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Temperature dependence of conductivity in electrolyte solutions and ionic channels of biological membranes

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Abstract

Temperature is a key parameter in the description of any physical system. Experimental study of the temperature dependence of conductivity is very valuable in building and testing theoretical models. This fact does not appear to be fully appreciated and exploited in the study of ionic channels of biological membranes owing in part to the lack of an adequate theory for the temperature dependence of conductivity in electrolyte solutions. To redress this imbalance, and to encourage further temperature-dependence studies in ionic channels, we first give explicit expressions for the conductivity of ions in electrolyte solutions in terms of the microscopic parameters of the liquid. We then propose that the dynamics of ion transport in membrane channels are similar to that in bulk electrolyte solutions, except that ions permeating the pore need to surmount a potential barrier, the height of which can be deduced experimentally. Finally, we use our model to analyze the conductance–temperature relationships obtained in two types of single ionic channels.

Key words: Single ion channels; Temperature; Conductance-temperature relationship; Electrolytes; Ohm's law; Ion transport

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1. Introduction

Despite the continued efforts of many physicists this century, an understanding of electrolyte solutions at the microscopic level based on statistical mechanics is still not available [1]. Perhaps the most telling sign of this is the absence of a theory which can explain the temperature dependence of conductivity in electrolytes. In most textbooks on physical chemistry, this question is either ignored or the available data are simply fitted using a polynomial form (see, for example ref. [2]). Yet, temperature is one of the key dynamical parameters, and understanding of the temperature dependence of physical quantities is essential for a comprehensive description of any system.

In membrane channels, which are the focus of this paper, the study of the transport problem is further complicated by the presence of protein walls whose interaction with ions and water

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molecules is not well understood [3]. The thrust in theoretical studies of ionic channels has been, so far, mainly phenomenological. Among such phenomenological models proposed to explain the permeation of ions through narrow channels in membranes are reaction-rate theory [4] and continuum theory [5,6]. More ambitious approaches based on molecular dynamics [7] and statistical physics [8] are still at early stages to be useful in the analysis of experimental observations. In tandem with electrolyte solutions, the question of temperature dependence of conductivity in ionic channels has not been adequately addressed. Although there are many experimental studies, due to lack of theoretical interest and guidance, these have had little impact on the field. The prevailing conclusion in the literature is that temperature dependence of conductivity in ionic channels is similar to the corresponding electrolyte which tacitly suggests that there is little new to be learned from such studies.

In this paper, we would like to draw attention to the importance of temperature-dependence study of conductivity in ionic channels. With this aim in mind, we first present a phenomenological but still microscopic formulation of conductivity in electrolytes which is based on the Brownian motion of hydrated ions. This formulation can explain the temperature dependence of conductivity in terms of the microscopic parameters of electrolyte, and, as far as we know, has not been considered in the literature previously. We then apply the above formalism to study the temperature dependence of conductivity in ionic channels. In order to isolate any temperature dependence due to ion–protein wall interaction from that of electrolyte, we consider a simple model for ionic channels, namely that of a bi-conical shape with a potential barrier at the neck region. We assume that in the access region, ions move as in an electrolyte solution, unhindered by the walls, and only in the neck region do they need to surmount a potential barrier which arises from electrostatic and dynamic interactions between the hydrated ion and the charge multipoles on the protein wall. We apply the formalism to Na and K channels and show how one can use the temperature data to extract the potential barrier heights. Our primary aim is to encourage further experimental studies of temperature dependence of conductivity which could be used in devising and testing realistic models of ionic channels in future.

2. Conductivity in electrolyte solutions

There is no microscopic theory which relates all the experimental observations associated with electrolytes to the details of intermolecular interactions between the particles in the solution. Part of the difficulty arises from the strong dipole moment of the water molecules which leads to correlations between the molecules and to the hydration of ions [9]. Here we first give a simple derivation for Ohm's law and then discuss how these correlations can be taken into account in a phenomenological way.

