

Energy of an Ion crossing a Low Dielectric Membrane : Solutions to Four Relevant Electrostatic Problems

by

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The influences on ion energy of membrane thickness, ion-pair formation, "pores" and "carriers" have been estimated. Only "pores" and "carriers" lower the energy barrier significantly.

THE cell membrane has been pictured as a region of low polarizability acting as a barrier to the passage of solute material between two aqueous solutions^{1,2}. Models of real membranes³ and of artificial bilayer membranes⁴⁻⁶ describe a thin (40-100 Å) hydrocarbon layer dividing media containing proteins and water soluble material. The energy required to put ionic particles into an oil phase suggests that such membranes will show great resistance to ion flow⁷. Indeed the specific resistance of artificial membranes can be as high as $10^8 \Omega \text{ cm}^{-2}$ (ref. 8). In cases of lower resistances the energy barrier presented by the membrane to the ion is reduced. Addition of tiny amounts of certain small neutral cyclic peptides can lower this ionic resistance by a factor of one million⁹⁻¹¹. Reason for this lowering must be found in terms of alteration of the membrane model structure or of the ion membrane interaction.

The leading term in the energy of a charge in a given medium is the "self energy" or "energy of charging". It depends on charge magnitude, e , and particle size as well as the structure and polarizability of the surrounding medium. For a spherical conducting charge of radius a in an infinite medium of dielectric constant ϵ the self energy will formally be $e^2/2\epsilon a$, the Born charging energy¹². For e =electronic charge the difference in this quantity between aqueous medium ($\epsilon_w \approx 80$) and hydrocarbon ($\epsilon_{hc} \approx 2$) will be in tens of kcalories/mole for ion-size particles.

Several factors have been suggested that might lower the energy estimated from $e^2/2\epsilon a$ for an ion crossing a low dielectric membrane. They are considered here. (a) The membrane is actually a region of finite thickness, not an infinite medium. (b) The ion may be next to another small ion of opposite sign and the charges in the "ion-pair" will cancel. (c) The membrane may have high dielectric "pores" through which the ion can pass. (d) The ion may be wrapped in a neutral molecule or "carrier" of high polarizability which tends to solvate it (increase effective radius a) in the low dielectric medium.

What is being calculated here is the decrease in the electrostatic self energy of a single ion when it is not in a uniform infinite medium. Neither of the first two schemes appreciably lowers the energy required to enter the membrane. The "pore" and "carrier" pictures give a substantially lower energy. The "pore" energy is less than that of the "carrier", however, by an energy which is large compared with the energies stabilizing lipid aggregates. It is possible that the membrane deforms under the influence of electrostrictive forces at the point of ion crossing (in association with a small protein molecule) and the "carrier" material may also be a "pore" through the thinned point. This kind of shape transition when an ion is associated with membrane is easily visualized in terms of electrostrictive forces and helps to blur the artificial distinction between "pores" and "carriers" that plague empirical explanations of ion transport.

The Model

For simplicity and clarity I have used a continuum dielectric model. A more detailed molecular picture is desirable but unnecessary for the limited conclusions drawn here; further, it would depend on unavailable knowledge of molecular organization in the membrane. The membrane pictured in Fig. 1 is a planar slab of thickness l and dielectric constant ϵ_{hc} bounded on two sides by semi-infinite regions of dielectric constant ϵ_w .

Results of calculations are as follows.

(a) The finite thickness l of the membrane material of dielectric ϵ_{hc} will cause a lowering of the self energy because of the presence of high dielectric material ϵ_w outside. For an ion at the centre of such a dielectric slab the energy is less by

$$\frac{e^2}{\epsilon_{hc} l} \ln \left(\frac{2\epsilon_w}{\epsilon_w + \epsilon_{hc}} \right)$$

from that in bulk hydrocarbon.

Because $\epsilon_w \gg \epsilon_{hc}$ this change is $\approx -\frac{c^2}{\epsilon_{hc} l} \ln 2$. Using $c^2/2\epsilon_{hc} a$ as an estimate for the energy in an infinite medium, the effect of finite l is

$$1.39 \frac{a}{l} \approx 1.4 \left(\frac{\text{charge radius}}{\text{membrane thickness}} \right)$$

and is negligible for a membrane 40-100 Å across.

