THE THEORY OF MEMBRANE EQUILIBRIA[1]

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In 1890 Wilhelm Ostwald (1) drew attention to the peculiar electrical and other effects which must occur in a system in which two solutions containing electrolytes are separated by a membrane which is freely permeable to most of the ions, but impermeable to at least one of them. It is a curious fact that the interesting ionic equilibria and potential differences which must occur in such a system, and which provide a very striking proof of the existence of ionization in solution, were not more fully investigated at an early stage in the development of the theory of Arrhenius.

In 1911 the author in collaboration with Harris (2) noticed the occurrence of these peculiar ionic equilibria during the course of an investigation of the osmotic pressure of aqueous solutions of Congo red. As the equilibrium equations resulting from the second law of thermodynamics are extremely simple if we assume that the electrolytes are completely ionized and that the ions act like ideal solutes, a statement of these approximate equations in a number of typical cases was given by the author (3). The exact equations can, however, be stated only in terms of the chemical potentials of Willard Gibbs, or of the ion activities or ionic activity-coefficients of G. N. Lewis. Indeed an accurate experimental study of the equilibria produced by ionically semi-permeable membranes may prove to be of value in the investigation of ionic activity coefficients.

It must therefore be understood that, if in the following pages ionic concentrations and not ionic activities are used, this is done in order to present a simple, though only approximate,

statement of the fundamental relationships. A good idea of the nature of the phenomena in question may be obtained by considering a very simple case. Let us suppose that a membrane M separates two solutions (1) and (2) of equal and constant volume containing initially only the salts NaA and KA respectively, the membrane being permeable to the sodium and potassium ions but not to the anion A. Evidently the ions Na and K can exchange places by means of diffusion across the membrane, but this exchange is subject to the restraint condition of equimolar quantities. The whole system is therefore subject to two conditions of restraint. At first sight one might be inclined to think that the interchange of sodium and potassium ions would proceed until these ions were equally distributed throughout the whole volume of solution. This would occur if the membrane were permeable also to the ion A; but that it will not generally occur in the present case can be readily seen. We may (assuming complete ionization) represent the initial and final states as follows:

$$M$$

Initial	c_1 Na$^+$	K$^+$ c_2
	c_1 A$^-$	A$^-$ c_2
	(1)	(2)

Equilibrium	$c_1 - x$ Na$^+$	Na$^+$ x
	x K$^+$	K$^+$ $c_2 - x$
	c_1 A$^-$	A$^-$ c_2

If F denote the free energy of the system, then the equilibrium state is characterized by the condition $(\delta F)_{p,t} = 0$. Consider the variation

$$\delta n \text{ mols } \text{Na}^+ \ (1) \ \rightarrow \ (2)$$
$$\delta n \text{ mols } \text{K}^+ \ (2) \ \rightarrow \ (1)$$
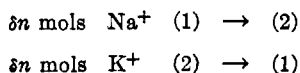
Electrical work terms vanish, and we have simply

$$\delta F = RT \left\{ \delta n \, \log \frac{[Na^+]_1}{[Na^+]_2} + \delta n \, \log \frac{[K^+]_2}{[K^+]_1} \right\} = 0$$
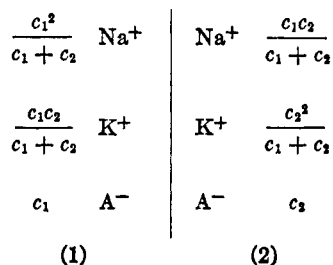
so that

$$\frac{[Na^+]_1}{[K^+]_1} = \frac{[Na^+]_2}{[K^+]_2}$$

Thus

$$\frac{c_1 - x}{x} = \frac{x}{c_2 - x}, \quad x = \frac{c_1 c_2}{c_1 + c_2}$$

The equilibrium state of the system is therefore:

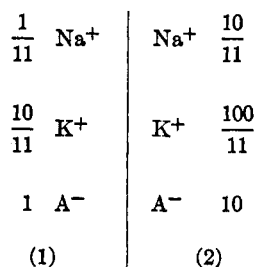|			
$\dfrac{c_1{}^2}{c_1 + c_2}$ Na$^+$		Na$^+$	$\dfrac{c_1 c_2}{c_1 + c_2}$
$\dfrac{c_1 c_2}{c_1 + c_2}$ K$^+$		K$^+$	$\dfrac{c_2{}^2}{c_1 + c_2}$
c_1 A$^-$		A$^-$	c_2
(1)		(2)	

$$\frac{[Na^+]_1}{[K^+]_1} = \frac{[Na^+]_2}{[K^+]_2} = \frac{c_1}{c_2}$$

Thus only when $c_1 = c_2$ is it true that for equilibrium

$$[Na^+]_1 = [K^+]_1 \text{ and } [Na^+]_2 = [K^+]_2$$

Suppose $c_1 = 1$, $c_2 = 10$. Then the equilibrium state is:

$\dfrac{1}{11}$ Na$^+$		Na$^+$	$\dfrac{10}{11}$
$\dfrac{10}{11}$ K$^+$		K$^+$	$\dfrac{100}{11}$
1 A$^-$		A$^-$	10
(1)		(2)	

In other words, 9.1 per cent of the potassium ions originally present in (2) diffuse to (1), while 90.9 per cent of the sodium

ions originally present in (1) diffuse to (2). Thus the fall of a relatively small percentage of the potassium ions down a concentration gradient is sufficient in this case to pull a very high percentage of the sodium ions up a concentration gradient. The equilibrium state represents the simplest possible case of two electrically interlocked and balanced diffusion-gradients. These ionic exchange equilibria have been experimentally investigated (4) in the case of the ferrocyanides of sodium and potassium separated by a membrane of copper ferrocyanide gel supported in the pores of a sheet of parchment paper. The concentration ratios at equilibrium were found to be in fair agreement with the simple theory sketched above. The same result was obtained in the equilibrium between sodium caseinate and potassium caseinate across a membrane of parchment paper.[2]

A very interesting case occurs when the valencies of the two exchanging ions are unequal. Thus suppose we substitute the divalent calcium ion for the potassium ion: the second restraint condition (equivalent inter-diffusion) requires that for every calcium ion passing from (2) to (1) *two* sodium ions must simultaneously diffuse from (1) to (2). Hence

$$\delta F = RT \left\{ \delta n \; 2 \log \frac{[Na^+]_1}{[Na^+]_2} + \delta n \log \frac{[Ca^{++}]_2}{[Ca^{++}]_1} \right\} = 0$$
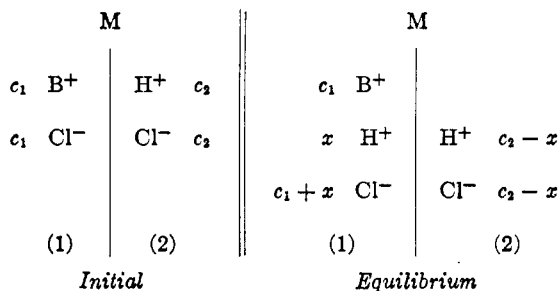
or

$$\frac{[Ca^{++}]_1}{[Na^+]_1{}^2} = \frac{[Ca^{++}]_2}{[Na^+]_2{}^2}$$

or

$$\frac{[Ca^{++}]_1}{[Ca^{++}]_2} = \left\{ \frac{[Na^+]_1}{[Na^+]_2} \right\}^2$$

This relationship has been tested (4) in the case of solutions of the ferrocyanides of sodium and calcium separated by a copper-ferrocyanide gel membrane, and found to be in fair agreement with the facts.

[2] Unpublished results.

