. In §2 we start from the premise that the distribution of ions of each species is governed by a Boltzmann equation with a collision term such as Fokker–Planck. Then, we show that, for times long compared to the time between collisions with the water molecules, these equations for the ion distributions can be approximated by the familiar Nernst–Planck equations. In §3 we adopt this macroscopic-deterministic approach and formulate the basic steady-state open channel boundary value problem, which consists of the above-mentioned Nernst–Planck equations for the concentration of ion species coupled to Poisson's equations for the electric field. In the dielectric slab, only Laplace's equation needs be considered since no ions are present. We stress at this point that, along the edge of the channel, neither the electric potential nor the electrical charge distribution is prescribed. Rather, we impose the usual jump conditions that hold along the interface of two dielectrics, and we let the solution of the equations determine the charge and the potential. Since the resulting problem is mathematically untractable, we rely on the fact that the aspect ratio of channels, i.e., the radius divided by the length, is typically of the order of 10^{-2} to simplify the analysis. The resulting singular perturbation analysis is discussed in §4 for the case in which the ratio of the permittivities of the aqueous solution and the membrane is order one; for this case, the membrane plays an inert role. In §5 we consider the more interesting case in which the ratio of permittivities is small; making

use of asymptotics, we find that the potential down the channel is governed by an equation other than a one-dimensional Poisson equation. This version of the problem is further discussed in §6.

2. The Nernst–Planck equations. In this section we want to give one possible interpretation of the Nernst–Planck equation. The derivation to be presented might be used to explain the randomness observed in the current measurements.

We start by defining the distribution function $f_i(\mathbf{x}, \mathbf{u}, t)$ for the i th species of ions. We recall that by definition $f_i(\mathbf{x}, \mathbf{u}, t) d\mathbf{x}d\mathbf{u}$ represents the number of i -ions in the cube $(\mathbf{x}, \mathbf{x} + d\mathbf{x}) \times (\mathbf{u}, \mathbf{u} + d\mathbf{u})$ of phase space. Consequently,

$$(2.1) \quad \int_{-\infty}^{+\infty} d\mathbf{u} \int_{-\infty}^{+\infty} d\mathbf{x} f_i = N_i,$$

where N_i is the total number of i th ions in the system.

For simplicity, we consider the one-dimensional case only. Then the equations governing the evolution of $f_i(z, u, t)$ are the one-dimensional Boltzmann equations

$$(2.2) \quad \frac{\partial f_i}{\partial t} + u \frac{\partial f_i}{\partial z} - \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} \frac{\partial f_i}{\partial u} = \left(\frac{\delta f_i}{\delta t} \right)_{\text{coll}}.$$

In this equation, ϕ is the electric potential; $Z_i e$ and m_i are the electrical charges and masses of the i th ions. The term on the right-hand side represents the effect of collisions.

We envision that these collisions are primarily with the water molecules of the aqueous solution. (Typically, ionic solutions of physiological interest are about 55.5 moles of water to 0.3 moles of solute.) As such, these collisions are very frequent. The effect of these numerous collisions can be approximated as follows (see, e.g., [13, p. 38]):

$$(2.3) \quad \left(\frac{\delta f_i}{\delta t} \right)_{\text{coll}} \equiv \frac{\omega}{\theta} \left\{ \frac{\partial}{\partial u} (u f_i) + \frac{kT}{m_i} \frac{\partial^2 f_i}{\partial u^2} \right\},$$

where ω is a parameter with units of (time)⁻¹ related to the frequency of collisions, and

$$\theta = \frac{\text{time between collisions}}{\text{characteristic time}}$$

is a dimensionless parameter measuring the ratio of the time between collisions and another, longer characteristic time such as the spatial evolution from an initial state.

With this parameter, (2.2) becomes

$$(2.4) \quad \frac{\partial f_i}{\partial t} + u \frac{\partial f_i}{\partial z} - \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} \frac{\partial f_i}{\partial u} = \frac{\omega}{\theta} \left\{ \frac{\partial}{\partial u} (u f_i) + \frac{kT}{m_i} \frac{\partial^2 f_i}{\partial u^2} \right\}.$$

Since θ is assumed to be very small, we look for an asymptotic series solution of this equation via the method of two-timing [6, p. 115]. To that effect, we define a slow time

$$(2.5) \quad \tau = \theta t,$$

rewrite (2.4) as follows:

$$(2.6) \quad \theta \frac{\partial f_i}{\partial t} + \theta^2 \frac{\partial f_i}{\partial \tau} + \theta u \frac{\partial f_i}{\partial z} - \theta \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} \frac{\partial f_i}{\partial u} = \omega \left\{ \frac{\partial}{\partial u} (u f_i) + \frac{kT}{m_i} \frac{\partial^2 f_i}{\partial u^2} \right\},$$

and look for a solution of the form

$$(2.7) \quad f_i(z, u, t, \tau, \theta) = f_i^{(0)}(z, u, t, \tau) + \theta f_i^{(1)}(z, u, t, \tau) + \theta^2 f_i^{(2)}(z, u, t, \tau) + \dots$$

Clearly,

$$(2.8) \quad \left(\frac{\delta f_i^{(0)}}{\delta t} \right)_{\text{coll}} \equiv \omega \left\{ \frac{\partial}{\partial u} (u f_i^{(0)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(0)}}{\partial u^2} \right\} = 0,$$

that is,

$$(2.9) \quad f_i^{(0)} = N_i \left(\frac{m_i}{2\pi kT} \right)^{1/2} p_i^{(0)}(z, t, \tau) \exp[-m_i u^2 / 2kT].$$

In other words, because of the frequent collisions, the velocity distribution equilibrates rapidly to a Maxwellian distribution. The factor $N_i(m_i/2\pi kT)^{1/2}$ has been introduced for normalization purposes. As a result of this factor, $p_i^{(0)} dz$ is the probability of finding an i -ion in the interval $(z, z + dz)$. The next-order equation reads

$$(2.10) \quad \frac{\partial f_i^{(0)}}{\partial t} + u \frac{\partial f_i^{(0)}}{\partial z} - \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} \frac{\partial f_i^{(0)}}{\partial u} = \omega \left\{ \frac{\partial}{\partial u} (u f_i^{(1)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(1)}}{\partial u^2} \right\},$$

that is,

$$(2.11) \quad \begin{aligned} & N_i \left(\frac{m_i}{2\pi kT} \right)^{1/2} \left(\frac{\partial p_i^{(0)}}{\partial t} \exp[-m_i u^2 / 2kT] \right. \\ & \quad \left. + \left\{ \frac{\partial p_i^{(0)}}{\partial z} + \frac{Z_i e}{kT} p_i^{(0)} \frac{\partial \phi}{\partial z} \right\} u \exp[-m_i u^2 / 2kT] \right) \\ & = \omega \left\{ \frac{\partial}{\partial u} (u f_i^{(1)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(1)}}{\partial u^2} \right\}. \end{aligned}$$

If we integrate this equation over all possible values of the velocity and anticipate that $f^{(1)}$ tends to zero exponentially fast as $u \rightarrow \pm\infty$, we see that

$$(2.12) \quad \frac{\partial p_i^{(0)}}{\partial t} = 0.$$

In other words, $p_i^{(0)}$ evolves on the slow timescale. As a result, (2.11) can be written thus:

$$(2.13) \quad \begin{aligned} & N_i \left(\frac{m_i}{2\pi kT} \right)^{1/2} \left\{ \frac{\partial p_i^{(0)}}{\partial z} + \frac{Z_i e}{kT} p_i^{(0)} \frac{\partial \phi}{\partial z} \right\} \frac{\partial}{\partial u} \left(-\frac{kT}{m_i} \exp[-m_i u^2 / 2kT] \right) \\ & = \omega \left\{ \frac{\partial}{\partial u} (u f_i^{(1)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(1)}}{\partial u^2} \right\}. \end{aligned}$$