(b) "Charge-pairing" between contiguous spheres also will not make a great difference as long as the interaction between positive and negative charges is ionic. The

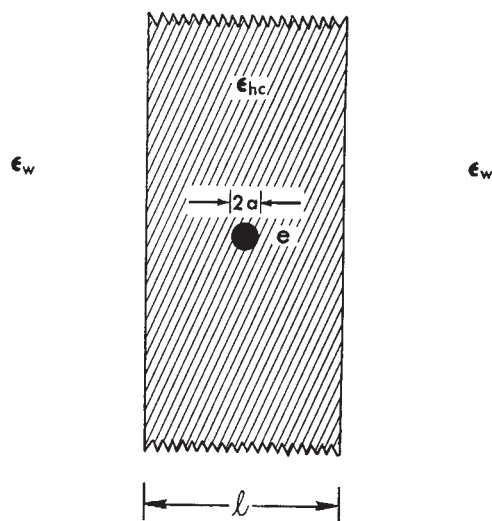


Fig. 1. Ion in centre of dielectric slab.

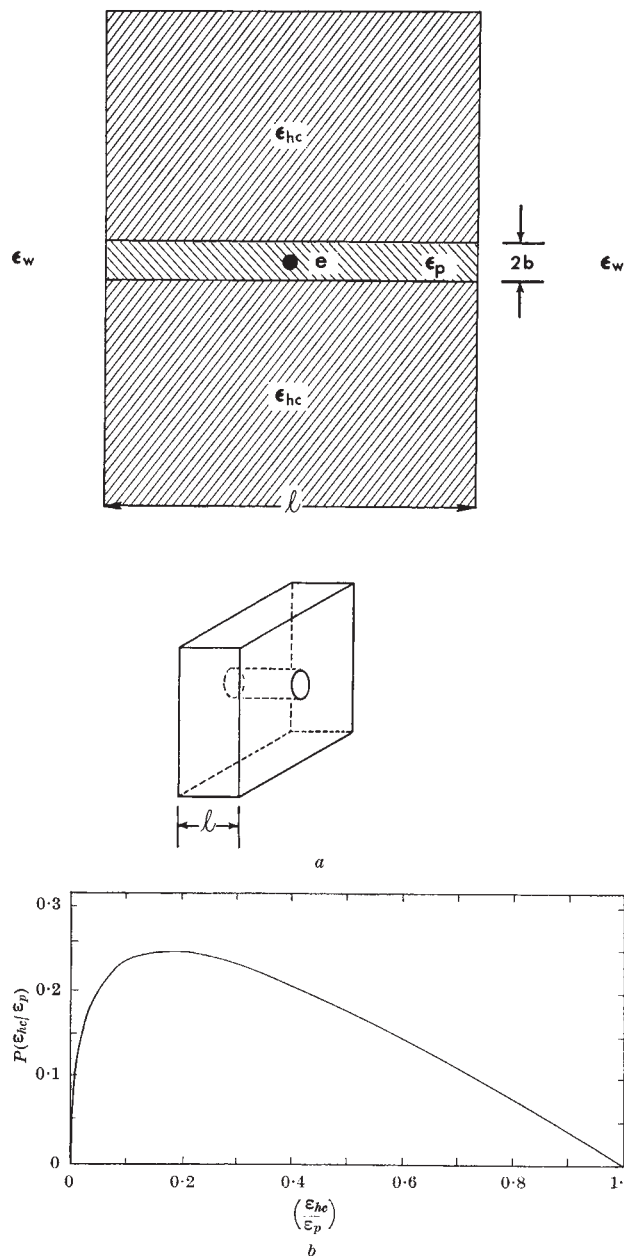


Fig. 2. a, Ion in centre of cylindrical "pore"; b, plot of $P(\epsilon_{hc}/\epsilon_p)$ against $(\epsilon_{hc}/\epsilon_p)$.

electrostatic energy of two particles of radii a_+ and a_- separated by a distance d is

$$E_{+-} = \frac{e^2}{2\epsilon a_+} + \frac{e^2}{2\epsilon a_-} - \frac{e^2}{\epsilon d}$$

where $d \geq (a_+ + a_-)$. For minimum energy take $d = a_+ + a_-$. Then

$$E_{+-} = \frac{e^2}{2\epsilon} \left(\frac{1}{a_+} + \frac{1}{a_-} - \frac{2}{a_+ + a_-} \right)$$

For equal size charges $a_+ = a_- = a$, $E_{+-} = \frac{e^2}{2\epsilon a}$ and is still equal to the energy of a single charge. For $a_+ \gg a_-$, $E_{+-} \geq \frac{e^2}{2\epsilon a_-}$ which is the greater of the original self energies at infinite separation.

Only if there is a covalent association between charged particles will the electric fields around them be reduced sufficiently to be energetically unimportant. This would

be tantamount to discharging the two associated particles. The requirements for such an association are rather stringent and unlikely to be met by strong electrolytes which form ionic crystals in vacuum.

