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HYDRATION ENERGY AND THE TRANSPORT OF IONS THROUGH MEMBRANES

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SUMMARY

In order to obtain a proper understanding of the transport of ions in membranes one must know the hydration energies of ions in water and the equivalent quantities arising from the electrostatic interaction of the ion with the membrane material. In this paper the effect of dielectric saturation on these quantities is discussed and a simple theoretical treatment of this phenomenon is proposed. The results are compared with values obtained from thermodynamic data.

INTRODUCTION

In a former publication[1] a study was made of the problem of transport of ions through membranes and analytical solutions were obtained corresponding to certain particular models. It was shown that the dielectric behaviour of the membrane material was critical in determining the insertion energy of the ions and hence the choice of model. Unless the dielectric constant of the membrane is comparable to or greater than that of water only a minute ion current is possible. Now the dielectric constant of the hydrocarbon part of phospholipids is probably approx. 7 or less and thus one can discount the lipid part of the membrane as contributing to ion transport. There remain the very large protein molecules which are now known to penetrate the cell wall. It is at least highly plausible that these proteins provide the regions containing the channels through which ions pass. Little is known about the dielectric constants of proteins viewed as solids but the results of Takashima and Schwan[2] indicate that dielectric constants greater than 200 are possible. Substantially higher values have been obtained for some β structure materials currently under investigation in this laboratory. The insertion energies discussed in the earlier paper referred to[1] were obtained using the Born[3] expression (Eqn 37 of the present paper) but this formula presupposes a linear relationship between polarisation and electric field even for the very high fields experienced in the immediate region of an ion. Clearly this approximation is rather crude and something better is required. The literature does not appear to contain any really satisfactory discussion of this type of problem and this paper is thus devoted to the development of a theoretical treatment of non linear dielectrics and its application to a partially phenomenological model for hydrated ions. A brief discussion of earlier work in this field is given in the penultimate section of this paper.

DISCUSSION OF THE MODEL AND DERIVATION OF ENERGY FORMULAE

Consider an isotropic dielectric medium and divide its polarisation into two components:

$\mathbf{P}_i$ which is associated with the displacement of ions and charged groups or the rotation of polar groups and

$\mathbf{P}_e$ which is associated with the polarisation of the electronic charge clouds relative to the positive atomic cores.

It is assumed that $\mathbf{P}_i$ saturates at some value $\mathbf{P}_m$ but below this value is linearly related to the local electric field. $\mathbf{P}_e$ is linearly related to the local field for all attainable values of this field.

We wish to calculate the energy density associated with the polarisation for this simple model. We begin by considering the energy associated with $\mathbf{P}_i$ and assume N polarisable units m^{-3} each having an effective charge, q, and an effective displacement, $\mathbf{x}$.

Then

$$\mathbf{P}_i = qN\mathbf{x} \tag{1}$$

Below saturation let the restoring force per unit be $\beta\mathbf{x}$ so that in this region

$$\beta\mathbf{x} = q(\mathbf{E}_0 + \mathbf{E}_L + \mathbf{E}_D) \tag{2}$$

where $\mathbf{E}_0$ is the applied field, $\mathbf{E}_L$ the Lorentz field and $\mathbf{E}_D$ the field resulting from polarisation remote from the region under consideration (*i.e.* the effect of polarisation not included in $\mathbf{E}_L$).

Then, dividing the interaction energy evenly between the interacting parts, the energy per polarisable unit associated with $\mathbf{P}_i$ will be

$$u_i = \tfrac{1}{2}\beta\mathbf{x}^2 - q\mathbf{x}\cdot(\mathbf{E}_0 + \tfrac{1}{2}\mathbf{E}_L + \tfrac{1}{2}\mathbf{E}_D) \tag{3}$$