Integrating once over u , we obtain

$$(2.14) \quad -N_i \left(\frac{m_i}{2\pi kT} \right)^{1/2} \left\{ \frac{\partial p_i^{(0)}}{\partial z} + \frac{Z_i e}{kT} p_i^{(0)} \frac{\partial \phi}{\partial z} \right\} = \omega \frac{\partial}{\partial u} \left\{ f_i^{(1)} \exp[m_i u^2 / 2kT] \right\}.$$

Since $p_i^{(0)}$ is not a function of u , it follows that

$$(2.15) \quad f_i^{(1)} = \frac{2N_i}{\sqrt{\pi}} \left(\frac{m_i}{2kT} \right)^{3/2} Q_i^{(0)} u \exp[-m_i u^2 / 2kT],$$

where

$$(2.16) \quad Q_i^{(0)} = -\frac{kT}{\omega m_i} \left\{ \frac{\partial p_i^{(0)}}{\partial z} + \frac{Z_i e}{kT} p_i^{(0)} \frac{\partial \phi}{\partial z} \right\}.$$

In deriving (2.15), we have set various constants of integration equal on account of the fact that

$$(2.17) \quad \int_{-\infty}^{+\infty} f_i^{(1)} du = 0.$$

We should also note at this stage that because of (2.12) and (2.16)

$$(2.18) \quad \frac{\partial f_i^{(1)}}{\partial t} = 0.$$

We next turn to the $O(\theta^2)$ equation, which reads

$$\frac{\partial f_i^{(1)}}{\partial t} + \frac{\partial f_i^{(0)}}{\partial \tau} + u \frac{\partial f_i^{(1)}}{\partial z} - \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} \frac{\partial f_i^{(1)}}{\partial u} = \omega \left\{ \frac{\partial}{\partial u} (u f_i^{(2)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(2)}}{\partial u^2} \right\},$$

or, in view of (2.15) and (2.17),

$$(2.19) \quad \begin{aligned} & \frac{N_i}{\sqrt{\pi}} \left(\frac{m_i}{2kT} \right)^{1/2} \frac{\partial p_i^{(0)}}{\partial \tau} \exp[-m_i u^2 / 2kT] \\ & + \frac{2N_i}{\sqrt{\pi}} \left(\frac{m_i}{2kT} \right)^{3/2} \frac{\partial Q_i^{(0)}}{\partial z} u^2 \exp[-m_i u^2 / 2kT] \\ & + \frac{Z_i e}{m_i} \frac{\partial \phi}{\partial z} Q_i^{(0)} \frac{\partial}{\partial u} \left\{ \frac{2N_i}{\sqrt{\pi}} \left(\frac{m_i}{2kT} \right)^{3/2} u \exp[-m_i u^2 / 2kT] \right\} \\ & = \left\{ \frac{\partial}{\partial u} (u f_i^{(2)}) + \frac{kT}{m_i} \frac{\partial^2 f_i^{(2)}}{\partial u^2} \right\}. \end{aligned}$$

Integrating this equation over all velocities, we deduce that

$$(2.20) \quad \frac{\partial p_i^{(0)}}{\partial \tau} + \frac{\partial Q_i^{(0)}}{\partial z} = 0.$$

Equations (2.16) and (2.20) are the equations proposed by Nernst [9] and Planck [11], provided (i) that

$$(2.21) \quad D_i = \frac{kT}{\omega m_i},$$

and (ii) that $Q_i^{(0)}$ can be identified as a flux of i-ions.

Equation (2.21) is the famous Einstein relation. The question of the flux can be settled as follows. By definition, the flux of ions is given by

$$(2.22) \quad F_i = \int_{-\infty}^{+\infty} u f_i du.$$

Therefore substituting the asymptotic series (2.7) with the help of (2.9) and (2.15), we have that

$$(2.23) \quad \begin{aligned} F_i = N_i \left(\frac{m_i}{2\pi kT} \right)^{1/2} p_i^{(0)} \int_{-\infty}^{+\infty} u \exp[-m_i u^2 / 2kT] du \\ + \theta \frac{2N_i}{\sqrt{\pi}} \left(\frac{m_i}{2kT} \right)^{3/2} Q_i^{(0)} \int_{-\infty}^{+\infty} u^2 \exp[-m_i u^2 / 2kT] du + O(\theta^2), \end{aligned}$$

that is,

$$(2.24) \quad F_i = \theta N_i Q_i^{(0)} + O(\theta^2).$$

In summary, dropping the superscripts and relabelling τ as t , we can rewrite (2.15), (2.20), and (2.21) as

$$(2.25) \quad \begin{aligned} \frac{\partial p_i}{\partial t} + \frac{\partial Q_i}{\partial z} &= 0, \\ Q_i &= -D_i \left\{ \frac{\partial p_i}{\partial z} + \frac{Z_i e}{kT} p_i \frac{\partial \phi}{\partial z} \right\}. \end{aligned}$$

The above approach is necessary for the microscopic study of ion flow through channels. However, at the present time, such a microscopic approach is not needed because of the limitation of the measuring devices. To understand this, we recall that because of frequent collisions with water molecules an ion takes a diffusion time to cross a channel. If the diffusion coefficient is $10^{-5} \text{ cm}^2 \text{ sec}^{-1}$ and the channel is 10^{-6} cm , then the diffusion time is of order 10^{-7} sec . This implies a current of the order of 10^{-12} A , which is about right. Now, the recording instruments have a characteristic time of the order of 10^{-5} sec . Therefore the experimental results are averages over at least hundreds of ions. We use this observation as a justification for using a continuum, macroscopic approach to the problem, adopting the same microscopic equations but now giving macroscopic interpretations to the various variables. In particular, we discuss concentrations c_i instead of probability distributions p_i . Finally, to further emphasize the macroscopic viewpoint, we denote the flux of the i -ions by the traditional symbol J_i instead of Q_i . The resulting equations are the classical Nernst-Planck equations.

3. Mathematical formulation. We idealize the membrane to be a dielectric layer of thickness d with a cylindrical hole, or channel, of radius a . Inside the channel, we assume that the Nernst-Planck equations hold. For the steady state, this means that the flux \mathbf{J}_i of i -ions satisfies the continuity equation

$$(3.1) \quad \nabla \cdot \mathbf{J}_i = 0,$$

which is the three-dimensional generalization of (2.20) for the steady-state case. The flux \mathbf{J}_i is given by the following "constitutive" equation:

$$(3.2) \quad \mathbf{J}_i = -D_i \left\{ \nabla c_i + \frac{Z_i e}{kT} c_i \nabla \phi \right\},$$

which generalizes (2.16). As before in the above formula, D_i is the diffusion coefficient of the i -ions, eZ_i their electric charge, k Boltzmann's constant, T the absolute temperature, and ϕ is the electrical potential, where as usual

$$(3.3) \quad \mathbf{E} = -\nabla\phi.$$

This electrical potential arises partly from the distribution of the ions in the aqueous solution. Thus, if \mathbf{D} is the dielectric displacement field, then, according to Gauss' law, $\nabla \cdot \mathbf{D} = \sum_i Z_i e c_i$, or if ϵ_a stands for the permittivity of the aqueous solution in the channel region and