Returning to the case of NaA and KA, let us consider the single variation

$$\delta n \text{ mols } K^+ \ (2) \ \longrightarrow \ (1)$$

If there existed no electrical potential gradient across the membrane, this would lead to the equation of equilibrium $[K^+]_1 = [K^+]_2$, which is contrary to the experimentally ascertained facts. A potential difference ϵ must therefore exist between solutions (1) and (2). If ϵ denote the excess of the positive potential of solution (1) above that of (2), the variational criterion of equilibrium now becomes

$$\delta n \ RT \log \frac{[K^+]_2}{[K^+]_1} - F \ \delta n \ \epsilon = 0$$

or

$$\epsilon = \frac{RT}{F} \log \lambda$$

where

$$\frac{[K^+]_2}{[K^+]_1} = \frac{[Na^+]_2}{[Na^+]_1} = \lambda$$

This relationship has been experimentally tested (5) in the simpler case of two solutions of potassium ferrocyanide of unequal concentrations separated by a copper ferrocyanide membrane. The experimental results were in fair agreement with the theory.

Such a membrane must produce a concentration polarization on the passage of an electrical current. Thus considering the two layers of solution on either side of the membrane and the passage of $1F$ of positive electricity from (2) to (1):

As a result (2) loses $(1-n)$KA and (1) gains an equal amount. The stationary state will be reached when the rates of change of concentration produced by the current are balanced by diffusion. This simple state of affairs may, however, be complicated by other actions, such as streaming effects due to inequalities of density, precipitations, electrostenolysis, etc. (compare Ostwald, loc. cit.).

Another interesting case of ionic equilibria across a semipermeable membrane arises when the system contains two electrolytes with a common ion, the non-dialyzing ion being, however, one of the other ions (whether cation or anion). Suppose, for example, we have the chlorides BCl and HCl, the membrane being freely permeable to H^+ and Cl^- but not to B^+. Considering equal volumes and complete ionization, the initial and equilibrium states may be represented thus:

		M				M		
c_1	B^+		H^+	c_2	c_1	B^+		
c_1	Cl^-		Cl^-	c_2	x	H^+		H^+ $c_2 - x$
					$c_1 + x$	Cl^-		Cl^- $c_2 - x$
	(1)		(2)			(1)		(2)
	Initial					*Equilibrium*		

The variation δn mols H^+ (2)$\rightarrow$(1), δn mols Cl^- (2)$\rightarrow$(1) gives for the equilibrium state $[H^+]_1 \cdot [Cl^-]_1 = [H^+]_2 \cdot [Cl^-]_2$ so that $x(c_1 + x) = (c_2 - x)^2$, whence $x = \dfrac{c_2^2}{c_1 + 2c_2}$. The equilibrium state is therefore:

c_1 B^+Cl^-	
$c_2 \cdot \dfrac{c_2}{c_1 + 2c_2}$ H^+Cl^-	H^+Cl^- $(c_1 + c_2) \cdot \dfrac{c_2}{c_1 + 2c_2}$
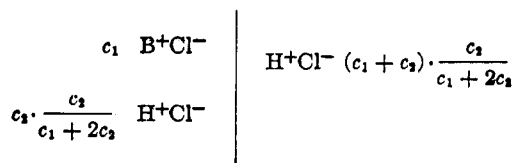
Thus

$$\frac{[H^+]_2}{[H^+]_1} = \frac{[H^+Cl^-]_2}{[H^+Cl^-]_1} = 1 + \frac{c_1}{c_2}$$

If c_1 be large compared with c_2 the expression $1 + \dfrac{c_1}{c_2}$ will be much greater than unity. The peculiarity of this equilibrium is therefore that the presence of the ionized salt BCl with the non-diffusible cation B^+ acts so as to hinder the diffusion of hydrochloric acid to the side where BCl occurs, or conversely to expel hydrochloric acid to the other side. The inequality of the ionic concentrations on either side shows that an electrical potential difference must exist across the membrane. Considering either of the single variations

$$\delta n \text{ mols } H^+ \ (2) \longrightarrow (1), \ \delta n \text{ mols } Cl^- \ (2) \longrightarrow (1)$$
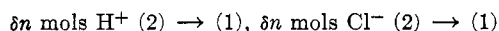
and calling ϵ the excess of the positive potential of (1) over that of (2), it follows that

$$\epsilon = \frac{RT}{F} \log \frac{[H^+]_2}{[H^+]_1} = \frac{RT}{F} \log \frac{[Cl^-]_1}{[Cl^-]_2} = \frac{RT}{F} \log \left(1 + \frac{c_1}{c_2} \right)$$