Ions in liquid water execute a random Brownian motion with an average collision time τ. When an electric field $\mathscr{E}$ is applied, an ion of mass m_i and charge q_i accelerates, on the average, for a time τ, gaining a drift velocity

$$v_\mathrm{d} = \frac{q_\mathrm{i}\mathscr{E}}{m_\mathrm{i}}\tau. \tag{1}$$

With n_i ions per unit volume, this leads to a current density of

$$J = n_\mathrm{i} q_\mathrm{i} v_\mathrm{d} = n_\mathrm{i}\frac{q_\mathrm{i}^2}{m_\mathrm{i}}\tau\mathscr{E}, \tag{2}$$

which is Ohm's law. From Eq. (2), the conductivity follows as

$$g = \frac{J}{\mathscr{E}} = n_\mathrm{i}\frac{q_\mathrm{i}^2}{m_\mathrm{i}}\tau. \tag{3}$$

Experimental verification of Ohm's law (i.e. constant conductivity) is sufficient proof of the validity of Eq. (3) and the existence of an average collision time for the transporting ions. To obtain a microscopic expression, we need to express the mean collision time in terms of the properties of ions and water molecules. First note that τ is related to the mean free path l and average relative speed $\bar{v}$ of the ions by $\tau = l/\bar{v}$. In a dilute solution where ions collide mainly with water molecules, a simple estimate of the mean free path can be obtained from $l=[n_w\sigma_{iw}]^{-1}$, where n_w refers to the number of water molecules per unit volume and σ_{iw} is the ion–water scattering cross section. Substituting these results in Eq. (3) gives

$$g=\frac{q_i^2}{m_i}\frac{n_i}{n_w\sigma_{iw}\bar{v}} \tag{4}$$

The average relative speed in Eq. (4) follows from the equipartition theorem as

$$\bar{v}=\left[\bar{v}_i^2+\bar{v}_w^2\right]^{1/2}=\left[3kT\left(\frac{1}{m_i}+\frac{1}{m_w}\right)\right]^{1/2} \tag{5}$$

For the cross section, we assume a hard-sphere model which is a good approximation for molecular collisions

$$\sigma_{iw}=\pi\left(r_i^2+r_w^2\right). \tag{6}$$

Here r denotes the radius and the subscripts i and w refer to ion and water molecules respectively. Substituting Eqs. (5) and (6) in Eq. (4), we obtain a simple microscopic expression for the conductivity in electrolytes

$$g=\frac{n_i}{n_w}\frac{q_i^2}{\pi\left(r_i^2+r_w^2\right)}\left(\frac{m_w}{3kTm_i(m_i+m_w)}\right)^{1/2}. \tag{7}$$

To illustrate the importance of the hydration effects, we give an estimate of g when such effects are ignored. Using the appropriate values for a 150 mM salt solution at room temperature ($T_r = 293$ K) in Eq. (7), we obtain for the conductivity of Na ions $g = 0.25\ \Omega^{-1}\ \mathrm{cm}^{-1}$, which is 47 times larger than the experimental value. (By convention, we express the conductivity in units of $\Omega^{-1}\ \mathrm{cm}^{-1}$. Length is thus given in cm throughout). A similar calculation for K ions gives $g = 0.12\ \Omega^{-1}\ \mathrm{cm}^{-1}$, which is 14 times larger than the experimental value. Thus a theory based on free (unhydrated) ions explains neither the magnitude of conductivities nor their variations. Moreover, from Eq. (7), the temperature dependence of conductivity is predicted to decrease as $T^{-1/2}$ (the temperature dependence of densities cancel). The conductivity for all ions actually increases with temperature [2,10].

These discrepancies can be naturally explained once water–ion interactions are taken into account. The ions in water are not free but hydrated with the first shell relatively firmly bound, followed by a more loosely bound second shell [9]. Thus the apparent radius and mass of ions in water are correspondingly larger. A similar interaction manifests itself for water molecules which however has negligible effect on conductivity. With increasing temperature, ion–dipole and dipole–dipole bonding becomes weaker, leading to a smaller effective radius and mass for the ions. These changes provide an intuitive explanation for the increase in conductivity. As stressed previously, a microscopic formulation of this problem entails considerable mathematical complexity and, as yet, does not exist. For our purposes, a simple phenomenological derivation will be sufficient. The effective radius and mass of ions depend on N_i, the number of correlated water molecules, as