$$(3.4) \quad \mathbf{D} = \epsilon_a \mathbf{E},$$

then, in view of (3.3),

$$(3.5) \quad \nabla^2 \phi = -\frac{1}{\epsilon_a} \sum_i Z_i e c_i.$$

Outside the channel, but still in the membrane, no ions are present, and hence the only field to consider is the potential that satisfies

$$(3.6) \quad \nabla^2 \psi = 0.$$

Strictly speaking, we should complete the analysis of the various regions with a discussion of the baths on either side of the membrane. However, incorporation of these regions makes for a much more complicated geometry and renders an analytical treatment of the problem impossible. For this reason, we instead assume that the ions on either side of the membrane are uniformly distributed and in neutral electric equilibrium. As a result, if z stands for the coordinate along the axis of the channel, then, at the right and left ends of the channel, we can state that

$$(3.7a) \quad \begin{aligned} c_i &= l_i c_0 c_L & \text{at} & \quad z = 0, \\ c_i &= r_i c_0 c_R & \text{at} & \quad z = d, \end{aligned}$$

where l_i and r_i are the fractional amounts of each species chosen to satisfy the charge neutrality conditions, viz.,

$$(3.7b) \quad \begin{aligned} 0 &< l_i, r_i \leq 1, \\ \sum_{Z_i > 0} l_i Z_i &= - \sum_{Z_i < 0} l_i Z_i = 1, \\ \sum_{Z_i > 0} r_i Z_i &= - \sum_{Z_i < 0} r_i Z_i = 1. \end{aligned}$$

In anticipation of the nondimensionalization process, we have written the concentrations on the right- and left-hand sides as $c_0 c_R$ and $c_0 c_L$, where c_0 has units of concentration (number/cm³), whereas c_L and c_R are dimensionless quantities.

The most important physiological case is that for which there are three species of ions such that $Z_1 = Z_2 = 1$ and $Z_3 = -1$; this describes, for example, the case of K^+ , Na^+ , and Cl^- in solution. Another relevant case is that where $Z_1 = 1$, $Z_2 = 2$, and

$Z_3 = -1$, which occurs if Ca^{++} is present. To consider both of these cases at once, we write the boundary conditions (3.7)

$$(3.8) \quad \begin{aligned} c_1 &= (1-l) c_0 c_L, & c_2 &= \chi l c_0 c_L, & c_3 &= c_0 c_L, & \text{at } z &= 0, \\ c_1 &= (1-r) c_0 c_R, & c_2 &= \chi r c_0 c_R, & c_3 &= c_0 c_R, & \text{at } z &= d, \end{aligned}$$

where $\chi = 1$ in the first case, and $\chi = 1/2$ in the second. Note that if we set $l = r = 0$, then we can also treat the case of two ion species with equal charge number.

It is obviously appropriate to use the cylindrical coordinates r, θ, z to study this problem, where θ is now the angular coordinate. In fact, we assume that all the fields are axially symmetric, i.e., independent of θ ; hence no confusion need arise over the meaning of θ . To complete the formulation of the problem, we must join the fields along the edge $r = a$ of the cylinder. Standard "pillbox" arguments [4, p. 110] imply that

$$(3.9) \quad \begin{aligned} \phi(a, z) &= \psi(a, z), \\ \frac{\partial \phi}{\partial r}(a, z) &= \epsilon \frac{\partial \psi}{\partial r}(a, z), \end{aligned}$$

where ϵ is the ratio of the permittivity ϵ_m , and ϵ_a of the membrane and aqueous solution, respectively, viz., $\epsilon = \epsilon_m/\epsilon_a$.

We translate the fact that the ions are confined to the channel by the requirement that

$$(3.10) \quad \mathbf{J} \cdot \mathbf{r} \equiv \left\{ \frac{\partial c_i}{\partial r} + \frac{Z_i e}{kT} c_i \frac{\partial \phi}{\partial r} \right\} \Bigg|_{(a,z)} = 0.$$

Finally, in addition to the concentration gradient, we allow for a second driving mechanism, namely, an applied potential difference across the membrane. Therefore

$$(3.11) \quad \begin{aligned} \phi(r, 0) &= \psi(r, 0) = V, \\ \phi(r, d) &= \psi(r, d) = 0, \end{aligned}$$

where V is the applied potential difference.

The next step is to introduce dimensionless variables to bring out a feature of the problem, namely, the fact that the channel is long and narrow. Denoting dimensionless quantities by a prime, we write

$$(3.12a) \quad \begin{aligned} r &= a r', \\ z &= d z', \\ \phi, \psi &= \frac{kT}{e} \phi', \psi', \\ c_i &= c_0 c'_i, \\ \mathbf{J}_i &= \frac{D_i c_0}{d} \mathbf{J}'_i. \end{aligned}$$

We are also interested in the current I flowing out of the channel mouth

$$I = \sum_i e Z_i 2\pi \int_0^a \mathbf{J}_i(r, d) \cdot \hat{\mathbf{k}} r dr,$$

or, if \bar{D} stands for an average diffusion coefficient, then we can define

$$I = \frac{\pi a^2 c_0 e \bar{D}}{d} I',$$

where

$$(3.12b) \quad I' = 2 \int_0^1 \sum_i Z_i \frac{D_i}{\bar{D}} \mathbf{J}'_i(r, d) \cdot \hat{\mathbf{k}} r dr.$$

Substituting (3.12) in (3.1) and (3.2) and in (3.5)–(3.11) and dropping the primes, we arrive at a complete mathematical formulation of the problem, which we state together with a program for its solution. We first solve the Nernst–Planck equations

$$(3.13) \quad \frac{1}{r} \frac{\partial}{\partial r} r \left[\frac{\partial c_i}{\partial r} + Z_i c_i \frac{\partial \phi}{\partial r} \right] + \alpha^2 \frac{\partial}{\partial z} \left[\frac{\partial c_i}{\partial z} + Z_i c_i \frac{\partial \phi}{\partial z} \right] = 0$$

for the concentrations c_i , subject to the impermeability boundary conditions

$$(3.14) \quad \frac{\partial c_i}{\partial r} + Z_i c_i \frac{\partial \phi}{\partial r} = 0 \quad \text{for } r = 1,$$

and the neutral left and right baths

$$(3.15) \quad \begin{aligned} c_i(r, 0) &= l_i c_L, \\ c_i(r, 1) &= r_i c_R, \end{aligned}$$

as if the potential ϕ were known. Incidentally, in (3.15), we have redefined l_i, r_i to conform to (3.8), namely,

$$(3.16) \quad \left. \begin{aligned} l_1 &= (1 - l) \\ l_2 &= l\chi \\ l_3 &= 1 \end{aligned} \right\} \quad \left\{ \begin{aligned} r_1 &= (1 - r), \\ r_2 &= r\chi, \\ r_3 &= 1. \end{aligned} \right.$$

