A Thermodynamic Approach to the Calibration of Ion Selective Membrane Electrodes in the Presence of Interfering Species

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The applicability of ion selective membrane electrodes is often limited by interference effects from species other than that one wishes to monitor. Such effects can be described in terms of an interference potential, E^+, which is the difference in the measured electrode response in the solution of interest minus that which would be observed in a solution where the activity of the species to be studied is the same but which contains no interfering species. Previous work, based on thermodynamic arguments, that identifies the variables that determine E^+ is amplified. This leads to calibration procedures that enable E^+ in an unknown solution to be determined from appropriate measurements using known solutions and also to criteria that must be met for these procedures to apply. In contrast with previous work, no models for equilibria and transport processes in the membrane interior are required. The method is extended to species involved in multiple dissociation equilibria such as polyacids and polyamines.

Introduction

A major goal in the development of ion selective membrane electrodes is to obtain a Nernstian response to changes in the activity in solution of the species one wishes to monitor. This goal is rarely met completely because the electrode response is modified by interference effects from other species. The traditional method of correcting for interference effects is to use the well-known Nikolsky equation[1] or some variant thereof.[2] Unfortunately this approach suffers from two drawbacks. The original equation is inconsistent for ions of different charge,[3] and the derivation is based on assumptions and model considerations that cannot be expected to be generally valid. In particular the conditions under which the Nernst−Planck equations[4] can be expected to hold are unlikely to be met in practice and their application requires knowledge that is not easily obtained about transport processes and equilibria such as ion association in the membrane interior. A recent alternative approach based on ion-extraction equilibria[3] circumvents the difficulties associated with ions whose charges differ. However, this is achieved at the expense of neglecting diffusion potentials and making other assumptions concerning ion pair formation and activity coefficients in the membrane interior. Although these assumptions lead to good agreement between theory and experiment in some cases,[3] it seems unlikely that they are generally valid. Clearly there is a need for an approach to correcting for interference effects that avoids these limitations. The aim of this paper is to provide one.

The treatment that results differs from conventional approaches in two important respects. First, transport processes within the membrane interior are described by applying the general formalism of irreversible thermodynamics, and no attempt is made to model them in detail. As a result the arguments concerned are quite general. Second, splitting the total potential change across the membrane into the sum of phase boundary potentials and a diffusion potential is avoided.

The Interference Potential

It is useful to describe interference effects in terms of an interference potential E^* whose significance may be understood by considering the following three cells where || denotes a liquid junction, all three solutions contain species i and solution II contains interfering species that are absent from solution III but that may be present in reference solution I.

reference electrode	test solution II ϕ_1^{II}	membrane giving Nerstian response to *i*	reference solution I ϕ_1^{I}	reference electrode	cell 1
reference electrode	test solution II ϕ_2^{II}	membrane of interest	reference solution I ϕ_2^{I}	reference electrode	cell 2
reference electrode	test solution III ϕ_3^{III}	membrane of interest	reference solution I ϕ_3^{I}	reference electrode	cell 3

The respective emf's of these cells are given by

$$E_1 = E^0(T,p) + (\phi_1^{I} - \phi_1^{II}) + \phi_{lj} \quad (1a)$$

$$E_2 = E^0(T,p) + (\phi_2^{I} - \phi_2^{II}) + \phi_{lj} \quad (1b)$$

$$E_3 = E^0(T,p) + (\phi_3^{I} - \phi_3^{III}) + \phi'_{lj} \quad (1c)$$

where E^0 is a reference potential that includes the potential differences across phase boundaries and junctions common to all three cells and where ϕ_{lj} and ϕ'_{lj} are the liquid junction potentials between the left-hand reference electrode and solutions II and III, respectively. Equation 1a also applies if the membrane in cell 1 is replaced by two electrodes that give a Nernstian response to species *i* placed back to back.

The interference potential E^* may be defined by

$$E^* = E_2 - E_1 \quad (2)$$

This definition is entirely equivalent to that given previously in ref 5. Clearly, if a membrane giving a Nernstian response to *i* is available, then $E_2 - E_1$ may be measured directly and in

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this case liquid junction effects cancel completely. Since

$$(\phi_1^{\mathrm{I}} - \phi_1^{\mathrm{II}}) = \frac{RT}{\nu_i F} \ln \frac{a_i^{\mathrm{II}}}{a_i^{\mathrm{I}}} \tag{3}$$

it follows that

$$E^* = (\phi_2^{\mathrm{I}} - \phi_2^{\mathrm{II}}) - \frac{RT}{\nu_i F} \ln \frac{a_i^{\mathrm{II}}}{a_i^{\mathrm{I}}} \tag{4}$$

where a_i denotes the activity in solution of species i and the superscript denotes the solution concerned. Hence

$$E_2 = \left(E^0 - \frac{RT}{\nu_i F} \ln a_i^{\mathrm{I}}\right) + E^* + \frac{RT}{\nu_i F} \ln a_i^{\mathrm{II}} + \phi_{\mathrm{lj}} \tag{5}$$