If we keep c_1 constant and increase c_2 both the ratio of unequal distribution of acid and the membrane P.D. will diminish, approaching unity and zero respectively in the limit. Similar phenomena will occur in the case of BCl and NaCl (or KCl), or in the case of NaA and NaCl (where A^- is a non-diffusible anion). If any of the diffusible ions possess different valencies, the equations given above must be modified in a manner which will be evident to the reader.

These unequal distributions have been investigated in the cases of Congo red and sodium chloride (2), potassium chloride and potassium ferrocyanide (6), sodium caseinate and sodium chloride.[3] In the latter case a fair agreement between theory and experiment is obtained if the sodium chloride be assumed to be completely ionized and if Pauli's values for the ionization of the caseinate be adopted. It will be noticed that in the case of such ionic equilibria the effect of the unequal distribution of

[3] Unpublished results.

the diffusible electrolyte will be to produce an osmotic pressure acting counter to that of the non-diffusible electrolyte. Thus in the example discussed above, the O.P. of BCl will be (assuming ideal ionic behavior) $2RTc_1$. The counter O.P. due to the unequal distribution of HCl =

$$2RT\frac{c_1c_2}{c_1 + 2c_2}$$

The *apparent* O.P. of the BCl will therefore be

$$2RTc_1 \frac{c_1 + c_2}{\cdot c_1 + 2c_2}$$

If c_2 be large compared to c_1, the apparent O.P. of the BCl will be approximately equal to RTc_1. A high value of the ratio $\frac{c_2}{c_1}$ will therefore *appear* to repress completely the ionization of the salt BCl, even though both c_1 and c_2 are individually small. Thus if B were a "colloidal" cation (or ionic micelle) of molecular weight, say, 5000, then for a 1 per cent solution of BCl c_1 = 0.002 molar approximately. If c_2 = 0.02, the apparent osmotic pressure of BCl would be only 5 per cent greater than the value corresponding to zero ionization.

It is worthy of remark that these ionic equilibria may be treated from the standpoint of the second law of thermodynamics in another manner. Thus in the case last dealt with, suppose reversible hydrogen electrodes be placed in both (1) and (2). If the system be in true equilibrium, the total e.m.f. will be zero, and therefore the membrane P.D. must be equal to

$$\frac{RT}{F} \log \frac{[H^+]_2}{[H^+]_1}$$

A similar consideration of reversible chlorine electrodes leads to the value

$$\frac{RT}{F} \log \frac{[Cl^-]_1}{[Cl^-]_2}$$

Hence

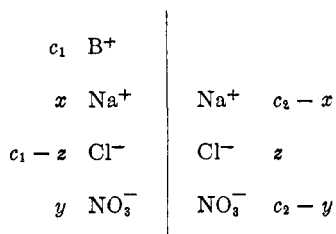$$[H^+]_1 \cdot [Cl^-]_1 = [H^+]_2 \cdot [Cl^-]_2$$

The two methods rest, of course, on the same basis, namely, the second law and the assumption that the system is in equilibrium. The primary condition of constraint assumed in the preceding discussion will be satisfied if for the semi-permeable membrane there be substituted an immiscible liquid layer which dissolves one of the electrolytes but not the other. It is easy to show that in this case the sum of the two "phase-interface potential differences" is equal to the value calculated above for the total difference of potential ϵ between the two aqueous solutions (7). Whether we deal with semi-permeable gel membranes or with layers of a very slightly miscible liquid, the condition of non-permeability may not be always an absolute one, i.e., the "non-permeable" electrolyte may be very slowly diffusing through the separating barrier. In such cases the true equilibrium state may be practically attained if the speed of diffusion of the "diffusible" ions be very great in comparison.