Once the concentrations are found as functionals of the potential, we then find this potential by solving the Poisson and Laplace equations

$$(3.17) \quad \begin{aligned} \frac{1}{r} \frac{\partial}{\partial r} r \frac{\partial \phi}{\partial r} + \alpha^2 \frac{\partial^2 \phi}{\partial z^2} &= -\alpha^2 \lambda^2 \sum_i Z_i c_i \quad \text{for } r < 1 \\ \frac{1}{r} \frac{\partial}{\partial r} r \frac{\partial \psi}{\partial r} + \alpha^2 \frac{\partial^2 \psi}{\partial z^2} &= 0 \quad \text{for } r > 1 \end{aligned}$$

subject to

$$(3.18) \quad \begin{aligned} \phi(r, 0) &= \psi(r, 0) = \Delta, \\ \phi(r, 1) &= \psi(r, 1) = 0, \end{aligned}$$

and the jump conditions

$$(3.19) \quad \left. \begin{aligned} \phi &= \psi \\ \frac{\partial \phi}{\partial r} &= \epsilon \frac{\partial \psi}{\partial r} \end{aligned} \right\} \quad \text{at } r = 1,$$

as well as the condition at infinity

$$(3.20) \quad \psi - (1 - z)\Delta \rightarrow 0 \quad \text{as} \quad r \rightarrow \infty.$$

In the process of solving the second half of the problem, we use the results obtained in [2]. When doing so, we recall that analogues of the fields u and v are $\phi - (1 - z)\Delta$, and $\psi - (1 - z)\Delta$, and not ϕ and ψ . Incidentally, we should note that the analogue of the forcing f is $\lambda^2 \sum_i Z_i c_i$, which does vanish at both ends of the channel and which is z differentiable.

The dimensionless parameters that appear in the problem are the aspect ratio

$$(3.21) \quad \alpha = \frac{a}{d},$$

the applied potential difference V expressed in units of kT/e , namely,

$$(3.22) \quad \Delta = \frac{eV}{kT},$$

and the relative size of the Debye length κ^{-1}

$$(3.23) \quad \lambda = d\kappa,$$

where

$$(3.24) \quad \kappa^2 = \frac{e^2 c_0}{\epsilon_a kT}.$$

We solve problems (3.13)–(3.20) under the assumption that α is very small.

4. Inert channels. Under this heading, we consider the case in which the ratio ϵ of the permittivities is $O(1)$. Making use of the results derived in [2], and more particularly on the form (8.1) of [2] of the asymptotic expansions, we look for solutions of the form

$$(4.1) \quad \begin{aligned} c_i &= C_i^{(0)}(z) + (-\alpha^2 \ln \alpha) C_i^{(1)}(z) + \alpha^2 c_i^{(2)}(r, z) + \dots, \\ \phi &= (1 - z)\Delta + (-\alpha^2 \ln \alpha) \Phi_i^{(1)}(z) + \alpha^2 \phi_i^{(2)}(r, z) + \dots, \\ \psi &= (1 - z)\Delta + (-\alpha^2 \ln \alpha) \Psi_i^{(1)}(z) + \alpha^2 \psi_i^{(2)}(r, z) + \dots. \end{aligned}$$

In the above expansions, we use capitals to emphasize that we have already anticipated some results about the lower-order terms, namely, that they are independent of r . Following the program outlined previously, we begin with the Nernst–Planck equations (3.13). The first two orders are trivially satisfied. The third order, which is $O(\alpha^2)$, yields

$$(4.2) \quad \frac{1}{r} \frac{\partial}{\partial r} r \left[\frac{\partial c_i^{(2)}}{\partial r} + Z_i C_i^{(0)} \frac{\partial \phi^{(2)}}{\partial r} \right] + \frac{d}{dz} \left[\frac{dC_i^{(0)}}{dz} - \Delta Z_i C_i^{(0)} \right] = 0.$$

Integrating this equation over r and using the impermeability boundary conditions (3.14) yields

$$(4.3) \quad \frac{d}{dz} \left[\frac{dC_i^{(0)}}{dz} - \Delta Z_i C_i^{(0)} \right] = 0.$$

These equations are, of course, the one-dimensional version of the Nernst–Planck equations for a constant gradient potential. We can solve for the concentrations and summarize the results as follows:

$$c_i = \frac{r_i c_R (\exp\{Z_i \Delta z\} - 1) + l_i c_L (\exp\{Z_i \Delta\} - \exp\{Z_i \Delta z\})}{\exp\{Z_i \Delta\} - 1} + O(-\alpha^2 \ln \alpha),$$

$$\phi = (1 - z)\Delta + O(-\alpha^2 \ln \alpha).$$

Note that the ratio of the permittivities is totally absent from the lowest-order fields. In that sense, the properties of the channel protein are not felt by the ions. Because its dielectric properties are not involved in ionic movement, we say that the channel is inert. The case we next investigate shows that when ϵ is small the situation can be significantly altered.

5. Active channels. We now investigate the case in which the aspect ratio α as well as the ratio of permittivities constants ϵ are small. In this case, we find that the dielectric properties of the channel protein affect the ion movement, as we feel they must if we are to explain biological phenomena such as selectivity and gating.

The small parameters α and ϵ are physically unrelated. However, mathematically (and perhaps physiologically), the most interesting behaviour of the potential down the channel occurs when a very specific relation between these parameters is assumed. Such a distinguished ordering is not at all unusual in the theory of asymptotics. Perhaps the most famous example of such an ordering occurs in the theory of water waves [6, p. 510]. There it is found that when a small parameter, which measures the ratio of the wave amplitude to the depth of the water (i.e., the nonlinear breaking tendency), is comparable to the square of another parameter, which measures the ratio of the depth to the wavelength (i.e., the dispersion), then the equations of motion allow for a new breed of waves, viz., the solitary waves governed by the Korteweg–DeVries equation. Similarly, we see that the richest behaviour for the potential occurs if we consider that

$$(5.1) \quad \epsilon = (-\alpha^2 \ln \alpha) \tilde{\epsilon},$$

where $\tilde{\epsilon}$ is an order-one quantity.

Once again using the results in [2], and more specifically of the form [2, (9.2)] of the asymptotic expansions, we look for the solutions of the form

$$(5.2) \quad c_i(r, z; \alpha, \tilde{\epsilon}) = C_i^{(0)}(z) + \frac{1}{(-\ln \alpha)} C_i^{(1)}(z) + \alpha^2 c_i^{(2)}(r, z) + \dots,$$

$$\phi(r, z; \alpha, \tilde{\epsilon}) = \Phi^{(0)}(z) + \frac{1}{(-\ln \alpha)} \Phi_i^{(1)}(z) + \alpha^2 \phi_i^{(2)}(r, z) + \dots,$$

$$\psi(r, z; \alpha, \tilde{\epsilon}) = \psi^{(0)}(r, z) + \frac{1}{(-\ln \alpha)} \psi_i^{(1)}(r, z) + \alpha^2 \psi_i^{(2)}(r, z) + \dots.$$

Just as before, the third-order Nernst–Planck equations yield

$$(5.3) \quad \frac{1}{r} \frac{\partial}{\partial r} r \left[\frac{\partial c_i^{(2)}}{\partial r} + Z_i C_i^{(0)} \frac{\partial \phi^{(2)}}{\partial r} \right] + \frac{d}{dz} \left[\frac{dC_i^{(0)}}{dz} + Z_i C_i^{(0)} \frac{d\Phi^{(0)}}{dz} \right] = 0,$$

which imply that

$$(5.4) \quad \frac{d}{dz} \left[\frac{dC_i^{(0)}}{dz} + Z_i C_i^{(0)} \frac{d\Phi^{(0)}}{dz} \right] = 0.$$