$$r_i=r_{i0}+\Delta r_i N_i^{1/3},\quad m_i=m_{i0}+m_w N_i, \tag{8}$$

where the subscript 0 refers to the bare ion radius and mass, and Δr_i is determined from the packing of water molecules. For example, assuming a cubing packing in the first hydration shell, we obtain for Na ions $\Delta r_i = 2r_w/6^{1/3} = 1.52 \times 10^{-8}$ cm. Since K and Cl have larger volumes avalable in the first shell, Δr_i for these ions are proportionally smaller (see Table 1). An appropriate parametrization for N_i is given by the Boltzmann factor [9]

$$N_i=A_i\,\mathrm{e}^{-U_i/kT}, \tag{9}$$

Table 1
Experimental conductivities of 150 mM ion solutions at T = 293 K. Also shown are the parameters of Eqs. (8) and (9) used to calculate the curves in Fig. 1

	g (10^{-3} Ω^{-1} cm^{-1})	r_{i0} (10^{-8} cm)	Δr_i (10^{-8} cm)	A_i	U_i (10^{-20} J)
Na	5.3	0.95	1.52	0.0397	−2.23
K	8.4	1.33	1.38	0.0114	−2.53
Cl	8.6	1.81	1.24	0.0049	−2.82

where A_i is a constant and U_i represents the average binding energy of water molecules. As an intermediate step in fitting the conductivity, we first extract the effective hydration numbers N_i from the conductivity data using Eqs. (7) and (8), and fit the resulting N_i data with a function of the form Eq. (9). The parameters A_i and U_i in Eq. (9), estimated from experimental data, are given in Table 1, together with the incremental coefficient of the radius of the first shell (Δr_i), and the radius of the unhydrated ion (r_{i0}). Fig. 1a shows the temperature dependence of effective hydration numbers for Na, K and Cl ions. We emphasize that these effective numbers are derived from the conductivity data which include effects of the higher hydration shells beyond the primary shell. Therefore they are somewhat larger than the measured or calculated hydration numbers which are sensitive to the primary shell only (see, for example, ref. [11]). Using the theoretical value of N_i and Eqs. (7) and (8), we obtained conductivity-temperature curves for the three ionic species, shown as solid lines in Fig. 1b. Superimposed on the curves are the experimental values [2,10]. Thus, we provide a phenomenological yet microscopic explanation for temperature dependence of conductivity in electrolyte solutions.

In contrast to temperature, the electric field and concentration dependence of conductivity in electrolytes is rather ordinary. At very high field strengths (10^5 V/cm), conductivity increases by a few percent due to the Wien effect [2], which is an almost negligible breaking of Ohm's law. From Eq. (4), conductivity is expected to increase linearly with concentration. Experimentally, it is slightly less than linear which, as explained by Debye and Hückel [2], is due to the ionic atmosphere. These deviations are quite small for concentration variations in ionic channels and, for practical purposes, can be ignored.

3. Conductivity in ionic channels

We now contrast the experimental information on conductivity in ionic channels with that for electrolytes. There exist many reports in the literature relating the conductance changes in a wide variety of single channels with temperature. All these studies demonstrate that single channel