Let ε_0 be the electrical permittivity of free space and define χ_{0i} by

$$\mathbf{P}_i = \varepsilon_0\chi_{0i}(\mathbf{E}_0 + \mathbf{E}_L + \mathbf{E}_D) \tag{4}$$

then

$$\chi_{0i} = \frac{q^2 N}{\varepsilon_0 \beta} \tag{5}$$

From Eqns 3, 4 and 5 one can show that this energy m^{-3} is given by

$$U_i = Nu_i = \frac{\mathbf{P}_i^2}{2\varepsilon_0\chi_{0i}} - \mathbf{P}_i\cdot(\mathbf{E}_0 + \tfrac{1}{2}\mathbf{E}_L + \tfrac{1}{2}\mathbf{E}_D) \tag{6}$$

We further assume that the same Lorentz factor, L, applies to both $\mathbf{P}_i$, $\mathbf{P}_e$ and their interaction *via* the Lorentz field.

Thus

$$\mathbf{E}_L = \frac{L}{\varepsilon_0}(\mathbf{P}_i + \mathbf{P}_e) \tag{7}$$

Thus from Eqns 6 and 7

$$U_i=\frac{P_i^2}{2\varepsilon_0\chi_{0i}}-\frac{P_i}{2}\cdot\left[2E_0+E_D+\frac{L}{\varepsilon_0}(P_i+P_e)\right] \tag{8}$$

In a similar manner one can show that

$$U_e=\frac{P_e^2}{2\varepsilon_0\chi_{0e}}-\frac{P_e}{2}\cdot\left[2E_0+E_D+\frac{L}{\varepsilon_0}(P_i+P_e)\right] \tag{9}$$

where χ_{0e} is analogous to χ_{0i} and is associated with the electronic polarisation. Hence the total energy density is given by

$$U=\frac{P_i^2}{2\varepsilon_0\chi_{0i}}+\frac{P_e^2}{2\varepsilon_0\chi_{0e}}-\frac{L}{2\varepsilon_0}(P_i+P_e)^2-R \tag{10}$$

where

$$R=\tfrac{1}{2}(P_i+P_e)\cdot(2E_0+E_D) \tag{11}$$

It is convenient to define

$$\chi=\frac{\chi_{0e}+\chi_{0i}}{1-L(\chi_{0e}+\chi_{0i})} \tag{12}$$

$$\chi_h=\frac{\chi_{0e}}{1-L\chi_{0e}} \tag{13}$$

and

$$\chi_i=\frac{\chi_{0i}}{1-L\chi_{0i}} \tag{14}$$

where χ is the low frequency susceptibility, χ_h is the high frequency susceptibility and χ_i is not directly observable. Then rearranging Eqns 10 and using 13 and 14 one obtains

$$U=\frac{P_i^2}{2\varepsilon_0\chi_i}+\frac{P_e^2}{2\varepsilon_0\chi_h}-\frac{L}{\varepsilon_0}P_i\cdot P_e-R \tag{15}$$

From Eqns 12, 13 and 14 one can show that

$$\frac{1}{\chi_i}=\frac{(1+L\chi_h)^2}{\chi-\chi_h}+L^2\chi_h \tag{16}$$

Hence

$$U=\frac{(1+\chi_hL)^2P_i^2}{2\varepsilon_0(\chi-\chi_h)}+\frac{L^2\chi_hP_i^2}{2\varepsilon_0}+\frac{P_e^2}{2\varepsilon_0\chi_h}-\frac{L}{\varepsilon_0}P_i\cdot P_e-R \tag{17}$$

To proceed further one must specify a particular model. For the model discussed in this paper, outside the region of saturation one obtains the well known result

$$U=-\tfrac{1}{2}E_0\cdot(P_i+P_e) \tag{18}$$

In the region of saturation

$$\mathbf{P}_\mathrm{i}=\mathbf{P}_\mathrm{m} \tag{19}$$

and

$$\mathbf{P}_\mathrm{e}=\varepsilon_0\chi_{0\mathrm{e}}(\mathbf{E}_0+\mathbf{E}_\mathrm{L}+\mathbf{E}_\mathrm{D}) \tag{20}$$