So, once again, the leading-order concentrations satisfy one-dimensional Nernst–Planck equations. We can integrate these equations once and write

$$(5.5) \quad \frac{dC_i^{(0)}}{dz} + Z_i C_i^{(0)} \frac{d\Phi^{(0)}}{dz} = -J_i^{(0)},$$

where J_i are constants of integrations equal to the dimensionless fluxes of the i th species. To solve for the concentrations in terms of the potential, we first must compute these fluxes

$$(5.6) \quad -J_i^{(0)} = \frac{r_{iC_R} - l_{iC_L} e^{Z_i \Delta}}{\int_0^1 e^{Z_i \Phi^{(0)}(\zeta)} d\zeta}.$$

We should remark at this stage that the fact that these fluxes are different from zero is a distinguishing feature of the physiological channel problem, although a great deal of the previous work on the Nernst–Planck equations dealt with situations in which the fluxes were zero (see, e.g., [14, pp. 19–41]). We can next find the concentrations

$$(5.7) \quad C_i^{(0)}(z) = \frac{l_{iC_L} e^{Z_i \Delta} \int_z^1 e^{Z_i \Phi^{(0)}(\zeta)} d\zeta + r_{iC_R} \int_0^z e^{Z_i \Phi^{(0)}(\zeta)} d\zeta}{e^{Z_i \Phi^{(0)}(z)} \int_0^1 e^{Z_i \Phi^{(0)}(\zeta)} d\zeta}.$$

We proceed with the determination of the potentials. It is easy to deduce from the third-order terms of the Poisson equation that

$$(5.8) \quad \phi^{(2)} = -\frac{r^2}{4} \left\{ \lambda^2 \sum_i Z_i C_i^{(0)}(z) + \frac{d^2 \Phi^{(0)}}{dz^2} \right\} + \Phi^{(2)}(z).$$

As a result, the potential inside the channel is given by

$$(5.9) \quad \begin{aligned} \phi = & \Phi^{(0)}(z) + \frac{1}{(-\ln \alpha)} \Phi^{(1)}(z) \\ & + \alpha^2 \left(-\frac{r^2}{4} \left\{ \lambda^2 \sum_i Z_i C_i^{(0)}(z) + \frac{d^2 \Phi^{(0)}}{dz^2} \right\} + \Phi^{(2)}(z) \right) + O(\alpha^2 / \ln \alpha). \end{aligned}$$

Similarly, the potential in the membrane is

$$(5.10) \quad \psi = A^{(0)}(z) + B^{(0)}(z) \ln r + \frac{1}{(-\ln \alpha)} \left(A^{(1)}(z) + B^{(1)}(z) \ln r \right) + O(\alpha^2).$$

For the potential to be continuous at $r = 1$ as required in (3.19), we must set

$$(5.11) \quad \begin{aligned} A^{(0)}(z) &= \Phi^{(0)}(z), \\ A^{(1)}(z) &= \Phi^{(1)}(z). \end{aligned}$$

The other half of (3.19) requires that the normal derivative of the potential suffers the correct discontinuity, namely,

$$(5.12) \quad \frac{\partial \phi}{\partial r}(1, z; \alpha, -\alpha^2 \ln \alpha \tilde{\epsilon}) = -\alpha^2 \ln \alpha \tilde{\epsilon} \frac{\partial \psi}{\partial r}(1, z; \alpha, -\alpha^2 \ln \alpha \tilde{\epsilon}).$$

This implies that

$$(5.13) \quad \begin{aligned} B^{(0)}(z) &= 0, \\ B^{(1)}(z) &= -\frac{1}{2\tilde{\epsilon}} \left\{ \lambda^2 \sum_i Z_i C_i^{(0)}(z) + \frac{d^2\Phi^{(0)}}{dz^2} \right\}. \end{aligned}$$

In summary, the exterior near-field now reads

$$(5.14) \quad \psi = \Phi^{(0)}(z) + \frac{1}{(-\ln \alpha)} \left(\Phi^{(1)}(z) - \frac{1}{2\tilde{\epsilon}} \left\{ \lambda^2 \sum_i Z_i C_i^{(0)}(z) + \frac{d^2\Phi^{(0)}}{dz^2} \right\} \ln r \right) + O(\alpha^2).$$

The last step is to impose the boundary condition (3.20) far from the channel. We saw in [2] that this can be done via the method of matched asymptotic expansions. Since, in fact, the question we confronted in [2] for the exterior v field is identical to that for the field $\psi - (1 - z)\Delta$, we can simply copy the needed results. In particular, from [2, eq. (9.2)], we immediately see that the coefficient of the $O(1)$ term must be set equal to minus the coefficient of the $\ln r$ in the term of order $(-1/\ln \alpha)$. As a result,

$$(5.15) \quad \Phi^{(0)} - (1 - z)\Delta = \frac{1}{2\tilde{\epsilon}} \left\{ \lambda^2 \sum_i Z_i C_i^{(0)}(z) + \frac{d^2\Phi^{(0)}}{dz^2} \right\},$$

or, better still,

$$(5.16) \quad -2\tilde{\epsilon} \left\{ \Phi(z) - (1 - z)\Delta \right\} + \frac{d^2\Phi}{dz^2} = -\lambda^2 \sum_i Z_i C_i.$$

This is the equation for the potential in the channel that we have been seeking. In summary, where the leading-order potential and concentrations are pure functions of the distance down the channel, and where the one-dimensional Nernst–Planck equations are in force, the electrostatic field is governed by an equation other than the strict one-dimensional Poisson equation.

Since we now focus on this equation, we have dropped all superscripts. The concentrations entering in this equation are given by expressions (5.7), so that, in fact, (5.16) is an integrodifferential equation for Φ , viz.,

$$(5.17) \quad \begin{aligned} \frac{d^2\Phi}{dz^2} - 2\tilde{\epsilon}\Phi &= -2\tilde{\epsilon}(1 - z)\Delta \\ &- \lambda^2 \sum_i Z_i \frac{l_i c_L e^{Z_i \Delta} \int_z^1 e^{Z_i \Phi} d\zeta + r_i c_R \int_0^z e^{Z_i \Phi} d\zeta}{e^{Z_i \Phi} \int_0^1 e^{Z_i \Phi} d\zeta}. \end{aligned}$$

To avoid problems with the shooting method, we transform (5.17) into the integral equation

$$(5.18) \quad \Phi(z) = (1 - z)\Delta - \lambda^2 \int_0^1 G(\zeta, z) F[\Phi(\zeta)] d\zeta,$$

where

$$(5.19) \quad F[\Phi(\zeta)] = \sum_i Z_i \frac{l_i c_L e^{Z_i \Delta} \int_\zeta^1 e^{Z_i \Phi(\eta)} d\eta + r_i c_R \int_0^\zeta e^{Z_i \Phi(\eta)} d\eta}{e^{Z_i \Phi(\zeta)} \int_0^1 e^{Z_i \Phi(\eta)} d\eta},$$

and the Green function G is given by

$$(5.20) \quad G(\zeta, z) = \frac{\sinh \sqrt{2\bar{\epsilon}} z_{<} \sinh \sqrt{2\bar{\epsilon}}(z_{>} - 1)}{\sqrt{2\bar{\epsilon}} \sinh \sqrt{2\bar{\epsilon}}}$$

As usual, in the above expression, $z_{<}, z_{>}$ stand for the “greater” and the “smaller” of the arguments.