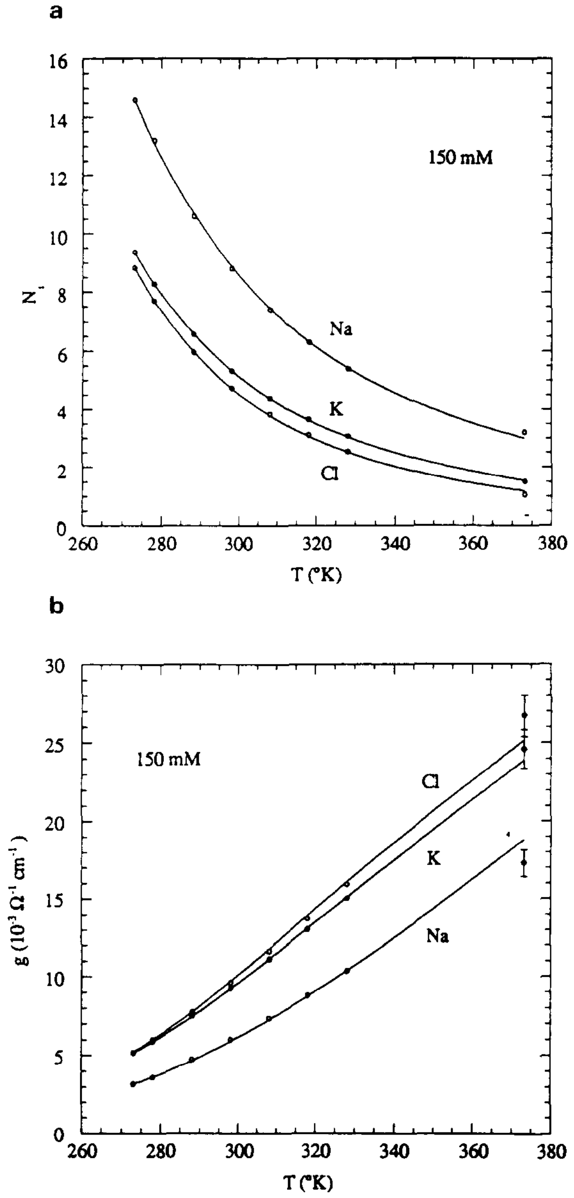

Fig. 1. Temperature dependence of effective hydration numbers and of conductivity. (a) The predicted number of water molecules transported with an ion is calculated from Eq. (9), using the parameters given in Table 1, and plotted against temperature. (b) The predicted increase in conductivity with temperature was calculated from Eq. (7) for Na, K and Cl ions. The circles are the bulk conductivity data extracted from Harned and Owen [2] and Robinson and Stokes [10].

conductance increases with temperature in a way similar to that of the conductivity of electrolyte solutions [12–14], but the slopes for ion channels are much steeper than those shown in Fig. 1b; conductance increases with temperature more steeply in an ionic channel than in an electrolyte solution. The measurements reveal that the Arrhenius plots of conductance yield an activation energy of between 25 to 35 kJ mol^{-1} or between 10 to 14 kT_r [14–24]. In contrast, the activation energy of conductivity of 150 mM Na$^+$ or K$^+$ electrolyte solutions, deduced from the Arrhenius plot, is about 6 kT_r. The similarity implies that the dynamics of ion transport in ionic channels are broadly the same as in bulk water. The major part of the channel must be wide enough so that the channel walls do not affect the bulk conductivity. The difference, on the other hand, points to the presence of a potential barrier in the channel that would enhance the temperature dependence.

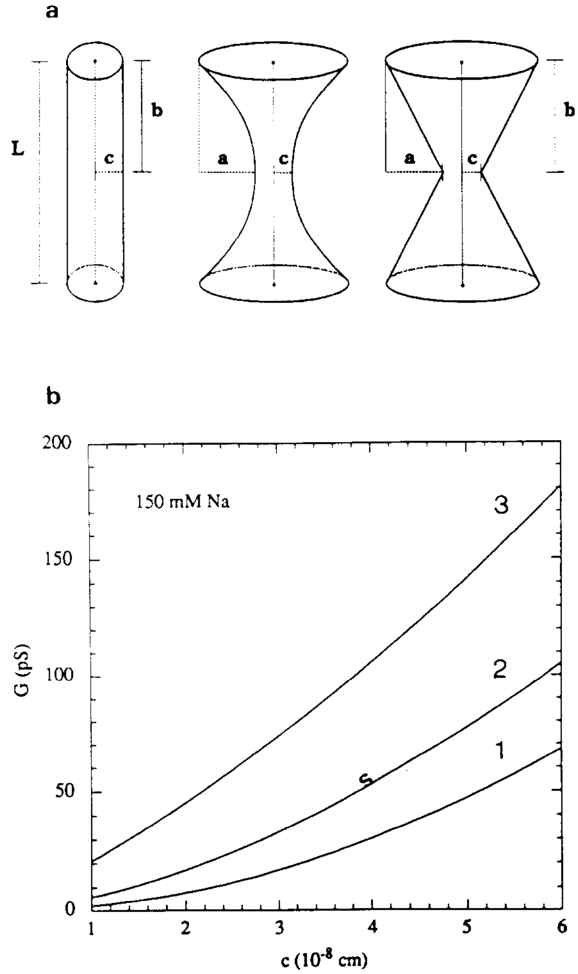

Fig. 2. The theoretical conductance of three idealized pores. (a) Three limiting cases of channel shapes considered for the evaluation of theoretical conductance are shown schematically. The letters, a, b, c and L, represent the dimensions of the pore featuring in Eqs. (10) and (11). (b) Pore conductance for the three shapes are shown as a function of the neck radius c. The numbers 1, 2 and 3 accompanying the curves denote respectively the cylindrical pore, hourglass-shaped pore and bi-conical pore. The conductance value represents that of a fictitious pore which has no potential barrier.