Using Eqn 7

$$\mathbf{P}_\mathrm{e}=\chi_\mathrm{h}L\mathbf{P}_\mathrm{m}+\varepsilon_0\chi_\mathrm{h}(\mathbf{E}_0+\mathbf{E}_\mathrm{D}) \tag{21}$$

Using Eqns 11, 17, 19 and 21 it can be shown that

$$U=\frac{\mathbf{P}_\alpha^{\,2}}{2\varepsilon_0(\chi-\chi_\mathrm{h})}-\frac{\mathbf{P}_\alpha\cdot\mathbf{P}_\mathrm{e}}{2\varepsilon_0\chi_\mathrm{h}}-\frac{\mathbf{E}_0}{2}\cdot(\mathbf{P}_\alpha+\mathbf{P}_\mathrm{e}) \tag{22}$$

where $\mathbf{P}_\alpha$ is defined by

$$\mathbf{P}_\alpha=(1+L\chi_\mathrm{h})\mathbf{P}_\mathrm{m} \tag{23}$$

SPHERICAL CHARGE, *e*, IMMERSED IN THE MODEL DIELECTRIC

As the medium is isotropic only the radial components of field and displacement are non zero.

Thus

$$E_0=\frac{1}{4\pi\varepsilon_0}\frac{e}{r^2} \tag{24}$$

$$D=\frac{1}{4\pi}\frac{e}{r^2} \tag{25}$$

Outside the region of saturation

$$E_0+E_\mathrm{D}=\frac{e}{4\pi\varepsilon_0\kappa r^2} \tag{26}$$

where κ is the dielectric constant.

Inside the region of saturation

$$D=\varepsilon_0\kappa_\mathrm{h}(E_0+E_\mathrm{D})+P_\alpha=\frac{1}{4\pi}\frac{e}{r^2} \tag{27}$$

where

$$\kappa_\mathrm{h}=1+\chi_\mathrm{h} \tag{28}$$

(this expression allows for the polarization of the electronic component by P_m *via* the Lorentz field).

Hence

$$E_0+E_\mathrm{D}=\frac{1}{\varepsilon_0\kappa_\mathrm{h}}\left(\frac{e}{4\pi r^2}-P_\alpha\right) \tag{29}$$

At the interface between the two regions the fields must join smoothly hence

$$r_c^{\,2} = \frac{e}{4\pi P_\alpha \kappa}(\chi - \chi_h) \tag{30}$$

where r_c defines the interface. From Eqn 29 in the region of saturation

$$P_e = \frac{\chi_h}{\kappa_h}\left(\frac{e}{r^2} - 4\pi P_\alpha\right) \tag{31}$$

Outside this region it is easy to show that

$$U_{\text{out}} = -\frac{\chi}{2\varepsilon_0 \kappa}\left(\frac{e}{4\pi r^2}\right)^2 \tag{32}$$

Inside this region using Eqns 22, 24 and 31 one obtains

$$U_{\text{in}} = \frac{1}{2\varepsilon_0 \kappa \kappa_h}\left[\frac{P_\alpha^{\,2}\kappa^2}{\chi - \chi_h} - 2P_\alpha \kappa\left(\frac{e}{4\pi r^2}\right) - \chi_h \kappa\left(\frac{e}{4\pi r^2}\right)^2\right] \tag{33}$$

If there were no saturation Eqn 32 would apply in both regions and thus the change in energy density due to saturation is given by the difference between Eqns 32 and 33

$$U_{\text{in}} - U_{\text{out}} = \frac{1}{2\varepsilon_0 \kappa \kappa_h(\chi - \chi_h)}\left[P_\alpha \kappa - (\chi - \chi_h)\left(\frac{e}{4\pi r^2}\right)\right]^2 \tag{34}$$

If one defines the total change of energy due to saturation as ΔU, then

$$\Delta U = 4\pi \int_{r_0}^{r_c} (U_{\text{in}} - U_{\text{out}}) r^2 \, \mathrm{d}r \tag{35}$$

where r_0 is the radius of the inserted charge.