Although there are no interfering species in solution III there may be interfering species in reference solution I, affecting cell 3 but not cell 1, in which case there is an interference potential for cell 3, E_0^*, given by

$$E_0^* = (\phi_3^{\mathrm{I}} - \phi_3^{\mathrm{III}}) - \frac{RT}{\nu_i F} \ln \frac{a_i^{\mathrm{III}}}{a_i^{\mathrm{I}}} \tag{6}$$

so that

$$E_2 - E_3 = \frac{RT}{\nu_i F} \ln \frac{a_i^{\mathrm{II}}}{a_i^{\mathrm{III}}} + (E^* - E_0^*) + (\phi_{\mathrm{lj}} - \phi'_{\mathrm{lj}}) \tag{7}$$

If a_i^{III} and a_i^{II} are both known and $(\phi_{\mathrm{lj}} - \phi'_{\mathrm{lj}})$ is negligibly small, then eq 7 may be used to estimate $(E^* - E_0^*)$ from $(E_2 - E_3)$.

The uncertainties involved in ignoring the final term in eq 7 can be avoided by replacing the left-hand reference electrode in cells 1−3 with an electrode reversible to some species in the test solution other than i. If the species concerned is species c then the expressions for E_1, E_2, and E_3 now contain terms in a_c such that when all activities are combined they refer to electrically neutral combinations of ions. As was pointed out over 60 years ago[6] cells of this kind without liquid junctions are clearly preferable to cells with liquid junctions for accurate thermodynamic studies. Despite this the use of reference electrodes with liquid junctions together with the associated notation remains almost universal in analytical applications of ion selective electrodes such as measurement of pH and will be familiar to most readers. Consequently this viewpoint rather than the more precise alternative is adopted in this paper. The discussion in chapters 3 and 4 of ref 7 indicates that for dilute solutions of inorganic electrolytes the two approaches are not expected to give widely different results so that estimates of $(E^* - E_0^*)$ using eq 7 should agree fairly closely with estimates obtained from cells without liquid junctions. The difference in principle between the two approaches is outlined in Appendix 1.

Deductions from Thermodynamics

In this section the variables on which E^* depends are identified. The arguments involved are an extension of those developed in the second section of ref 5. Within the framework of irreversible thermodynamics these arguments are completely general and are *not* confined to situations where interference effects are small. Consider a membrane separating two electrolyte solutions which contain species i, some interfering species j, k, etc. and other ionic species that are excluded from the membrane. We suppose that the membrane/solution interfaces are sharp and that there are no discontinuities in $\check{\mu}_i$ and $\check{\mu}_j$ on crossing these interfaces. It follows that immediately adjacent to such an interface the membrane phase on one side and the solution phase on the other are effectively at equilibrium even when transport processes across the interface are occurring.

Under steady-state conditions and at constant T and p the entire state of the membrane interior globally and locally is determined by the compositions within the membrane immediately adjacent to the two interfaces. These compositions in turn are fixed by the nature of the solutions separated by the membrane. Moreover this remains true even when changing only one solution alters the conditions in the membrane immediately adjacent to the other solution as a result of altering the distribution of species confined within the membrane.

The dissipation function across the membrane, $T\dot{S}$, is given by[8]

$$T\dot{S} = \sum_{i \neq j} J_j \Delta\check{\mu}_j + J_i \Delta\check{\mu}_i + \sum_{\alpha} J_\alpha \Delta\mu_\alpha \tag{8}$$

where $\Delta\check{\mu}$ denotes the difference in $\check{\mu}$ on the two sides of the membrane, the J terms denote fluxes per unit area, $\dot{S}$ is the rate of entropy production per unit area, and the summations over j and α include all species other than i, charged and uncharged, respectively, that are common to the membrane and either of the solutions it separates. When there is zero current flow across the membrane

$$\sum_{j \neq i} J_j \nu_j + J_i \nu_i = 0 \tag{9}$$

where ν denotes ionic valency including the sign. Consequently

$$T\dot{S} = \sum_{j \neq i} J_j \Delta\theta_j + \sum_{\alpha} J_\alpha \Delta\mu_\alpha \tag{10}$$

where

$$\theta_j = \left(\check{\mu}_j - \frac{\nu_j}{\nu_i}\check{\mu}_i\right) \tag{11}$$

Equation 10 shows that $\dot{S} = 0$ when all $\Delta\theta_j$ and $\Delta\mu_\alpha$ are zero. Under these circumstances, the membrane interior is at equilibrium and we have Donnan equilibrium across it. Thus, when all $\Delta\theta_j$ and $\Delta\mu_\alpha$ are zero we may vary one or both of the solutions keeping their θ_j and μ_α constant without making any difference whatsoever to the membrane interior or to those parts of the membrane immediately adjacent to the membrane/solution interfaces. In other words no part of the membrane interior sees changes in solution composition that leave all θ_j and μ_α unaltered. Similar considerations can be expected to apply under nonequilibrium steady-state conditions. When all ionic species in the bulk solution are also present in significant amounts in the membrane then, at constant T and p, it is no longer possible to vary the solution phase keeping all θ_j and μ_α constant. The above argument still applies, but in this case it has no practical value.