The electric field and concentration dependence, in contrast, deviate markedly from that of bulk electrolyte, showing early saturation [3]. This together with ionic selectivity can be explained by the presence of a narrow neck region in the channel which limits the rate of ions processed to some maximum value. The picture of channels which emerges from these considerations is that of a funnel consisting of 4–5 proteins. Following our simple model, we first consider the conductance in such a channel using the formalism developed in the last section, and then introduce the effect of the protein walls as a potential barrier. Since the precise shape of protein subunits forming a channel is not known, we consider as limiting cases three shapes for the pore: cylindrical, hourglass and bi-conical (see Fig. 2a). The last two pore shapes result depending on whether the α-helical bundles forming the channel are gently curved or sharply curved near their midsections. The resistance of the channel is given by

$$R = \frac{2}{\pi g}\int_0^b \frac{\mathrm{d}z}{x^2},$$

$$x = \begin{cases} c, & \text{cylindrical},\\ c + a - a\left[1 - z^2/b^2\right]^{1/2}, & \text{hourglass},\\ c + az/b, & \text{bi-conical}. \end{cases} \qquad (10)$$

The integrals in Eq. (10) can be evaluated analytically to yield

$$R = \frac{L}{\pi c^2 g} \begin{cases} 1, & \text{cylindrical,} \\ \dfrac{1}{1+2a/c} + \dfrac{2a/c}{(1-2a/c)^{3/2}} \\ \quad \times \tan^{-1}\sqrt{1+2a/c}, & \text{hourglass} \\ \dfrac{1}{1+a/c}, & \text{bi-conical.} \end{cases} \tag{11}$$

where $L = 2b$ is the channel length. Using typical dimensions for proteins ($a = 10^{-7}$ cm and $L = 10^{-6}$ cm) , we plot in Fig. 2b the conductance, $G = 1/R$, for various channel shapes as a function of the neck radius. As will become clear later, the cylindrical pore results in a conductance far lower than the experimental value, and it is therefore unlikely to be a realistic approximation of the actual biological channel. If the fictitious membrane channel were to present no potential barrier to the passage of ions, the channel conductance could easily be calculated by Eqs. (10) and (11), and from the measured current amplitude one would be able to deduce the radius of the channel when it is open. However, the neck region plays an important role in reducing the current and needs to be considered before making such numerical evaluations.

To set a lower limit for the radius of an open channel, we need to consider whether an ion in the channel undergoes partial or complete dehydration at the neck region before traversing the membrane. A simple estimate of the electrostatic binding energy of a water molecule in the first hydration shell can be obtained, assuming a cubic structure, by

$$U = \frac{-q\mu}{r^2} + \left(\frac{3}{\sqrt{2}} + \frac{1}{4}\right)\frac{\mu^2}{r^3}, \tag{12}$$

where μ is the dipole moment of the water molecule. For $r = (0.95 + 1.38) \times 10^{-8} = 2.33 \times 10^{-8}$ cm, we obtain $U = -10^{-19}$ J or $-24\ kT_r$ in room temperature units. This is a huge energy compared to the average kinetic energy of ions $\frac{3}{2}kT$, and strongly suggests that ions move across the neck with their first shell mostly intact. A plausible scenario is that ions in transit are partially dehyrated and the hydrogen bonds are temporarily substituted by groups at the neck. This process would naturally lead to an effective potential barrier which is dynamic in character.