Then

$$\Delta U = \frac{e^2}{8\pi\varepsilon_0 r_c}\left(\frac{1}{\kappa_h} - \frac{1}{\kappa}\right)\left[\left(\frac{r_c}{r_0}\right) - \frac{8}{3} + 2\left(\frac{r_0}{r_c}\right) - \frac{1}{3}\left(\frac{r_0}{r_c}\right)^3\right] \tag{36}$$

The hydration energy, ignoring saturation effects (originally obtained by Born[3]) is given by

$$U_B = 4\pi \int_{r_0}^{\infty} U_{\text{out}} r^2 \, \mathrm{d}r = -\frac{e^2}{8\pi\varepsilon_0 r_0}\left(1 - \frac{1}{\kappa}\right) \tag{37}$$

HYDRATION ENERGIES OF ALKALI IONS

It is assumed in this discussion that it is legitimate to treat water as a continuum having κ given by the static dielectric constant and κ_h given by the square of the refractive index as measured in the middle of the visible range.

If one takes $\kappa = 78$ and $\kappa_h = 1.778$ and makes use of Eqns 36 and 37 it is easy to obtain the following expression for the hydration energy of singly charged ions.

$$U_H = -\frac{7.1068}{r_0}\left[1 - 0.5568F\left(\frac{r_0}{r_c}\right)\right] \tag{38}$$

where the radii are in Ångstrom units, the energy is in electron volts and

$$F(Z) = 1 - \tfrac{8}{3}Z + 2Z^2 - \tfrac{1}{3}Z^4 \tag{39}$$

r_c is defined in terms of the saturation polarisation *via* Eqn 30 and r_0 is the effective radius of the ion in solution. Clearly the r_0 values should be somewhat larger than the radii estimated by Pauling on the basis of the packing in ionic crystals. It is assumed that

$$r_0 = r_p + \beta \tag{40}$$

where r_p is the Pauling radius and β is a constant applicable to all the alkali ions. β is chosen to reproduce the experimental values of U_H deduced from thermodynamic data by Noyes[4]. Before carrying through this calculation however one must determine a value of P_α to be inserted into Eqn 30 so that one can calculate r_c. Buckingham[5] has argued that the first hydration shell consists exclusively of water molecules whose dipole moments point directly away from the ion. Using this model he was obliged to assume that the first shell consists of only four molecules tetrahedrally coordinated. Unfortunately such an arrangement involves a large amount of unoccupied space near the ion. The introduction of more nearest neighbour molecules into this model leads to less satisfactory agreement with experimental results. The present author believes that one should employ a model which does not involve unfilled space near the ion. Furthermore one would expect the hydrogen bonds between the molecules to introduce constraints and prevent all the molecules orienting themselves in a radial manner. At the present time it does not seem possible to make an accurate estimate of the value of P_m and hence, *via* Eqn 23, P_α. One can however obtain a reasonable value of P_m if it is assumed that, over a few atomic spacings and at physiological temperatures, the structure of water is like ice. One can then work out the various arrangements which water molecules can take on if it is required that there be a maximum in the electric polarisation but that the tetrahedral coordination characteristic of ice is preserved. Taking for the electric moment of the free water molecule $\mu_w = 1.83$ Debye Units[6], the maximum mean component along a particular direction becomes

$$\overline{\mu_w} = \frac{1}{2}\left(\frac{1}{\sqrt{3}} + \frac{1}{3}\right)\mu_w = 0.8332 \text{ Debye Units} \tag{41}$$

The increase of this quantity resulting from electronic polarisation brought about by the Lorentz field is taken into account in the relationship between P_m and P_α.