We have restricted our attention to the case of three species of ions such that $Z_1 = Z_2 = -Z_3 = 1$. For this important case, the solution of (5.18) is identical to that of *two* species of ions since (5.19) reduces to

$$(5.21) \quad F[\Phi(\zeta)] = \frac{c_L e^{\Delta} \int_{\zeta}^1 e^{\Phi(\eta)} d\eta + c_R \int_0^{\zeta} e^{\Phi(\eta)} d\eta}{e^{\Phi(\zeta)} \int_0^1 e^{\Phi(\eta)} d\eta} - \frac{c_L e^{-\Delta} \int_{\zeta}^1 e^{-\Phi(\eta)} d\eta + c_R \int_0^{\zeta} e^{-\Phi(\eta)} d\eta}{e^{-\Phi(\zeta)} \int_0^1 e^{-\Phi(\eta)} d\eta}$$

We have solved (5.18) iteratively. For each iteration, we have used M points (usually 48) to evaluate the integral involving the Green function by means of Legendre–Gauss quadratures. For each of these points, i.e., choices of ζ in (5.18), we computed the corresponding value of the functional $F[\Phi]$. For this purpose, we used another set of Legendre–Gauss quadratures with N points (usually 20) for *each* integral appearing in (5.21). Altogether, we evaluated Φ at $(2N + 1)M$ points. As a result, we were led to consider the system

$$(5.22) \quad \Phi_K^{(n+1)} = (1 - z_K)\Delta - \frac{\lambda^2}{2} \sum_{i=1}^M G_{K,i} F_i^{(n)} W_i(M), \quad K = 1, \dots, (2N + 1)M,$$

where

$$F_i = e^{-\Phi_i} \frac{c_R \cdot \frac{\zeta_i}{2} \cdot \sum_{\nu=1}^N e^{\Phi_{i\nu}} W_{\nu}(N) + c_L e^{\Delta} \cdot \frac{1 - \zeta_i}{2} \cdot \sum_{\nu=N+2}^{2N+1} e^{\Phi_{i\nu}} W_{\nu-N-1}(N)}{\frac{\zeta_i}{2} \cdot \sum_{\nu=1}^N e^{\Phi_{i\nu}} W_{\nu}(N) + \frac{1 - \zeta_i}{2} \cdot \sum_{\nu=N+2}^{2N+1} e^{\Phi_{i\nu}} W_{\nu-N-1}(N)},$$

$$- e^{\Phi_i} \frac{c_R \cdot \frac{\zeta_i}{2} \cdot \sum_{\nu=1}^N e^{-\Phi_{i\nu}} W_{\nu}(N) + c_L e^{\Delta} \cdot \frac{1 - \zeta_i}{2} \cdot \sum_{\nu=N+2}^{2N+1} e^{-\Phi_{i\nu}} W_{\nu-N-1}(N)}{\frac{\zeta_i}{2} \cdot \sum_{\nu=1}^N e^{-\Phi_{i\nu}} W_{\nu}(N) + \frac{1 - \zeta_i}{2} \cdot \sum_{\nu=N+2}^{2N+1} e^{-\Phi_{i\nu}} W_{\nu-N-1}(N)},$$

and $W_k(I)$ is the Gauss–Legendre weight for an integration over the normalized interval $(-1,1)$ divided into $I + 1$ subintervals. Superscripts refer to iterations. Finally, the index K denotes the alphabetically ordered pair $(i, \nu), i = 1, \dots, M$ and $\nu = 1, \dots, 2N + 1$.

The iteration was stopped when the difference between two successive iterates was smaller than 10^{-12} . A crude analysis of the iteration suggests that convergence should occur as long as λ^2 is not too large.

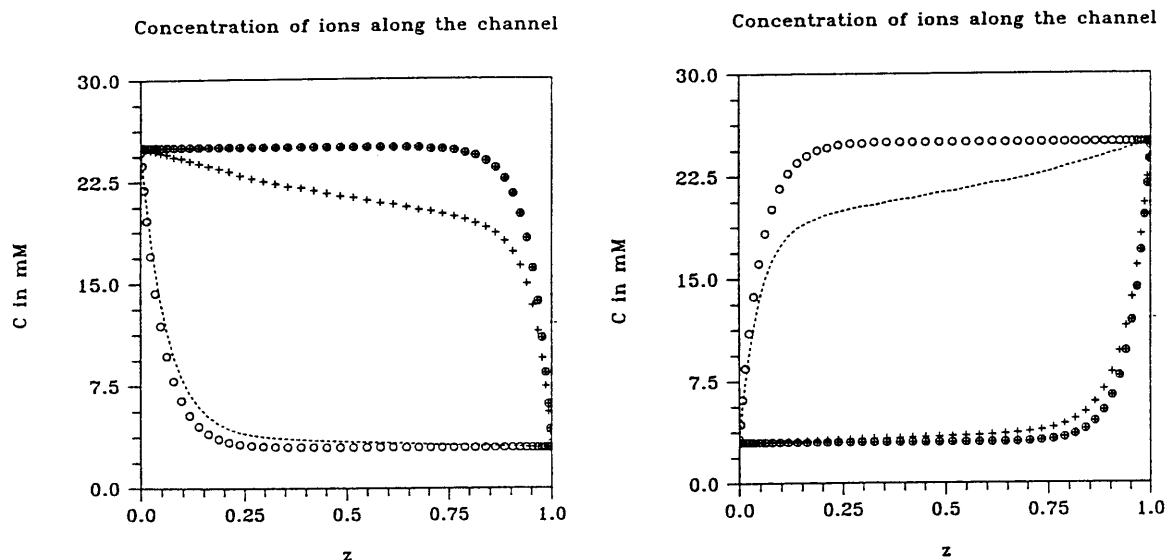


FIG. 3. Ion distributions versus distance along the channel. Positive and negative ions are indicated by crosses and dashes, respectively. The crossed and open circles represent the distributions that would have been obtained if the dielectric effects were neglected. The diagrams are for a channel 100 Å long with a radius of 5 Å; with dielectric constants of membrane and solution of 2 and 80, respectively, and voltage potential of 50 mV. In the (a) frame, the concentration in the left bath is 25 mM, and 3 mM in the right bath. In the (b) frame, the bath concentrations are reversed. In all cases, the voltage drop from right to left equals 50 mV. $C(+)$ our calculation +, $C(-)$ our calculation ----, $C(+)$ constant field \oplus , $C(-)$ constant field \circ .

Figures 3(a) and 3(b) show the distribution of positive (crosses) and negative (dashes) ions for a channel 100 Å long with a radius of 5 Å. The dielectric constants for the membrane and solution are 2 and 80, respectively. The applied potential consists of a drop of 50 mV (from left to right). In the (a) frame, the concentration in the left bath is equal to 25 mM, whereas the concentration in the right bath has the lower value of 3 mM. In the (b) frame, the concentration gradient is reversed but the electrical potential is not altered. Because of the nonlinearity of the governing equations, the results for these two situations need not be symmetric. However, for the parameters considered here, this appears to be the case. In both cases, the concentrations depart from a straight line profile, bowing either up or down, depending on the imposed gradients. Circles with crosses and open circles indicate the distribution of positive and negative ions that would be predicted if the dielectric effects were neglected. For these particular settings, $\alpha = 0.05$, $\bar{\epsilon} = 3.3$, and $\lambda^2 = 7.4$. Incidentally, for these settings, the next-order corrections, which are of order $1/(-\ln \alpha) = 0.33$, may be nonnegligible.

Figures 4(a) and 4(b) show the potential along the channel, or rather the deviation of the latter from the straight line profile, for the same settings as before. Note once again that the sign of the curvature of this deviation changes with the imposed gradients.