(c) "Pores" of high polarizability, filled with protein or water, through the low dielectric membrane can significantly lower the energy of a charge and possibly permit its passage through the membrane. In addition to direct interaction of the ion with the "pore" material, there is charge induced on the boundary between "pore" and membrane material which gives an additional, positive term to the self energy.

Consider a cylindrical "pore" of polarizability ϵ_p and radius $b \ll l =$ thickness of the membrane (Fig. 2a). With a membrane dielectric constant ϵ_{hc} the self energy of a charge will be the bulk term plus the induced energy

$$E_p = \frac{e^2}{2\epsilon_p a} + \frac{e^2}{\epsilon_{hc} b} P\left(\frac{\epsilon_{hc}}{\epsilon_p}\right)$$

where a is the ion radius (derived from ref. 13). The function $P(\epsilon_{hc}/\epsilon_p)$ is calculated numerically and plotted in Fig. 2b. The induced charge term is inversely proportional to "pore" radius b and that $P(\epsilon_{hc}/\epsilon_p)$ has a maximum value less than 1/4.

If, for example, the value of ϵ_p is comparable with that of water outside the membrane (≈ 80), then the barrier posed to an ion will be due simply to the second term in E_p . For $\epsilon_{hc} = 2$ this will be

$$\frac{e^2}{2b} P(1/40) = \frac{28.36}{b} \frac{\text{kcalories}}{\text{mole}}$$

when b is measured in \AA .

A charge lined water filled "pore" which forms an internal double layer will further lower the energy for the mobile counterions¹⁴. These interactions will be in addition to the dielectric aspects considered here.

(d) A "carrier" in the present model is simply a neutral molecule of high polarizability that can form a spherical complex (possibly including water) with the ion inside. This local "solvation" of the charge is expected to lower its energy in the hydrocarbon region. For an outer radius b of the entire complex (see Fig. 3) its energy in the medium ϵ_{hc} will be

$$E_c = \frac{e^2}{2\epsilon_{hc} b} + \frac{e^2}{2\epsilon_c} \left(\frac{1}{a} - \frac{1}{b} \right)$$

where again a is the original radius of the ion. The second

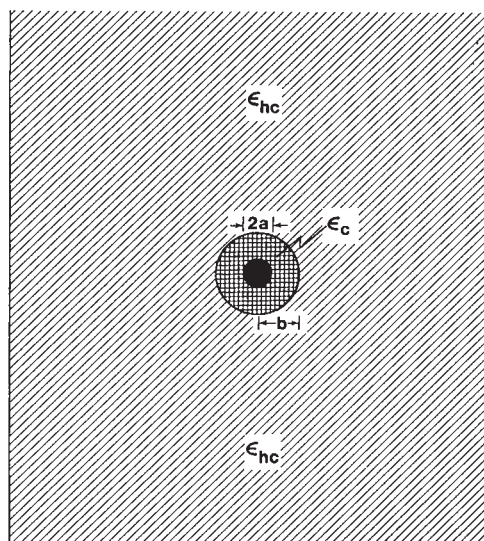


Fig. 3. Ion in centre of spherical "carrier".

term is a macroscopic but convenient form for the contribution to the energy of the ion by an effective carrier polarizability $\epsilon_c > 1$. If the jacket material is infinitely polarizable then $\epsilon_c \rightarrow \infty$ and the self energy of the complex is at a minimum, $e^2/2\epsilon_{hc}b$. In this best of all cases the energy E_c is still appreciable compared with thermal energy but much less than that for a bare ion. For example, in that case with $\epsilon_{hc}=2$, $b=5-10$ Å, E_c will be 16.5-8.2 kcalories/mole or 9.8-4.9 kT/ion at 25°C.

Fig. 4 summarizes these calculations for a charged particle of radius $a=2$ Å. Values used for ϵ_{hc} and ϵ_p are 2 and 80 respectively, membrane thickness is 70 Å, and radii of cylindrical and spherical structures are both 5 Å. These are credible values for these hypothetical models^{5,6,15}; consequences of other assumed numbers can be easily calculated from the formulae given here. Note again that cases (c) "pore" and (d) "carrier" give energies much lower than (a) thin membrane and (b) charge-pair. One can thus probably rule out models (a) and (b) for ion transport across low dielectric membranes on electrostatic grounds.

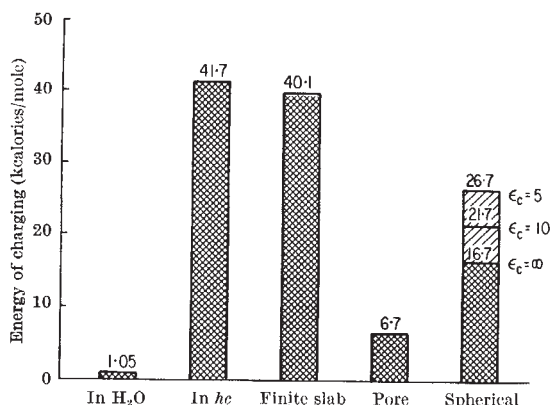


Fig. 4. Illustrative values of energies calculated here.