Consider now a membrane separating a test solution II from a reference solution I that is part of an electrode assembly designed to monitor species i. According to ref 5 the interference potential of solution II, E^*, is given by

$$FE^* = \frac{\check{\mu}_i^{\mathrm{I}} - \check{\mu}_i^{\mathrm{II}}}{\nu_i} = \int_{\mathrm{I}}^{\mathrm{II}} \left[\sum_{j \neq i} \frac{t'_j}{\nu_j}\left(\frac{\mathrm{d}\theta_j}{\mathrm{d}x}\right) + \sum_{\alpha} t'_\alpha \left(\frac{\mathrm{d}\mu_\alpha}{\mathrm{d}x}\right)\right] \mathrm{d}x \tag{12}$$

where x denotes a distance coordinate across the membrane. The t_j' and t_α' may be expressed in terms of local phenomenological coefficients in the membrane that are completely determined by its local state. Also the integrals may be taken entirely within the membrane phase provided that the solutions are uniform right up to the membrane surfaces. This will be the case when the solutions are stirred and when mobilities in the solution are much greater than in the membrane.

If solution II is now altered but all θ_j and μ_α remain the same, then according to the above arguments there should be no change whatsoever in the membrane interior. It may be concluded that for a given reference solution I E^* may be regarded as a function of the quantities θ_j^{II} and μ_α^{II}.

Expressing θ_j and μ_α in terms of standard chemical potentials and activities gives

$$\theta_j = \mu_j - \frac{\nu_j}{\nu_i}\mu_i = \mu_j^\theta - \frac{\nu_j}{\nu_i}\mu_i^\theta + RT \ln a_j - \frac{\nu_j}{\nu_i} RT \ln a_i \quad (13a)$$

$$\mu_\alpha = \mu_\alpha^\theta + RT \ln a_\alpha \quad (13b)$$

and it is apparent that at constant T and p E^* is a function of the a_α and the quantities $a_j a_i^{-\nu j/\nu i}$. Moreover, the limiting expressions derived in ref 5 indicate that this remains true in the limit that the activities of j and α approach zero even though θ_j and μ_α decrease indefinitely in this limit.

As has been noted previously these considerations apply equally to symmetrical and asymmetrical membranes. However, the interference potential of an asymmetrical membrane may alter when the solutions on either side of it are switched.

A feature of E^* as defined above and in ref 5 is that it is nonzero when the reference solution I contains interfering species and the test solution does not. In practice it is more convenient to work with an interference potential E^+ that is zero when the test solution contains no interfering species. Let E_0^* denote the value of E^* in systems of this kind. From the above arguments it is apparent that E_0^* depends only on the nature of the reference solution. It now follows from eq 5 that for any given reference solution the dependence of E_2 on a_i^{II} is Nernstian when test solution II contains no interfering species. Consequently

$$E^+ = E^* - E_0^* \quad (14)$$

and it is clear that for a given reference solution E^+ depends on the same variables as E^*.

The interference potential used in ref 9 corresponds to E^+. Since E^* and E^+ differ, the statement in ref 5 that the interference potential defined therein is *entirely* equivalent to that defined in ref 9 is incorrect.

It is of course an approximation to assume that the membrane/solution interface is absolutely sharp. The thickness concerned can be expected to be of the same order as the longer of the two Debye lengths of the solution and membrane phases. In most practical situations this length will be much smaller than the thickness of the membrane but may not be for membranes having very high resistivity where this is due to a low concentration of charged species rather than low ionic mobilities.

Determination of Activities in Solution When Interfering Species Are Present

(a) Single Interfering Species. Suppose that we have an electrode designed to sense species i, which, apart from interference by species j, exhibits a Nernstian response to i and a second electrode, which, apart from interference by i, gives a Nernstian response to j. We now show that if the potentials of both electrodes relative to a reference electrode are measured then from these measurements and suitable calibration graphs obtained from measurements on known solutions the activities of i and j in the unknown solution can be found.

Let E_i and E_j denote the potentials of the two electrodes relative to a suitable reference electrode. Ignoring liquid junction effects we write

$$E_i = E_i^0 + \frac{RT}{\nu_i F} \ln a_i + E_i^+ \quad (15a)$$

$$E_j = E_j^0 + \frac{RT}{\nu_j F} \ln a_j + E_j^+ \quad (15b)$$

where E_i^+ and E_j^+ are interference potentials for the two electrodes concerned. In the absence of interfering species in the test solutions, E_i^+ and E_j^+ are both zero and it is straightforward to determine E_i^0 from the dependence of E_i on a_i in known solutions where interfering species are absent. E_j^0 may be obtained similarly. In the case of interest, at constant T and p, it has been shown in the preceding section that, for a given reference solution, E_i^+ depends on the single variable $a_j a_i^{-\nu j/\nu i}$, which we denote as x. Similarly, E_j^+ depends on the single variable $a_i a_j^{-\nu i/\nu j}$, which is $x^{-\nu_i/\nu_j}$. Since

$$E_i - E_j = E_i^0 - E_j^0 - \frac{RT}{\nu_j F} \ln x + E_i^+ - E_j^+ \quad (16)$$

it follows that $(E_i - E_j)$, which is measurable, also depends only on x.