Accordingly we proceed on the assumption that the mean saturation moment per molecule is given by Eqn 41 and use Eqn 30 to obtain $r_c = 3.264$ Å for singly charged ions and $r_c = 4.615$ Å for doubly charged ions. The best choice of β for the ions of Na^+, K^+, Cs^+, Rb^+ is $\beta = 0.57$ Å from which one obtains the results displayed in Table I. As a check on this procedure one can take the values of P_α and β already employed and use them to obtain the hydration energies of the alkali earth ions. The results are presented in Table II.

It should be noted that the values of U_H here calculated only take into account the electrical energy involved. The quantities obtained by Noyes[4] with which comparison is made are corrected by him so as to correspond to the electrical energy only. The results for Na^+ and K^+ agree with the results of Noyes[4] to within 2% and the worst discrepancy between theory and experiment for any of the ions considered is 10%. The results of a similar calculation previously published by the present

TABLE I

COMPARISON OF THEORETICAL AND EXPERIMENTAL HYDRATION ENERGIES FOR THE ALKALI IONS

r_p is the Pauling radius in Ångstrom units, U_{exp} is the hydration energy derived from thermodynamic data in electron volts per ion, U_B is the hydration energy according to the simple Born theory and U_{TH} is this energy derived from the calculations presented in the present paper.

Ion	r_p	U_{exp}	U_B	U_{TH}
Na^+	0.97	4.27	7.33	4.18
K^+	1.33	3.49	5.34	3.56
Rb^+	1.47	3.27	4.83	3.36
Cs^+	1.67	2.94	4.26	3.10

TABLE II

COMPARISON OF THEORETICAL AND EXPERIMENTAL HYDRATION ENERGIES FOR THE ALKALI EARTH IONS

The notation is as for Table I.

Ion	r_p	U_{exp}	U_B	U_{TH}
Mg^{2+}	0.65	19.69	43.73	17.68
Ca^{2+}	0.99	16.45	28.71	14.94
Sr^{2+}	1.13	14.73	25.16	14.08
Ba^{2+}	1.35	13.61	21.06	12.93

author[7] gave a rather better fit with experiment. However they depended on scaling up the Pauling radius by a multiplicative factor rather than an additive factor. The use of an additive factor however seems physically more reasonable. Buckingham[5] and Ross[8] have both given some account of previous attacks on this problem and reference should be made to their papers. Even the most refined calculations have always been based on certain *ad hoc* assumptions about the values of the parameters to be employed. Thus, until a really complete theory of this subject is worked out, there seems some value in having available a simple theory such as the one presented here which leads to reasonably accurate results and could readily be extended to materials other than water.

APPLICATION TO MEMBRANE THEORY

It is evident that the relative "hydration energies" of an ionic species in water and in the material which surrounds membrane pores have a critical effect on the permeability of the membrane to that particular species[1]. Elsewhere the present author[7] has suggested that the negative resistance characteristics shown by excitable membranes could be explained by the assumption that the "hydration" energies of ions in the membrane are dependent on the electric potential across the membrane. Such a situation could be brought about if the material surrounding the pores was ferroelectric. Experimental work now being carried out by the author points to the probability of certain proteins being ferroelectrics. An understanding of their interaction with ions is beyond the scope of the present paper. However the theory outlined here should be applicable to non excitable membranes. The following conclusions then appear

(1) The effective ionic radius of cations should be taken to be about 0.6 Å larger than the Pauling radius when hydration effects are considered.

(2) The saturation effect is important for small monovalent ions and for divalent ions. It can be characterised by one additional parameter r_c which depends on P_m (this assertion supposes an isotropic material). In order to calculate the relative hydration energies of ions in water and in various biological materials one must know not only the values of κ but also of κ_h and P_m for these materials.

(3) It thus seems important to carry out both theoretical and experimental studies of dielectric saturation effects in biological materials. Experiments must be carried out at a sufficient level of humidity so that damage to the structure is avoided. At the present time no studies of this type appear to have been carried out and published. The only theoretical study of which the author is aware is the examination of the polarisability of the hydrogen bond made by Janoschek *et al.*[9].

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