The simple principles indicated in the preceding discussion may be easily applied to systems containing any number of different and diffusible ions. Suppose for example that we have present besides BCl an electrolyte with no ion in common, e.g., $NaNO_3$. The initial state is:

$$c_1 \ B^+ \quad \bigg| \quad Na^+ \ c_2$$
$$c_1 \ Cl^- \quad \bigg| \quad NO_3^- \ c_2$$
$$(1) \qquad \bigg| \qquad (2)$$
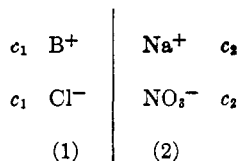
At first sight we might be led to suppose that in this case the sodium nitrate would distribute itself equally in the two equal volumes. Such a supposition neglects the fact that the system we are now considering possesses *both* the types of ionic interchange previously considered, since although Na^+ can pass from (2) to (1) only in company with a negative ion, Cl^- and NO_3^- can interchange without the assistance of Na^+.

The equilibrium state may be represented thus:

$$
\begin{array}{ll|ll}
c_1 & B^+ & & \\
x & Na^+ & Na^+ & c_2 - x \\
c_1 - z & Cl^- & Cl^- & z \\
y & NO_3^- & NO_3^- & c_2 - y
\end{array}
$$

with the condition $x = y - z$.

The equilibrium conditions for the diffusible ions give

$$\frac{[Na^+]_2}{[Na^+]_1} = \frac{[Cl^-]_1}{[Cl^-]_2} = \frac{[NO_3^-]_1}{[NO_3^-]_2} = \lambda$$

Hence

$$\lambda = \frac{[Na^+]_2 + [Cl^-]_1 + [NO_3^-]_1}{[Na^+]_1 + [Cl^-]_2 + [NO_3^-]_2} = \frac{c_2 - x + c_1 - z + y}{x + z + c_2 - y} = 1 + \frac{c_1}{c_2}$$

Thus the deductions as regards membrane P.D. and apparent osmotic pressure of BCl are the same as in the previous case. Solving the equilibrium equations

$$x = y - z$$
$$x(c_1 - z) = z(c_2 - x)$$
$$xy = (c_2 - x)(c_2 - y)$$

we get

$$x = \frac{c_2^2}{c_1 + 2c_2}, \quad y = \frac{c_2(c_1 \cdot c_2)}{c_1 + 2c_2}, \quad z = \frac{c_1 c_2}{c_1 + 2c_2}$$

The osmotic pressure of (1) against (2) $=$

$$2\,RT\,(c_1 - c_2 + 2x) = 2\,RT \cdot c_1 \frac{c_1 + c_2}{c_1 + 2c_2}$$

If c_2 be large compared with c_1, this expression reduces as in the previous case to RTc_1. If we suppose c_1 large compared with c_2, say $c_1 = 10\,c_2$, then $\lambda = 11$ and therefore

$$[Na^+]_2 = 11\,[Na^+]_1$$
$$[Cl^-]_1 = 11\,[Cl^-]_2$$
$$[NO_3^-]_1 = 11\,[NO_3^-]_2$$

Thus most of the sodium ions are prevented from diffusing from (2) into (1), whereas most of the NO^-_3 ions pass from (2) into (1) and only a small percentage of the Cl^- ions from (1) into (2). If the solution (1) inside its separating membrane be frequently dialyzed against fresh sodium nitrate solution and finally against pure water, the B^+Cl^- may be almost completely converted into $B^+NO^-_3$. This sort of action resembles the ionic exchanges which occur in the well-known "Permutite" process of water-softening.

Let us now consider the effect of a diffusible electrolyte with no common ion (e.g., $NaNO_3$) on the unequal distribution of HCl in presence of BCl previously considered.