Let us suppose now that from studies of known solutions we have graphs of E_i^+, E_j^+, and $(E_i - E_j)$ vs x. To determine a_i and a_j for an unknown solution we may proceed as follows.

(1) Measure E_i and E_j and determine $(E_i - E_j)$

(2) Find the value of x corresponding to this value from the graph referred to above. This is the value of x for the unknown solution.

(3) From the graphs referred to above find the E_i^+ and E_j^+ corresponding to this x. These are the values of E_i^+ and E_j^+ for the unknown solution.

(4) Given E_i, E_i^+ for the unknown solution and E_i^0, use eq 15a to obtain a_i. a_j may be found in the same way.

To obtain the information needed to implement the above procedure and to verify that E_i^+, E_j^+ and $(E_i - E_j)$ depend on x only is straightforward.

(1) Plot E_i vs ln a_i at several fixed concentrations of j including $c_j = 0$. Measure E_j for the solutions containing both species. Do the same for species j.

(2) From the results in 1 determine E_i^+ for each measurement and plot E_i^+ vs x. The points for different runs should all lie on the same curve. Treat the E_j^+ data in the same way.

(3) Plot $(E_i - E_j)$ vs x for all measurements where this is possible. Again a single curve should result.

(4) Check that E^0 has not changed during the course of the experiments.

Given that $(E_i - E_j)$ depends only on x it may be more economical to plot E_i^+ and E_j^+ vs $(E_i - E_j)$ and to use these graphs for calibration purposes.

If these procedures fail then either other interfering species are present or steady-state conditions do not apply. Obviously matters are simpler if either E_i or E_j conform to the Nernst equation.

The values of x for known solutions may be calculated using Debye−Huckel theory or some extended form thereof. Some

ambiguity may arise if there is more than one value of x corresponding to a given $(E_i - E_j)$, and it is not obvious that this possibility can be ruled out on a priori grounds.

When a precipitate of the salt formed from i and j is present so that θ_j is constant then E_i^+ is also constant. Hence, the dependence of E_i on a_i should be Nernstian despite interference from j. However a shift in E^0 is to be expected. Such behavior has been reported in ref 10.

(b) Two Interfering Species. When there are two interfering species, j and k, E_i^+ is a function of the variables $a_j a_i^{-\nu j/\nu i}$ and $a_k a_i^{-\nu k/\nu i}$, which we denote as x and y, respectively. However it is evident that we may work instead with the variables x and z where $z = a_j a_k^{-\nu k/\nu j}$. From studies using known solutions one may determine E_i^+ and $(E_i - E_j)$ as a function of x and z and, when electrodes that give a Nernstian response to j and k are available, z for any unknown solution may be obtained easily from measured values of $(E_j - E_k)$. To obtain x for this solution measure its $(E_i - E_j)$ and find the value of x in a known solution that has the same $(E_i - E_j)$ and the same z. The determination of E_i^+ and hence a_i is then straightforward. Evidently this procedure involves much more effort than is required when there is but one interfering species. Difficulties may arise if there is more than one x value corresponding to a given z and $(E_i - E_j)$.

(c) Several Interfering Species. In principle it may be possible to develop general calibration procedures when there are more than two ionic interfering species, but such procedures are probably too elaborate to implement in practice. Nevertheless, interference potentials for known solutions may be measured, and when interference effects are small and additive it may be reasonable to write when solution I contains no interfering species[5]

$$E_i^* = \sum_{j \neq i} A_{ij} a_j a_i^{-\nu j/\nu i} + \sum_{\alpha} A_{i\alpha} a_\alpha \qquad (17)$$

where for a given membrane at constant T and p the A_{ij} and $A_{i\alpha}$ are constants. The conditions under which eq 17 holds, if any, may be checked experimentally, and the constants therein may be measured. When electrodes giving a Nernstian response are available for all interfering species we have

$$E_i - E_j = E_i^0 - E_j^0 + \frac{RT}{\nu_i F} \ln a_i - \frac{RT}{\nu_j F} \ln a_j + E_i^* \qquad (18)$$

which on substitution for E_i^* gives

$$E_i - E_j = E_i^0 - E_j^0 + \frac{RT}{\nu_i F} \ln a_i - \frac{RT}{\nu_j F} \ln a_j + \sum_{j \neq i} A_{ij} a_j a_i^{-\nu j/\nu i} + \sum_{\alpha} A_{i\alpha} a_\alpha \qquad (19)$$

When $E_i^0 - E_j^0$, the A_{ij}, and the $A_{i\alpha}$ are all known and the a_j and a_α are measurable separately, eq 19 relates measured values of $(E_i - E_j)$ to the single unknown a_i. When there is but one solution of this equation the determination of a_i is straightforward. Unfortunately, again, the possibility of multiple solutions cannot be ruled out.