Figures 5(a) and 5(b) show the current flowing out of the channel as a function of the applied potential drop. The current is computed according to (3.12') with the following values for the diffusion constants: $D_+ = 1.0 \times 10^{-6} \text{cm}^2 \text{s}^{-1}$, and $D_- = 2.5 \times 10^{-7} \text{cm}^2 \text{s}^{-1}$. These values of the diffusion constants are not unrealistic, but they are picked simply to get the right order of magnitude current.

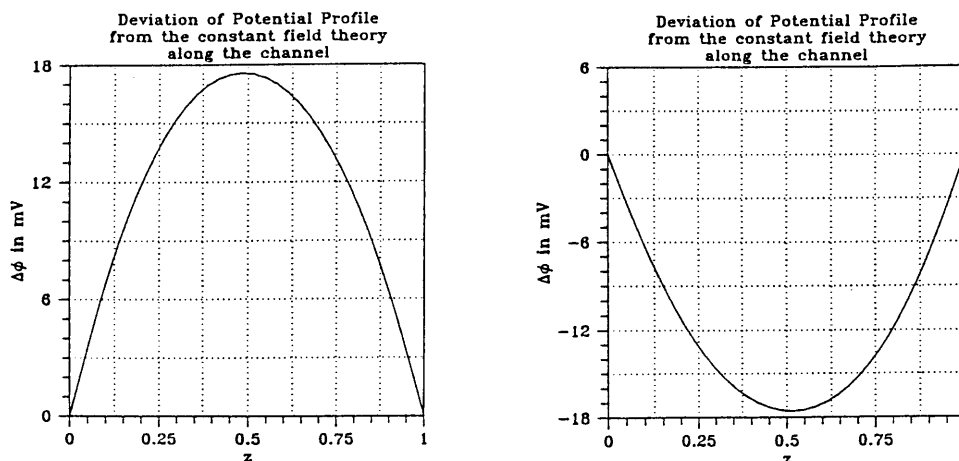


FIG. 4. Deviation of potential from a straight line versus distance along the channel. All the settings are identical to those in Fig. 3. In particular, frame (a) corresponds to concentrations in the left and right baths of 25 mM and 3 mM, respectively, whereas frame (b) corresponds to the reverse values.

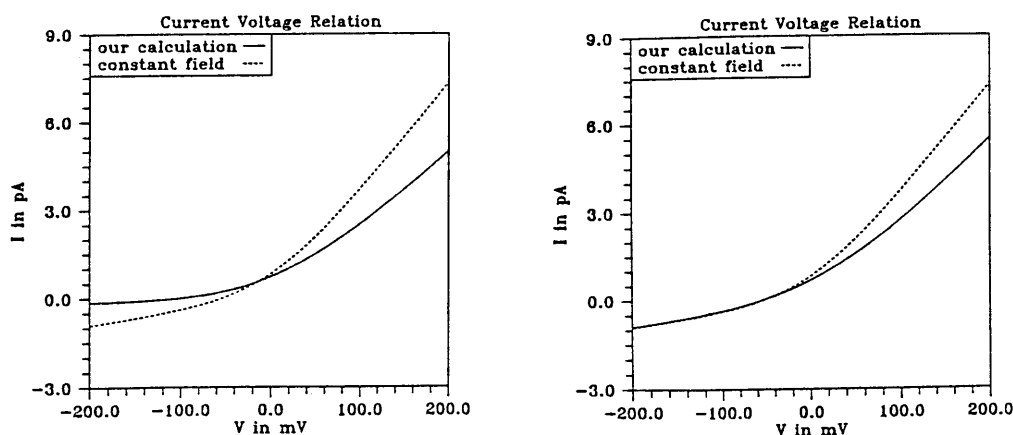


FIG. 5. Current versus voltage. The dashed lines represent what these current voltage relations would have been had we neglected the dielectric effect. As in the other figures, the channel is 100 Å long with a radius of 5 Å. The dielectric constants of the membrane and solution are 2 and 80, respectively. In the (a) frame, the left and right bath concentrations are, respectively, 25 mM and 3 mM. In the (b) frame, the concentrations in the left and right baths are reversed. The diffusion constants used to calculate the current are $D_+ = 1.0 \times 10^{-6} \text{ cm}^2\text{s}^{-1}$ and $D_- = 2.5 \times 10^{-7}$.

6. The small gradients case. To understand the results of our numerical analysis shown in Fig. 3, and, in particular, whether the departures of the potential from a linear profile are concave or convex, we have found it useful to treat the case in which both the concentration gradient and the potential difference are small and of

comparable magnitude. To fix the ideas, we consider the case in which c_L and c_R differ slightly from an average value c . Thus we define

$$(6.1) \quad \begin{aligned} c_R &= c(1 + \mu\Delta), \\ c_L &= c(1 - \mu\Delta), \end{aligned}$$

where

$$(6.2) \quad \Delta \ll 1.$$

The parameter μ introduced above represents the relative strength of the concentration gradient versus the electric potential. We restrict our attention to the 2-ion equations, viz.,

$$(6.3) \quad \begin{aligned} C_1' + C_1\Phi' &= -J_1, \\ C_2' - C_2\Phi' &= -J_2, \\ \Phi'' - 2\tilde{\epsilon}(\Phi - [1 - z]\Delta) &= -\lambda^2(C_1 - C_2), \end{aligned}$$

and look for solutions as power series expansions in Δ , viz.,

$$(6.4) \quad \begin{aligned} C_1 &= c + \Delta C_1^{(1)} + \Delta^2 C_1^{(2)} + \dots, \\ C_2 &= c + \Delta C_2^{(1)} + \Delta^2 C_2^{(2)} + \dots, \\ \Phi &= \Delta \Phi^{(1)} + \Delta^2 \Phi^{(2)} + \dots. \end{aligned}$$

As a result, the boundary conditions are as follows:

$$(6.5) \quad \begin{aligned} C_1^{(1)}(0) = C_2^{(1)}(0) &= -\mu c; & \Phi^{(1)}(0) &= 1, \\ C_1^{(1)}(1) = C_2^{(1)}(1) &= \mu c; & \Phi^{(1)}(1) &= 0, \\ C_1^{(n)}(0) = C_2^{(n)}(0) &= \Phi^{(n)}(0) = 0 & n > 1, \\ C_1^{(n)}(1) = C_2^{(n)}(1) &= \Phi^{(n)}(1) = 0 & n > 1. \end{aligned}$$

The first-order problem is

$$(6.6) \quad \begin{aligned} \frac{dC_1^{(1)}}{dz} + c \frac{d\Phi^{(1)}}{dz} &= -J_1^{(1)}, \\ \frac{dC_2^{(1)}}{dz} - c \frac{d\Phi^{(1)}}{dz} &= -J_2^{(1)}, \\ \frac{d^2\Phi^{(1)}}{dz^2} - 2\tilde{\epsilon}(\Phi^{(1)} - 1 + z) &= -\lambda^2(C_1^{(1)} - C_2^{(1)}). \end{aligned}$$

Clearly, the fluxes of positive and negative ions are given by

$$(6.7) \quad \begin{aligned} J_1^{(1)} &= -(2\mu - 1)c, \\ J_2^{(1)} &= -(2\mu + 1)c. \end{aligned}$$

Depending upon the magnitude of μ , these fluxes can either be positive or negative. The Nernst-Planck equations in (6.6) imply that

$$(6.8) \quad \begin{aligned} C_1^{(1)} &= \mu c(2z - 1) - (\Phi^{(1)} - 1 + z), \\ C_2^{(1)} &= \mu c(2z - 1) + (\Phi^{(1)} - 1 + z). \end{aligned}$$

The remaining equation for the potential becomes

$$(6.9) \quad \frac{d^2\Phi^{(1)}}{dz^2} - 2\tilde{\epsilon}(\Phi^{(1)} - 1 + z) = 2c\lambda^2(\Phi^{(1)} - 1 + z).$$

In view of the boundary conditions, we conclude that

$$(6.10) \quad \Phi^{(1)} = 1 - z,$$

and, after substituting this expression in (6.8),

$$(6.11) \quad C_1^{(1)} = C_2^{(1)} = \mu c(2z - 1).$$

Thus, to leading order, the so-called constant field approximation is, in fact, exact and the concentration of 1- and 2-ions are the same. To explain the bowing of the distribution profiles, we must go to the next order.