Initial state			H^+	c_2
	c_1	B^+	Cl^-	c_2
			Na^+	c_3
	c_1	Cl^-	NO_3^+	c_3
		(1)	(2)	
Equilibrium state	c_1	B^+		
	x	H^+	H^+	$c_2 - x$
	$c_1 + w$	Cl^-	Cl^-	$c_2 - w$
	y	Na^+	Na^+	$c_3 - y$
	z	NO_3^-	NO_3^-	$c_3 - z$

with the condition $x + y = w + z$.
The equilibrium conditions give

$$\frac{[H^+]_2}{[H^+]_1} = \frac{[Na^+]_2}{[Na^+]_1} = \frac{[Cl^-]_1}{[Cl^-]_2} = \frac{[NO_3^-]_1}{[NO_3^-]_2} = \lambda$$

Proceeding as in the previous case

$$\lambda = \frac{c_2 + c_3 - (x+y) + c_1 + (w+z)}{(x+y) + c_2 + c_3 - (w+z)} = 1 + \frac{c_1}{c_2 + c_3}$$

Thus, even though c_1 be relatively large in comparison with c_2, a condition which in the absence of $NaNO_3$ would lead to a

very unequal distribution of HCl and a considerable membrane potential, if c_3 be large in comparison with c_1, these effects will be practically annulled (λ not very different from unity).

Interesting types of equilibrium arise when we consider the phenomena of neutralization or hydrolysis across a semi-permeable membrane, and such cases have proved of interest in connection with the physical chemistry of the proteins. Suppose there is present on one side of the membrane a feeble mono-acid base B_0, the membrane being impermeable both to the base and to its cation B^+. Neglecting the ionization of the base, the initial state of the system may be represented thus:

$$c_0 \quad B_0 \quad \bigg| \quad \text{water}$$

$$(1) \quad \bigg| \quad (2)$$
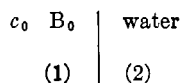
where c_0 denotes the molar concentration of B_0. The osmotic pressure will be RTc_0. If hydrochloric acid be added to the pure water side, H^+ and Cl^- ions will diffuse into (1) and produce a partial neutralization and ionization of B_0, forming B^+Cl^-. This will increase the osmotic pressure of solution (1), but the unequal distribution of the hydrochloric acid will produce a counter osmotic pressure tending to lessen the increase due to the ionization of B_0. The equilibrium state may be represented thus:

$$
\begin{array}{rl|rl}
c_0 - z & B_0 & & \\
z & B^+ & & \\
y & H^+ & H^+ & x \\
y + z & Cl^- & Cl^- & x
\end{array}
$$
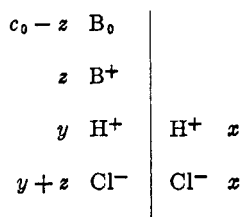
the equation for the membrane equilibrium being therefore

$$x^2 = y(y + z)$$

Also

$$z = \frac{c_0 y}{K + y}$$

where $K = \dfrac{K_w}{K_b}$, K_b being the ionization constant of the base and K_w the ionic product for water. Elimination of z between these equations gives

$$(x^2 - y^2)(K + y) = c_0 y^2 \dots\dots\dots\dots\dots\dots\dots(1)$$

The osmotic pressure P of (1) against (2) is given by

$$P = RT \{2y + z + c_0 - 2x\}$$

which may be written

$$P = RT \frac{(x - y)^2}{y} + RTc_0 \dots\dots\dots\dots\dots\dots\dots(2)$$

Equations (1) and (2) determine P as a function of x and $c^\bullet$ (at the given temperature T).

The first term on the right-hand side in the equation for P depends on the unequal distribution of H^+ ions. It vanishes for $x = 0$, and also tends asymptotically to zero for values of x large in comparison with c_0. Thus P, starting with the value RTc_0, will increase, reach a maximum, and then diminish asymptotically to its original value as x increases. These conclusions depend of course on the assumptions of complete ionization of HCl and BCl and the laws of ideal solutions.