The potential barrier presented by the protein wall ensures that only the ions with energies E larger than the barrier height will be allowed to go through the neck, so reducing the number of ions that can traverse a channel and suppressing the conductance level of a pore as deduced by Eq. (11) (see Fig. 2). Such a barrier could arise from two distinct sources which have very different temperature dependence. One is the dehydration and substitution process mentioned above and will be denoted by V_T. Since V_T depends on the hydration number which varies with temperature (see Fig. 1a), we expect V_T to exhibit a similar temperature dependence. Thus, as a first guess, we assume that V_T is proportional to N_i, as defined in Eq. (9). The other source, to be denoted by V_0, is due to the electrostatic interaction between ions and charge multipoles on the protein wall, and is assumed to be independent of temperature. Note that V_T, by its very nature, always presents a barrier whereas V_0 could lead to either a potential barrier or a well depending on the interaction. An *ab initio* calculation of these potentials is not possible since neither the dynamics nor the statics (i.e. the location and distribution of charges along the pore) are well known at present. It is likely that the actual profile of the potential is quite complex, fluctuating in space and time. However, the macroscopically measured quantity in studying single channels is current, which is the space-time average of ionic motions, and thus current measurements alone cannot probe the space-time details of the potential. For these reasons, we adopt a simple, static potential, characterized solely by its height of the form

$$V = V_T + V_0,\ V_T = \alpha N_i = \alpha A_i\ e^{-U_i/kT}, \tag{13}$$

where V_0 and α are constants to be determined from data. Since V_T is a more readily recognized parameter, we prefer to specify values of V_T at room temperature rather than α in the fits below. The probability of an ion surmounting a barrier of height V follows from the Boltzmann distribution as

$$\mathscr{P}(E>V) = (2\pi mkT)^{-3/2}\int_{p^2>2mV}^{\infty} \mathrm{e}^{-p^2/2mkT}\,\mathrm{d}^3p, \quad (14)$$

where p is the momentum of the ion. Changing variables to E, the integral becomes

$$\mathscr{P}(E>V) = \frac{2}{\sqrt{\pi}}(kT)^{-3/2}\int_V^{\infty}\mathrm{e}^{-E/kT}\sqrt{E}\,\mathrm{d}E \quad (15)$$

which is given by the incomplete Γ function

$$\mathscr{P}(E>V) = \frac{2}{\sqrt{\pi}}\Gamma(\tfrac{3}{2},\epsilon),\ \epsilon = V/kT \quad (16)$$

For $\epsilon > 1$, using the asymptotic expansion for the incomplete Γ function, this can be rewritten as

$$\mathscr{P}(E>V) = \frac{2}{\sqrt{\pi}}\mathrm{e}^{-\epsilon}\sqrt{\epsilon}\left(1+\frac{1}{2\epsilon}-\frac{1}{4\epsilon^2}+\frac{3}{8\epsilon^3}-\cdots\right). \quad (17)$$

For $\epsilon \sim 1$, Eq. (17) does not converge quickly, and one should use instead the alternative expansion

$$\mathscr{P}(E>V) = 1-\frac{4}{3\sqrt{\pi}}\mathrm{e}^{-\epsilon}\epsilon^{3/2} \times\left(1+\frac{2\epsilon}{5}+\frac{4\epsilon^2}{5\times 7}+\frac{8\epsilon^3}{5\times 7\times 9}+\cdots\right). \quad (18)$$

Thus, the probability that an ion entering the channel will successfully pass through it decreases exponentially as a function of the barrier height. An interesting question here is whether ions can tunnel through the barrier. From the Heisenberg uncertainty relation, quantum effects are not expected to be important for ions in the channel. This is also borne out by a quantum tunneling calculation using the Hill–Wheeler formalism [25] which gives the classical step function for the transmission probability. To appreciate how the potential barrier affects current flow through a channel, we give a few representative values

$$\mathscr{P}(E>24kT) = 2\times 10^{-10},$$
$$\mathscr{P}(E>8kT) = 2\times 10^{-3},$$
$$\mathscr{P}(E>3kT) = 0.11. \quad (19)$$

The first value roughly corresponds to a situation where an ion must be partially dehydrated before crossing the neck, and the bonds are not substituted. This leads to a reduction of the current by ten orders of magnitude and is clearly not acceptable. The second barrier height ($V = 8kT$) is typical of the values used in reaction rate theories and leads to a still stronger reduction in current than that warranted by experimental data (e.g. for a pore resistance of 10^{10} Ω, one would obtain 0.01 pA at 100 mV for the total current). Finally, the third value gives a current of 1 pA which is the same order of magnitude as the observed values. This value for the barrier height (1.23×10^{-20} J) is much smaller than the hydration energies involved which raises the crucial question of how many water molecules, if any, are carried through the neck with the ions. With the combined use of ^3H_2O and radioactive nuclides, such as ^{42}K and ^{24}Na, it should be possible to determine the number of water molecules transported with each ion. The result would be important in devising a working model of the neck region.