Extension to Species Involved in Dissociation Equilibria

We now discuss how the activities in solution of species involved in more than one dissociation equilibrium may be measured in unknown complex solutions using membrane electrodes given appropriate information about the membrane response in known solutions. Consider a polyacid with ν dissociable groups and let r denote the subspecies or set of subspecies for which r groups are dissociated. Evidently r can have integral values in the range $0-\nu$ inclusive where $r = 0$ denotes the undissociated polyacid. In general, all subspecies can be expected to be present in the membrane and in the solution albeit in some cases at very low levels indeed. When there is effectively only one subspecies present in the membrane and its $r \neq 0$, the membrane should show a Nernstian response to that subspecies. For hydrophobic membranes whose electrical permittivity is much lower than that of water subspecies with lower values of r can be expected to be taken up by the membrane preferentially so that even in solutions of high pH where the polyacid is effectively fully dissociated there may still be significant amounts of partially dissociated species in the membrane. However, the presence therein of undissociated polyacid is unlikely to contribute directly to the interference potential unless its transport number is significant. Hence, for a monobasic acid the membrane is likely to exhibit a Nernstian response to the ionized form. To deal with more complex cases dissociation equilibrium is assumed so that locally

$$\breve{\mu}_r + r\breve{\mu}_{H^+} = \mu_p \qquad (20)$$

for all r where μ_0 is the chemical potential of the undissociated polyacid. Let

$$\theta_r = \breve{\mu}_r - \frac{r}{\nu}\breve{\mu}_\nu \qquad (21)$$

where $\breve{\mu}_\nu$ is the electrochemical potential of fully dissociated polyions.

From eqs 20 and 21 it follows immediately that

$$\theta_r = (1 - r/\nu)\mu_p \qquad (22)$$

If the only species common to the membrane and the solutions it separates are the set $r = 0 \rightarrow \nu$, then taking the fully dissociated form as the species to be sensed we may write the interference potential due to the various other species as

$$E^* = \int_I^{II} \left[\sum_{r=1}^{\nu-1} \frac{t_r}{\nu_r} d\theta_r + t_0 d\mu_p \right] \qquad (23)$$

where t_r and t_0 respectively are the local transport numbers of species r and undissociated polyacid. Substituting for $d\theta_r$ in eq 23 as given by eq 22 gives

$$E^* = \int_I^{II} \frac{t_{H^+}}{\nu} d\mu_p \qquad (24)$$

where t_{H^+} is the local transport number of H^+ ions in the membrane when association in the membrane is treated implicitly so that the only species recognized as common to both the membrane and the solution are H^+ ions and fully dissociated polyions. Consequently the contribution of species $r = 0 \rightarrow (\nu - 1)$ to the interference potential may be considered as arising from the single interfering species H^+. Thus, if E_p and E_{H^+} respectively denote the potentials from a polyion electrode and an H^+ electrode then $(E_p - E_{H^+})$ should depend only on μ_p, and if this dependence can be obtained for known solutions the behavior of μ_p in unknown solutions may be studied. This in turn allows changes in the activities of the various species $r = 1 \rightarrow \nu$ to be determined if separate measurements of a_{H^+} are available. To obtain the activities themselves the dissociation constants of the various equilibria involved or equivalent information is needed. In favorable cases this information may be obtained from studies of known solutions.

The calibration procedures described above cannot be applied unless solutions are available in which the activities of the species one wishes to study are known. Polyacids pose two problems. First, E_p may never exhibit a Nernstian response because interference effects are always present. Second, hydrophobic species are likely to associate at low concentrations so that calculating activities from solution composition even at low concentrations is not feasible. Despite this, as is shown in Appendix 2, provided that it is monotonic, the dependence of $(E_p - E_{H^+})$ on μ_p may be obtained from studies of solutions made up from water, polyacid, and NaOH when electrodes are available that give a Nernstian response to H^+ and Na^+ ions. Also, if we have one solution of this kind for which a_ν is known, then a_ν may be found for any other solution made up of the same ingredients. This enables the calibration procedures described in the preceding section to be implemented and allows unknown solutions to be studied in the same way. However, the methods involved are rather elaborate and may not be very accurate. When there is no solution available for which a_ν is known a priori, a reference solution may be chosen for which $a_\nu = a_\nu^{ref}$. In this case a_ν/a_ν^{ref} may be determined. Since all activities are referred to some reference state the advantages of being able to assign a definite value to a_ν^{ref} are more apparent than real.

Analogous arguments apply to polyamines, to dyes and drugs, and to species such as amino acids that contain more than one kind of dissociable group.