To consider models (c) and (d) further, examine the difference in energy ($E_{\text{carrier}} - E_{\text{pore}}$)

$$E_c - E_p \approx \frac{e^2}{\epsilon_{hc}b} \left[\frac{1}{2} - P \left(\frac{\epsilon_{hc}}{\epsilon_p} \right) \right]$$

in the case where sphere and cylinder have the same radius b and hypothetical polarizability ($\epsilon_p = \epsilon_c \gg \epsilon_{hc}$). This difference then measures the importance of shape of the hydrocarbon-high dielectric boundary. Because $P(\epsilon_{hc}/\epsilon_p) < 1/4$ (Fig. 2b),

$$(E_c - E_p) \gtrsim \frac{e^2}{4\epsilon_{hc}b} = \frac{83}{\epsilon_{hc}b} \text{ kcalories/mole}$$

With $\epsilon_{hc}=2$, $b=5$ Å, for example, this is $\gtrsim 8$ kcalories/mole (actually equal to 10 kcalories/mole (Fig. 4)).

The inequality $E_c > E_p$ is not an argument for the likelihood of a "pore" mechanism; the energy required to form these two structures has not been considered here. Nevertheless this difference is comparable with the electrostatic and interfacial energies that suffice to explain phase transitions in liquid crystal phases of mixtures of lipid and water¹⁶.

Given an electrostatic self energy gain of more than 8 kcalories/mole by forming a pore, a membrane may well thin out at the point where an ion is forced across it by an applied electric field. Should the ion also be in association with a "carrier" the thinning out is such as to let the "carrier" be indistinguishable from a "pore" or bridge across the membrane. Fig. 5 is drawn simply as an illustration of the electrostrictive forces due to the field about a charged particle, at the centre of a low dielectric

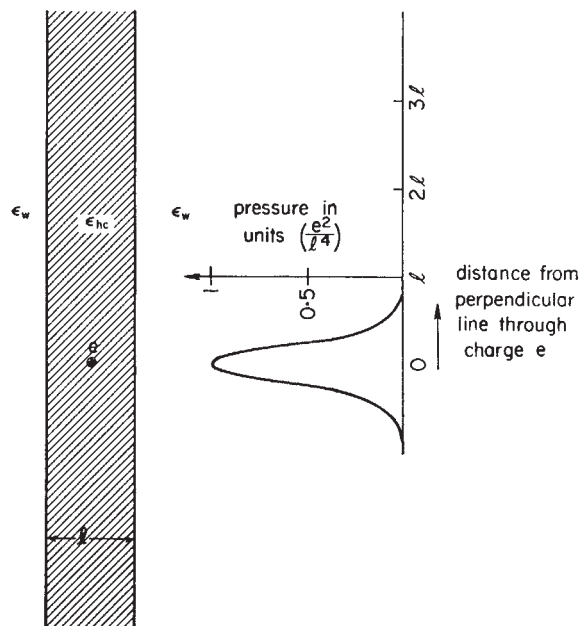


Fig. 5. The electrostrictive pressure due to a charge e at the centre of a slab of thickness l . The force is to pinch the slab about a line perpendicular to the slab and through the charge. The pressure curve is drawn for $\epsilon_{hc}=2$ and $\epsilon_w=80$; for $e=4.8 \times 10^{-19}$ statcoulombs (monovalent ion) and $l=70$ Å, $e^2/l^4=9.58 \times 10^6$ dynes/cm²=0.95 atmospheres. The force increases rapidly with decrease in l and with proximity of e to either surface of the slab.

slab (as in Fig. 1). Note that this pressure is focused over a small area of interface and for thin membranes can have a value of the order of atmospheres. If the charge is near a dielectric interface, forces will be much larger than those given in the illustration.

There have recently been some models proposed for changes in membrane structure when associated with ions¹⁷⁻¹⁹. These have been based formally on the principles of ligand formation and counterion association. The present calculations have examined the interaction of ion with membrane as a problem in dielectrics. It would be surprising if the simple thin film models used here represented the actual cell in membrane structure. Still, these models are useful as examples for calculation of ion-dielectric interaction. It is now clear that these electrostatic forces are strong on the scale of molecular interactions stabilizing a membrane. Electrostrictive forces may deform the membrane to effect transient changes in membrane permeability during flow of ions across it.

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