Combining Eqs. (11) and (16), the conductance of an ion channel can be written as

$$G = \frac{1}{R}\mathscr{P}(E>V). \quad (20)$$

To illustrate the way Eq. (20) can be utilized to determine the potential barriers, we apply our model to temperature data in Na and K channels. The conductance-temperature measurements we selected for illustration were obtained from an NMDA-activated glutamate channel from an inside-out membrane patch of a cultured hippocampal neuron (Chung and Kuyucak, unpublished observation) and a Ca^{2+}-activated K^+ channel in inside-out membrane patch of human erythrocytes [19]. In each case, the data are fitted using three parameters, namely an overall amplitude for conductance and the heights for V_T and

V_0. In presenting the results, we have converted the amplitude to an equivalent neck radius c using Eq. (11) for bi-conical shape. Since convergence in a three-parameter search is very slow, we first performed a two-parameter fit with $V_0 = 0$ and then included V_0 in the fitting process. In the case of Na channel (Fig. 3a), inclusion of V_0 did not lead to any visible improvement, suggesting that $V_0 \sim 0$. The other parameters were found to be, $c = 5.24 \times 10^{-8}$ cm and $V_T = 1.77\ kT_r$ at room temperature. For the K channel (Fig. 3b), inclusion of V_0 did improve the fit resulting in the values $c = 4.7 \pm 1.1 \times 10^{-8}$ cm, $V_T = 1.0 \pm 0.1\ kT_r$ and $V_0 = 1.8 \pm 0.4\ kT_r$. (The uncertainties were negligibly small for the Na channel.)

In Fig. 3, besides the fit results (solid lines), we have also shown the temperature dependence expected from a similar electrolyte solution (dashed lines), normalized to the former at zero temperature. The difference in the slopes, especially in the case of the Na channel, is quite large, and is the main reason for calling attention to importance of temperature studies in ionic channels. The potential barriers which explain these differences are rather small (a few kT_r). As demonstrated in Eq. (19) larger barriers would suppress the current too much in conflict with experiment. For example, ignoring V_T in the fit to the Na channel would lead to $V_0 \sim 8\ kT_r$ and $c = 200 \times 10^{-8}$ cm which are clearly inconsistent with the channel data. This example also underscores the importance of the temperature dependent barrier V_T for a consistent explanation of the data, and the ionic dehydration and substitution process at the neck region which gives rise to it. The larger value of V_T obtained for the Na channel compared to that of K channel is consistent with their hydration numbers (see Fig. 1a).