When highly charged aggregates such as ionic micelles are present in solution, it may not be legitimate to ignore changes in liquid junction potentials with solution composition.[11]

Discussion

Interference effects are described conventionally by using the Nikolsky equation.[1] When there is but one interfering species, this equation takes the form

$$E_i = E_i^0 + \frac{RT}{\nu_i F}\ln[a_i + K_{ij}a_j^{\nu i/\nu j}] \qquad (25)$$

Equation 25 may be regarded as defining the selectivity coefficient K_{ij}, which, in general, can be expected to depend on solution composition. Comparing eqs 25 and 15a it is apparent that

$$E_i^+ = \frac{RT}{\nu_i F}\ln\left[1 + K_{ij}\frac{a_j^{\nu i/\nu j}}{a_i}\right] \qquad (26)$$

Since E_i^+ depends only on the variable $(a_j a_i^{-\nu j/\nu i})$, it follows from eq 26 that K_{ij} should also depend only on the same variable. The data required to evaluate this prediction must be equivalent to that obtained by varying a_i (or a_j) at several fixed values of a_j (or a_i). As far as the author is aware, no extensive study of this kind has been reported for any system where significant changes in K_{ij} are likely to occur. Figures 2 of refs 9 and 12 provide some evidence in support of the prediction.

The above discussion has been couched in terms of the interference potential. An alternative approach is to use a matched potential method in which the activities of *i* giving the same measured potential in the presence and absence of interference are compared.[3,13] When liquid junction effects are negligible the relationship between this activity difference and the interference potential E^+ may be obtained from eq 7 by setting $E_2 = E_3$. As is shown in Appendix 1, E^+ is well defined in terms of measurable quantities, and its definition does not involve assumptions about liquid junction potentials. The significance of situations where $E_2 = E_3$ is less clear.

Various explicit expressions for the potential difference across a membrane have been obtained by solving the Nernst−Planck equations.[4] Particular examples involving binary mixtures of mono- and divalent cations are eqs 40 and 41 of ref 3 and eq 14 of ref 14. It is readily established that all three expressions are entirely consistent with the notion that the interference potential is a function of θ_j. The fact that the expressions in ref 3 give good agreement with experiment indicates that the data concerned also conforms to the more general theory described above. Evidently this theory provides a useful means of evaluating expressions for membrane potentials obtained from treatments based on models. In particular, expressions for membrane potentials giving interference potentials that are not functions of the θ_j and the μ_α are inconsistent with the thermodynamic arguments given above and are therefore presumably incorrect.

The main advantage of the procedures described above is that they rely on general considerations whose applicability may be tested without any detailed knowledge concerning the behavior of the membrane interior. Hence no knowledge of such details is required to obtain activities in solution from membrane electrodes. However, detailed information about membrane properties is useful if one wishes to understand their response characteristics and to design membranes for applications where interference effects are minimal. Overall the ideas expressed above offer considerable scope for extending the domain of applicability of ion selective membrane electrodes for the determination of activities in solution. This has important implications for analytical science and especially for thermodynamic studies of multicomponent solutions containing ions. For work of this kind it is obviously desirable to have electrodes that, under the conditions concerned, give a true Nernstian response to the species of interest. Unfortunately, this restricts somewhat the range of species one can study. The treatment described above shows that, in favorable cases, an electrode prone to interference from but one species in the system may be used to obtain thermodynamic information that should be reliable when the calibration procedures outlined above are sound. When the interfering species and the species to which the electrode is designed to respond have the same sign $(E_i - E_j)$ is governed by a ratio of activities so that a wide range of θ_j (or x) may be covered while working in dilute solutions where theoretical expressions for activity coefficients are most reliable. Hence it should be possible to measure the activities of a species such as SO_4^- in the presence of say Cl^- using a membrane electrode prone to some chloride interference. The situation where the sign of the interfering species is opposite to that of interest is more tricky because in this case $(E_i - E_j)$ is governed by a product of concentrations so that there is less scope for calibrating in solutions where activity coefficients can be calculated reliably.

We stress that, in contrast with classical work involving cells with transference, the procedures described above do not require any measurement of membrane transport properties and, for this reason among others, are convenient to implement.

Finally, we note that similar reasoning to that given above can be expected to apply to optode membranes that are allowed to equilibrate with the test solution in contact therewith.

Appendix 1. Liquid Junction Effects

When the left-hand reference electrode in cells 1−3 is replaced by an electrode reversible to species c the following expressions result

$$E_1 = E^{\oplus} + \frac{RT}{\nu_i F}\ln a_i^{\mathrm{II}} - \frac{RT}{\nu_c F}\ln a_c^{\mathrm{II}} \qquad \text{(A1a)}$$

$$E_2 = E^{\oplus} + \frac{RT}{\nu_i F}\ln a_i^{\mathrm{II}} - \frac{RT}{\nu_c F}\ln a_c^{\mathrm{II}} + E^* \qquad \text{(A1b)}$$

$$E_3 = E^{\oplus} + \frac{RT}{\nu_i F}\ln a_i^{\mathrm{III}} - \frac{RT}{\nu_c F}\ln a_c^{\mathrm{III}} + E_0^* \qquad \text{(A1c)}$$

where $E^{\oplus}$ is the same for all three cells and includes the term $-(RT)/(\nu_i F)\ln a_i^{\mathrm{I}}$.