We may arrive at the same conclusions in another way. Calling the expression $(2y + z + c_0 - 2x)$, e,

$$P = RTe$$

From the equations

$$x^2 = y(y + z) \text{ and } 2y + z + c_0 - 2x = e$$

it follows that

$$e = c_0 - 2x + \sqrt{4x^2 + z^2}$$

and hence

$$P = RT\{\sqrt{4x^2 + z^2} - 2x\} + RTc_0$$

When $x = 0$, $z = 0$; and with increasing x, z tends towards the limiting value c_0. Thus both for $x = 0$ and for values of x large in comparison with c, $P = RTc_0$. The variation of the membrane

potential ϵ with increasing x can be followed in a similar manner. If ϵ denotes the excess of the positive potential of solution (1) over that of solution (2), then, since $\dfrac{x^2}{y^2} = 1 + \dfrac{z}{y}$

$$\epsilon = \frac{RT}{F} \log \sqrt{1 + \frac{z}{y}} = \frac{RT}{2F} \log \left(1 + \frac{z}{y}\right)$$

When $x = 0$, $\epsilon = 0$, if we neglect the small ionization of the weak base B_o. As x increases continuously so does y, while z tends towards the finite value c_o. Thus with increasing x ϵ will increase, reach a maximum, and then sink asymptotically to zero.

If B_o be a poly-acid $(n-\text{acid})$ base, the preceding equations for the osmotic pressure of solution (1) against solution (2) become more complex. For values of y corresponding to nearly complete neutralization (ionization) according to the equation

$$B_o + n\text{HCl} = B^{n(+)} + n\text{Cl}^-$$
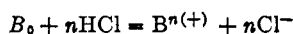
we may represent the equilibrium thus:

y	H^+			
y	Cl^-		H^+	x
$\dfrac{z}{n}$	$B^{n(+)}$		Cl^-	x
z	Cl^-			
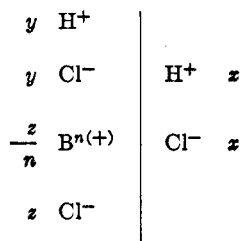
Under these conditions we have

$$P = RT \frac{(x-y)^2}{y} + RT \frac{z}{n}$$

which with increasing x tends towards

$$P = RT \frac{(x-y)^2}{y} + RT c_i$$

If B_o be a substance of very high molecular weight (say a protein molecule or aggregate) the second term in the equations for the osmotic pressure may be relatively small. However,

even though c_0 be small, the final value of $z(= n\ c_0)$ may not be negligible, since n may be large (regarding $B^{n(+)}$ as an "ionic micelle").

Very many interesting investigations based on this simple theory have been made by Jacques Loeb (8) and his collaborators. In this work, among other things, the effects of acids, alkalies and salts on the osmotic pressures and membrane potentials of the amphoteric proteins have been studied. Loeb has shown that the simple theory of membrane equilibria is capable of accounting fairly quantitatively for a great many of his experimental results, and regards this as a proof that the phenomena exhibited by the protein ampholytes are due to simple chemical reactions and not to the adsorption of ions by colloid aggregates or micelles. While this view may be correct in many instances, it is necessary to remember that the theory of membrane equilibria depends simply on two assumptions:

  a. The existence of equilibrium
  b. The existence of *certain constraints* which restrict the free
      diffusion of one or more electrically charged or ionised con-
      stituents

and that the equations which result from the theory will hold equally well whether we have to deal with "colloid units" which have acquired an ionic character (electrical charge) by adsorption of ions, or with simple molecules which have become ionized by the loss or gain of electrons. All that is necessary for the theory is that the simple ionized molecules or the ionic micelles be subject to the same constraint, namely inability to diffuse freely through the membrane. This constraint then imposes a restraint on the equal distribution on both sides of the membrane of other otherwise freely diffusible ions, thus giving rise to the concentration, osmotic, and electrical effects with which the theory deals. Thus, in the type of equilibrium last discussed, it is only necessary to assume that of the Cl^- ions which diffuse from (2) into (1), a certain proportion (of concentration z) are unable to wander freely back and forth because their average total electric charge is balanced by that of constituents which

for some reason or other cannot do so. The adsorption of
certain ions on the surface of a solid wall would provide an
equally effective constraint, and the "binding" of these ions
would impose a restraint on the free diffusion and mobility of
an electrically equivalent amount of oppositely charged ions.
In fact, J. A. Wilson and W. H. Wilson (9) have considered
ionic adsorption equilibria from this point of view.