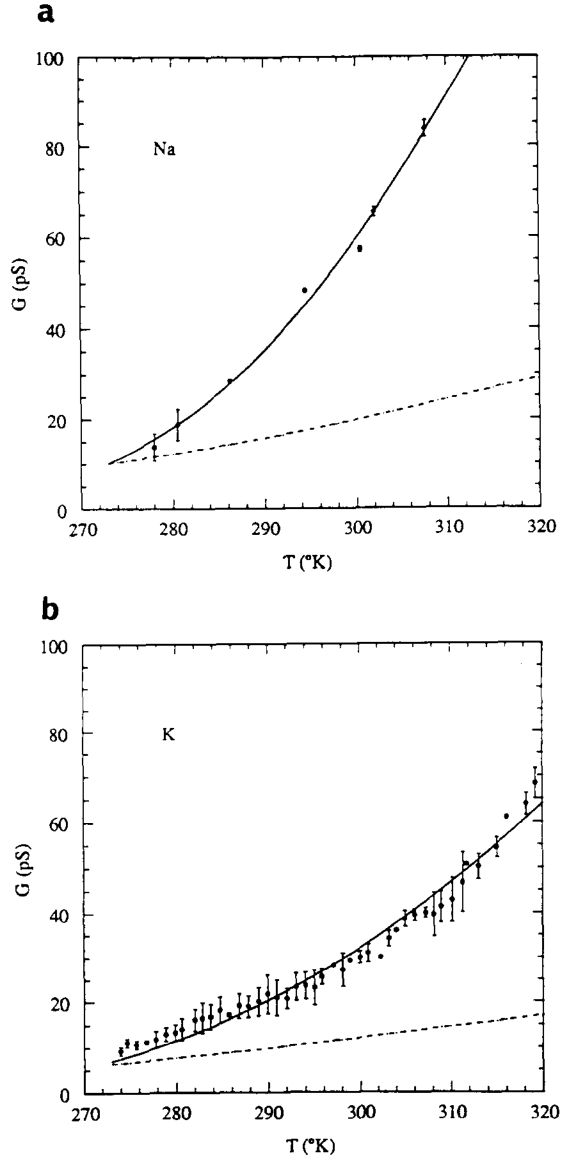

Fig. 3. Analyses of the conductance-temperature curves of single Na and K channels. The conductance-temperature relationships of two different types of single channels are fitted with theoretical curves (solid lines). Superimposed on the graphs are the conductivity of electrolyte solutions containing 0.15 M of Na^+ and K^+ (dotted lines). (a) Single channel currents were activated by 50 μM NMDA and 2 μM glycine from an excised membrane patch from a cultured hippocampal neuron. The patch was held at a pippete potential of +40 mV. The amplitudes of channel currents recorded at various temperatures were determined by using digital signal processing techniques. The pippete solution contained (mM): Na-gluconate, 145; $CaCl_2$, 2; Na-HEPES. 10, pH 7.3. (b) The currents amplitudes of Ca^{2+}-activated K^+ channel recorded in the temperature range from 0 to 47°C were taken from Fig. 3A of Grygorczyk [19], converted in pS and then replotted in (b).

In fact, the ratio of N_i gives 1.65 which is very close to the ratio of V_T (1.77). This indicates that the assumption of V_T being proportional to N_i is consistent with the data. The neck radius, in both cases, comes out between the first and second hydration shells, supporting the idea that the first hydration shell is not disrupted in these channels.

Conventionally, the conductance changes of single channel currents have been used to derive the activation energy under the assumption that the transport process can be represented as a simple rate process that can be fitted by the Arrhenius equation. Because a part of the potential barrier is dependent on temperature, a plot of the logarithm of single channel current against the inverse of temperature can be markedly nonlinear for some ionic channels. In an Arrhenius plot, the effect of the temperature-dependent potential barrier will manifest itself as a downward curvature, i.e. a slow decline at high temperatures and a steep decline at low temperatures. Several investigators have noted such a downward curvature in the Arrhenius plot and offered various explanations for it [14,18,20]. Our interpretation of this nonlinearity is that a part of potential barrier presented by the channel to the permeating ion stems from the hydration shell. The height of this potential barrier decreases with increasing temperature, thus causing a systematic deviation from the relationship predicted by the Arrhenius or Eyring rate equation.

4. Discussion

We have presented simple microscopic models based on the concept of hydrated ions to describe the temperature dependence of conductivity in electrolyte solutions and ionic channels. Ionic hydration is essential in explaining why and how conductivity increases with temperature in electrolytes. It also plays a dominant role in determining the potential barrier in ionic channels, which have a steeper temperature dependence of conductance than electrolytes. Since our aim is to draw attention to the importance of temperature-dependence studies in ionic channels, and not sophisticated modeling of channels, we have been content with a schematic model which nevertheless captures the essential physics involved. The division of a channel into a wider access region where transport is similar to electrolyte solutions, and a narrow neck region where the potential barrier is localized is the main feature of the model, and simplifies the problem both conceptually and computationally.

According to our model, the shape of the pore and its radius at the neck give the theoretical maximum conductance level (Fig. 2). A potential barrier reduces this conductance level by a Boltzmann factor to give the actual conductance level of any given single channel. Although the radius of a channel in the open conformation cannot yet be determined experimentally, our results suggest that it is somewhere between the first and second hydration shell. If the open aperture were to be, for example, 10^{-7} cm, which is greater than the radius of the second hydration shell, the potential barrier arising from dehydration and electrostatic interaction would be negligible in height, and such a channel would not be selective to one ion species.

We hope the quantitative relationships between the conductance and the potential barrier proposed here will be useful in the analysis of experiments studying temperature dependence of conductivity in ionic channels. As demonstrated in the last section, temperature data can be used to extract information on potential barrier heights and neck radius within a simple model. Once systematic and accurate temperature data for various channels become available, improvements on the simple picture presented here may be possible, with more realistic potential barriers calculated from microscopic models.

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