The sums of activity terms in eqs A1a−c refer to electrically neutral combinations of ions. In principle they are measurable and when electrodes giving a Nernstian response to both species are available such measurements are straightforward. When this is not so it may still be possible in some instances to obtain the information required from nonelectrochemical data such as colligative properties or by adopting the procedures outlined in Appendix 2. Data of this kind can be compared with theoretical predictions and provides a basis for the development of empirical expressions[15] that may be applied to systems where direct measurements are unavailable or cannot be made. In contrast the activities that occur in eqs 3−7 cannot be estimated experimentally without making extrathermodynamic assumptions. In dilute solutions they may be calculated using Debye−Huckel theory or some other statistical mechanical approach. These calculations may then be compared with experimental estimates based on the assumption that liquid junction effects are negligible. Good agreement between such estimates indicates that this assumption is reasonable.

Appendix 2. Indirect Determination of Activities

Consider a solution made up by mixing N_0 moles of water, N_{Na} moles of NaOH, and N_{p} moles of a polyacid. At constant T and p it can be shown that the Gibbs−Duhem equation for the solution may be written as

$$\mathrm{d}\mu_{\mathrm{w}} = -c_{\mathrm{Na}}\,\mathrm{d}\theta_{\mathrm{Na}} - c_{\mathrm{p}}\,\mathrm{d}\mu_{\mathrm{p}} \qquad \text{(A2)}$$

where

$$c_{\mathrm{Na}} = \frac{N_{\mathrm{Na}}}{N_0 + N_{\mathrm{Na}}} \qquad \text{(A3a)}$$

$$c_{\mathrm{p}} = \frac{N_{\mathrm{p}}}{N_0 + N_{\mathrm{Na}}} \qquad \text{(A3b)}$$

$$\theta_{\mathrm{Na}} = (\breve{\mu}_{\mathrm{Na^+}} - \breve{\mu}_{\mathrm{H^+}}) \qquad \text{(A3c)}$$

$$\mu_{\mathrm{p}} = (\breve{\mu}_{\nu} + \nu\breve{\mu}_{\mathrm{H^+}}) \qquad \text{(A3d)}$$

Straightforward manipulation of eq A2 leads to the following expression

$$(\partial\theta_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}} = (\partial\mu_{\mathrm{p}}/\partial c_{\mathrm{Na}})_{c_{\mathrm{p}}} \qquad \text{(A4)}$$

from which we obtain

$$\mu_{\mathrm{p}}^{\mathrm{II}} - \mu_{\mathrm{p}}^{\mathrm{I}} = \int_{\mathrm{I}}^{\mathrm{II}} (\partial\theta_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}}\,\mathrm{d}c_{\mathrm{Na}} \qquad \text{(A5)}$$

where the integration refers to constant c_{p}. Equation A5 allows changes in μ_{p} with c_{Na} at constant c_{p} to be obtained if changes in θ_{Na} are measurable as is the case when Na^+ and H^+ electrodes are available.

It is also evident from the properties of partial derivatives that

$$(\partial\mu_{\mathrm{p}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}} = -(\partial\mu_{\mathrm{p}}/\partial c_{\mathrm{Na}})_{c_{\mathrm{p}}}(\partial c_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{\mu_{\mathrm{p}}} \qquad \text{(A6)}$$

which together with A4 leads to

$$(\partial\mu_{\mathrm{p}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}} = -(\partial\theta_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}}(\partial c_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{\mu_{\mathrm{p}}} \qquad \text{(A7)}$$

Consequently

$$\mu_{\mathrm{p}}^{\mathrm{II}} = \mu_{\mathrm{p}}^{\mathrm{I}} = \int_{\mathrm{I}}^{\mathrm{II}} -(\partial\theta_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{c_{\mathrm{Na}}}(\partial c_{\mathrm{Na}}/\partial c_{\mathrm{p}})_{\mu_{\mathrm{p}}}\,\mathrm{d}c_{\mathrm{p}} \qquad \text{(A8)}$$

where the integration is performed at constant c_{Na}. Equation A8 enables changes in μ_{p} with c_{p} at constant c_{Na} to be obtained when the right-hand side (rhs) of eq A7 is known. It has already been noted that the first of the two derivatives is measurable. When $(E_{\mathrm{p}} - E_{\mathrm{H}^+})$ is a single-valued function of μ_{p} only, the constraints constant μ_{p} and constant $(E_{\mathrm{p}} - E_{\mathrm{H}^+})$ are equivalent. Hence, the second derivative on the rhs of eq A7 is also measurable. It is, therefore, possible in principle to determine $(\mu_{\mathrm{p}} - \mu_{\mathrm{p}}^{\mathrm{ref}})$ for any solution where $\mu_{\mathrm{p}}^{\mathrm{ref}}$ refers to some reference state that may be chosen for convenience. Moreover, if a_{ν}^{ref} is known then a_{ν} may be obtained for any other solution.