H. R. Procter (10) and his collaborators have used the theory
of membrane equilibria to account for the effect of acids and
salts on the swelling of gelatine. The gelatine jelly is regarded
by Procter as an elastic structural network of gelatine molecules
into which molecules of water, acid, etc., can diffuse. The
hydrogen ions of the acid react chemically with the gelatin
molecules which thereby become ionized. Although there is
no membrane, the necessary condition of constraint is provided
by the inability of the gelatine ions to leave the structural net-
work owing to the forces of cohesion which hold it together.
This imposes a restraint on the free diffusibility of an equivalent
amount of the anions of the acid, and as a result there is produced
an unequal distribution of hydrogen ions and anions of the acid
between the gelatine jelly phase and the surrounding aqueous
solution, and an increase of the osmotic pressure of the jelly
solution against this external solution (although the gelatine
molecules and ions of the structural net-work make no contri-
bution thereto). On the basis of this theory Proter and Wilson
have been able to account quantitatively for the remarkable
effect of acids in low concenrations in first increasing and then
diminishing the swelling of the gelatine jelly. As in the case
previously discussed, $x^2 = y(y + z)$, and therefore $2y + z$,
the sum of the concentrations of the diffusible ions of the jelly
phase must be greater than $2x$, the sum of the ions of the external
aqueous solution. It is this difference of concentrations which
gives rise to the excess osmotic pressure of the jelly, and hence
the entrance of water into it and consequent swelling. The
osmotic equilibrium must be due to an increased hydrostatic
pressure inside the jelly, so that it is assumed that the stretch-
ing of the molecular net work or frame work gives rise to forces

which produce this increase of internal pressure. The important fact is that at equilibrium the concentration of acid inside the jelly is less than that of the external solution. From the equation $x^2 = y(y + z)$, it follows at once that $y < x$.

It may be remarked that Tolman and Stearn (11) have worked out an alternative theory of these swelling effects, on the assumption of electrical repulsions caused by the formation of electrical double layers due to adsorption of ions at the interfaces of a very fine two-phase structure.

A decision on these matters must await the complete elucidation of the internal physical structure and equilibrium of such jellies, though it may be said that a good deal of modern work lends support to the view taken by Procter. An adsorption of hydrogen ions by colloidal aggregates or micelles (constituting the units of the "molecular" network) would lead to the same constraint condition and the same general equations as the ionization of the amphoteric protein molecules assumed by Procter. The difference between these two points of view may not be very great, since the hydrogen ions may be "bound" in one case by primary and in the other case by secondary chemical forces (valencies). The researches of I. Langmuir on adsorption have thrown a great deal of light on this point.

Procter's theory of the effects of acids, etc., on the swelling of gelatine jellies has been adopted by Loeb (8), who considers that his own experiments are in support of it.

The ionic equilibria, osmotic pressures, and potential differences discussed in the preceding pages may have an interesting bearing on the ionic and other exchanges which take place between living cells or tissues and their circumnatant fluids. In these cases, however, the phenomena may be complicated by the variable permeability of the cell membranes and by many other factors, so that the extremely simple relationships which result from the ideal theory of membrane equilibria as sketched in this paper will represent only a very small part of the associated complex of phenomena which make up the reaction of the cell towards variations of its environment. But in the phenomena of living matter, as in other branches of

science, we can understand the complex only by analyzing it
into its simplest constituents and ascertaining, one by one, the
laws which govern the operation—the action and the equilib-
rium—of these constituent phenomena.   Since many living
cells do exhibit selective permeability as regards ions, it is pos-
sible that ionic exchanges and equilibria of the sort discussed
in this paper may occur between the cell and the external fluid
(12).

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