These second-order corrections are governed by

$$(6.12) \quad \begin{aligned} \frac{dC_1^{(2)}}{dz} + c\frac{d\Phi^{(2)}}{dz} - \mu c(2z - 1) &= -J_1^{(2)}, \\ \frac{dC_2^{(2)}}{dz} - c\frac{d\Phi^{(2)}}{dz} + \mu c(2z - 1) &= -J_2^{(2)}, \\ \frac{d^2\Phi^{(2)}}{dz^2} - 2\tilde{\epsilon}\Phi^{(2)} &= -\lambda^2(C_1^{(2)} - C_2^{(2)}). \end{aligned}$$

We can easily check that

$$(6.13) \quad J_1^{(2)} = J_2^{(2)} = 0;$$

i.e., there are no second-order corrections to the fluxes. Consequently,

$$(6.14) \quad C_1^{(2)} = -C_2^{(2)} = -c\Phi^{(2)} + \mu c(z^2 - z).$$

The equation for $\Phi^{(2)}$ reduces to

$$(6.15) \quad \frac{d^2\Phi^{(2)}}{dz^2} - 2(\tilde{\epsilon} + \lambda^2 c)\Phi^{(2)} = 2\lambda^2\mu cz(1 - z).$$

We can show that $\Phi^{(2)}$ is of one sign throughout the channel without resorting to its explicit form. Indeed, if $\Phi^{(2)}$ changed sign at, say, z_1 , then after multiplying (6.15) by $\Phi^{(2)}$ and integrating from 0 to z_1 , we would obtain

$$(6.16) \quad -\int_0^{z_1} \left(\frac{d\Phi^{(2)}}{dz}\right)^2 dz - 2(\tilde{\epsilon} + \lambda^2 c) \int_0^{z_1} (\Phi^{(2)})^2 dz = 2\lambda^2\mu c \int_0^{z_1} z(1 - z)\Phi^{(2)} dz$$

from which we would deduce that

$$(6.17) \quad \mu\Phi^{(2)} < 0 \quad \text{in } (0, z_1).$$

However, by repeating the same operations on the interval (z_1, z_2) , where z_2 is the next zero of $\Phi^{(2)}$ (which could coincide with the endpoint), we would obtain

$$(6.18) \quad \mu\Phi^{(2)} < 0 \quad \text{in } (z_1, z_2).$$

This contradicts our assumption that this correction changes sign at z_1 . Therefore

$$(6.19) \quad \mu\Phi^{(2)} < 0 \quad \text{in } (0, 1).$$

In other words, the sign of the deviation of the electric potential is the same as that of the concentration gradient.

The explicit expression for $\Phi^{(2)}$ is

$$(6.20) \quad \Phi^{(2)} = -\frac{\lambda^2\mu c}{\tilde{\epsilon} + \lambda^2 c} z(1-z) + \frac{\lambda^2\mu c}{(\tilde{\epsilon} + \lambda^2 c)^2} \left\{ 1 - \frac{\cosh \sqrt{2(\tilde{\epsilon} + \lambda^2 c)} (z - 1/2)}{\cosh \sqrt{2(\tilde{\epsilon} + \lambda^2 c)}/2} \right\}.$$

Substituting this expression in (6.14), we see that

$$(6.21) \quad C_1^{(2)} = -C_2^{(2)} = -\frac{\tilde{\epsilon}\mu c}{\tilde{\epsilon} + \lambda^2 c} z(1-z) + \frac{\lambda^2\mu c}{(\tilde{\epsilon} + \lambda^2 c)^2} \left\{ 1 - \frac{\cosh \sqrt{2(\tilde{\epsilon} + \lambda^2 c)} (z - 1/2)}{\cosh \sqrt{2(\tilde{\epsilon} + \lambda^2 c)}/2} \right\}.$$

Once again, the departure of the concentrations from the linear profile is dependent on μ , i.e., the sign of the overall concentration gradient. To understand this sign, we can imagine a situation in which the electric potential is first set equal to zero. In this case, the positive and negative ions diffuse throughout the channel and their identical distributions coincide with the linear profile $C_{1,2} = c_R z + c_L (1 - z)$.

Note that, for the perturbation analysis just considered, this profile is identical with the first two terms of the expansion. We then imagine that the potential is applied and that an electric field is generated. The positive ions are swept along in the direction of the electric field. The negative ions have the opposite behaviour. The sign of the net charge in the channel determines the curvature of the departure of the electric potential from a straight-line profile. The quantitative features of this behaviour are affected by the geometry of the channel as well as the dielectric constant, but the qualitative features are not.

7. Discussion. In closing, we summarize the salient results of this analysis and attempt to relate or contrast them to previous work in the literature.

The main result of the paper is the derivation of (5.17) for the electrical potential. Inside a long, narrow channel, this electric potential is one-dimensional and governed by three processes: (i) the classical axial spreading present in the one-dimensional Poisson equation, (ii) a channeling process that is most pronounced when the ratio of permittivities ϵ is of order $\alpha^2 \ln \alpha$; and, (iii) a source arising from the distribution of ions in the channel as given by the Nernst–Planck equations.

It is interesting to contrast this equation with that studied by Jordan et al. [4] and Mao Cai and Jordan [7]. They consider a channel with more realistic features than ours, since they are relying on numerical means, and, in particular, they do not restrict the size of the aspect ratio of their channels. They also consider surface charges that are very important, and absent from our analysis. They solve a classical Poisson equation in the channel with appropriate boundary conditions reflecting the disparity in electrical permittivities. However, it is not clear from their analysis what effect this disparity has. The other important difference between our approaches can

be traced to the distribution of ions. In their analysis, the distribution of ions is such that the flux of each different species is zero.

Levitt [6] also has considered the same problem and exploited the smallness of ϵ . In fact, in his paper, there is a hint that α and ϵ must be related for the analysis to be valid. The electrical potential is governed by a Poisson equation, and, as in our case, the distribution of ions satisfy Nernst–Planck equations. Furthermore, his analysis attempts to consider the finite size of the ions and, in particular, their confinement in a channel of roughly the same radius. However, this important feature of ion transport, absent here, may not have been done in a consistent manner. A time averaging might be required to go from the behaviour of a single ion to that of a distribution governed by the Nernst–Planck equations. Nevertheless, the fact remains that our less ambitious analysis makes many results contained in his paper systematic and rigorous.

Another shortcoming of our paper is the very unrealistic treatment of the entry and exit regions. The paper by Peskoff and Bers [10], in the same spirit as ours, is devoted exclusively to such a treatment. Ideally, we would like to merge the two treatments, but the analytical difficulties are too great.

The above remarks indicate that a satisfactory synthesis of all the important aspects of this problem is still in the future. For our part, we have embarked on an extension of the current work in which surface charges are present.

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