To show that equations A2 and A3a−A3d are mutually consistent we note that at constant T and p

$$G = G(N_0, N_{\mathrm{Na}}, N_{\mathrm{p}})$$

where G denotes the Gibbs free energy so that

$$\mathrm{d}G = \lambda_0\,\mathrm{d}N_0 + \lambda_{\mathrm{Na}}\,\mathrm{d}N_{\mathrm{Na}} + \lambda_{\mathrm{p}}\,\mathrm{d}N_{\mathrm{p}} \qquad \text{(A9)}$$

where λ denotes the appropriate derivative of G. However we may also write

$$\mathrm{d}G = \mu_{\mathrm{w}}\,\mathrm{d}N_{\mathrm{w}} + \breve{\mu}_{\mathrm{Na^+}}\,\mathrm{d}N_{\mathrm{Na^+}} + \breve{\mu}_{\mathrm{H^+}}\,\mathrm{d}N_{\mathrm{H^+}} + \breve{\mu}_{\mathrm{OH^-}}\,\mathrm{d}N_{\mathrm{OH^-}} + \breve{\mu}_{\nu}\,\mathrm{d}N_{\mathrm{p}} \qquad \text{(A10)}$$

where the N's refer to the amounts of the species concerned in the system, $N_{\mathrm{H^+}}$ includes all undissociated protons as well as those in solution, and the $\breve{\mu}$ denotes electrochemical potential. At equilibrium

$$\mu_{\mathrm{H^+}} + \breve{\mu}_{\mathrm{OH^-}} = \mu_{\mathrm{w}} \qquad \text{(A11)}$$

Also by virtue of electrical neutrality

$$N_{\mathrm{Na^+}} + N_{\mathrm{H^+}} = N_{\mathrm{OH^-}} + \nu N_{\mathrm{p}} \qquad \text{(A12)}$$

Equation A10 may now be rewritten as

$$\mathrm{d}G = \mu_{\mathrm{w}}\,\mathrm{d}N_{\mathrm{w}} + (\breve{\mu}_{\mathrm{Na^+}} + \mu_{\mathrm{OH^-}})\mathrm{d}N_{\mathrm{Na}} + (\breve{\mu}_{\mathrm{H^+}} + \mu_{\mathrm{OH^-}})\mathrm{d}(N_{\mathrm{OH^-}} - N_{\mathrm{Na}}) + (\breve{\mu}_{\nu} + \nu\breve{\mu}_{\mathrm{H^+}})\mathrm{d}N_{\mathrm{p}} \qquad \text{(A13)}$$

which is true for all variations where undissociated and free protons are in equilibrium. If water is regarded as $H^+ + OH^-$ then the total hydroxide in the system is what was there to start with plus what was added, i.e. $(N_0 + N_{\mathrm{Na}})$. But this is the same as $(N_{\mathrm{w}} + N_{\mathrm{Na}})$. Therefore,

$$\mathrm{d}N_0 = \mathrm{d}(N_{\mathrm{w}} + N_{\mathrm{OH^-}} - N_{\mathrm{Na}}) \qquad \text{(A14)}$$

and it is apparent on comparing eq A13 with eq A9 that for systems at equilibrium

$$\lambda_0 = \mu_{\mathrm{w}} \qquad \text{(A15a)}$$

$$\lambda_{Na} = (\check{\mu}_{Na^+} + \mu_{OH^-}) = (\check{\mu}_{Na} - \mu_{H^+} + \mu_w) \quad \text{(A15b)}$$

$$\lambda_p = (\check{\mu}_\nu + \nu\check{\mu}_{H^+}) = \mu_p \quad \text{(A15c)}$$

Hence

$$dG = \mu_w\, dN_0 + (\check{\mu}_{Na^+} + \check{\mu}_{OH^-})dN_{Na} + \mu_p\, dN_p \quad \text{(A16)}$$

The corresponding Gibbs−Duhem equation is

$$0 = N_0\, d\mu_w + N_{Na}d(\check{\mu}_{Na^+} + \check{\mu}_{OH^-}) + N_p\, d\mu_p \quad \text{(A17)}$$

Setting $\check{\mu}_{OH^-} = \mu_w - \check{\mu}_{H^+}$ we obtain

$$0 = (N_0 + N_{Na})d\mu_w + N_{Na}\, d(\check{\mu}_{Na} - \check{\mu}_{H^+}) + N_p\, d\mu_p \quad \text{(A18)}$$

Dividing by $(N_0 + N_{Na})$ and rearranging gives eq A2.

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