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GUIDELINES FOR THE DETERMINATION OF STABILITY CONSTANTS

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Introduction

During the resurgence of interest in coordination chemistry in the 50's and 60's, numerous scientists were involved in the determination of the stability constants for metal complexes in aqueous solution. The extent of these studies is represented by the cumulative tables of stability constants which were originally compiled under the auspices of the International Union of Pure and Applied Chemistry (1). These tabulations are probably the most complete to date and should be consulted for numerical results and references for particular systems. Perrin has published a further supplement of the tables of stability constants dealing with organic ligands (2). Although these tabulations are useful generally, the number of combinations of metals, ligands, ionic media, and temperature is so large that frequently even for simple systems, data for specific sets of conditions are absent. Furthermore, extrapolation of available data to regions of interest is often hampered either by inadequate theory to guide extrapolation or by the lack of reliable data describing such factors as temperature and ionic medium effects. Several ligands and/or metal ions may be present in the same system and internally consistent stability constants in such cases are difficult to find. A recent compilation by Smith and Martell (3) is aimed at providing for the user, a set of stability constants selected by these authors. Critical surveys of stability constants of metal complexes are also being prepared under the auspices of the International Union of Pure and Applied Chemistry (4,5) and in these reports, each system consisting of a series of metal ions or ligands is being treated by a scientist who is an expert in that particular field. These and other publications (6,7) will aid the user in selecting the best stability constant values from the literature.

In the past twenty years, interest in the formation of metal complexes in aqueous solutions has changed from the more basic purposes of interpreting the mechanism of formation and correlating stability constant data, to numerous applied fields ranging from the formation of complexes in biological fluids to the treatment of sewage. Recently (8), the toxicity of cadmium to the grass shrimp (Palaemonetes pugio) was studied in the presence of chloride ion and the chelating ligand, nitrilotriacetic acid (NTA). Taking into account both chloride and NTA complexes of the metal ion, it was shown that the degree of toxicity was directly related to the activity of the free cadmium ion. In these cases, stability data are used simply as tools to control systems or processes or to understand the mechanism of biological and other reactions. Another important application of

stability data for the design of metal ion buffers for use in biological systems and for standardizing ion-selective electrodes has been discussed by Perrin et al (9).

In view of the increasing need to understand the interactions between ions in diverse mixed electrolytes, investigators in almost all fields of science require reliable stability constants for their systems and conditions. Most workers in areas outside physical and inorganic chemistry are not trained in methods of stability constant determination. However, reliable stability constants are readily determined for most simple aqueous systems consisting of only one metal cation, which may have hydroxyl complexes, and one ligand, which may also have ionizable protons. Recent developments which have facilitated stability constant determination include:

(i) the availability of high speed computers, (ii) modern solid state electronics and (iii) the establishments of reliable standards.

The present article is intended as a guide for the determination of stability constants for those whose background is not in physical chemistry but who recognize such a need in their own systems. It is not aimed at scientists whose research interests are in the methodology of stability constant determination. The determination of stability constants will be described in detail from the design of the experimental methods to the final computer analysis of the data. The systems to be considered are ones for which closely related standards have been accepted; this will include aqueous media from 0 - 90°C, ionic strengths up to 0.2 mol dm^{-3}, a pH range from about 2 to 12 and species which are stable for the time needed to complete the measurements. Recently, acid-base standards have been proposed by Bates and his co-workers at ionic strengths up to 1 mol dm^{-3} (10). There is clearly a need to establish non-aqueous and mixed solvent standards over a wide range of temperature (eg. up to the critical point of water) which are internally consistent*.

In the present treatment, we shall restrict our discussion to complexes containing only one metal cation or ligand but with the possibility of several ionizable protons or hydroxyl ions. Extending the formulae and mathematics presented herein to mixed ligand complexes is formally straight forward. In practice, however, the experimental charac-

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* This is taken to mean setting up standards in such a way that operational definitions in one system transform smoothly into the second, third, etc. pure component properties. The present day standards of pH are a result of about two decades of very careful work. Similar sets of consistent standards for other common solvents and mixed solvents appear to be years in the future.

terization of mixed complexes is tedious and has been accomplished in only a few cases. The discussion will be centered on the most widely used potentiometric method for determining stability constants but some of the problems involved in the application of other experimental methods will be outlined.

Thermodynamic stability constants for a given complex are defined with respect to the activities of the uncomplexed constituent ionic species.

$$\beta^{th}_{M_iH_jL_k} = \frac{\{M_iH_jL_k^{im+j-k\ell}\}}{\{M^{m+}\}^i \{H^+\}^j \{L^{\ell-}\}^k}$$

$$= \frac{[M_iH_jL_k^{im+j-k\ell}]y_{im+j-k\ell}}{[M^{m+}]^i [H^+]^j [L^{\ell-}]^k y_m^i y_1^j y_\ell^k} \qquad (1)$$

For example, in the calcium citrate system:-
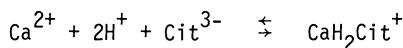
$$Ca^{2+} + 2H^+ + Cit^{3-} \;\rightleftharpoons\; CaH_2Cit^+$$

$$*\beta^{th}_{CaH_2Cit} = \frac{\{CaH_2Cit^+\}}{\{Ca^{2+}\} \{H^+\}^2 \{Cit^{3-}\}} = \frac{[CaH_2Cit^+]}{[Ca^{2+}][H^+]^2[Cit^{3-}]y_1y_2y_3} = 2.028 \times 10^{12}(dm^3mol^{-1})^3$$

In equation (1) $\{\;\}$ denotes activity, $[\;]$ concentration, and m and ℓ are the charges on the uncomplexed metal and ligand respectively[#]. The superscript "th" refers to thermodynamic stability constants which are functions only of temperature and pressure. y_z is the activity coefficient of an ion of charge $\pm z$.

* See Appendix A.

Hydroxide containing species can be represented formally in terms of the hydrogen ion activity by use of the thermodynamic ionic product for water K_w^{th}:

$$\{OH^-\} = K_w^{th} \{H^+\}^{-1}$$

Thus for the formation of $Pb(OH)_4^{2-}$ ionic complex:

$$\beta^{th}_{Pb(OH)_4^{2-}} = \frac{\{Pb(OH)_4^{2-}\}}{\{Pb^{2+}\} \{OH^-\}^4} = \frac{\{Pb(OH)_4^{2-}\} \{H^+\}^4}{\{Pb^{2+}\} K_w^4}$$

The conversion from proton stability constants to the more generally reported acid dissociation constants is given in Appendix A. In the determination of the thermodynamic stability constant $\beta_{M_iH_jL_k}^{th}$, attention must be given to the choice of standard states, units and activity coefficients. There are numerous methods to calculate the activity coefficients, y_z, of the species $Z^{\pm z}$(11). In the present report, the activity coefficients will either be assumed to be constant and incorporated into the stability constant for experiments made at constant ionic strength, or they will be calculated from the widely used Davies Equation (12).

$$\log_{10}y_{\pm z} = -Az^2[I^{1/2}/(1+I^{1/2}) - 0.31] \tag{2}$$

where I is the molar ionic strength

$$I = \sum_{\substack{\text{all ionic}\\ \text{species } Z^{\pm}}} 1/2\ z^2[Z]$$

and A can be taken as the constant of the Debye-Hückel equation
The Davies Equation has been shown to represent the activity coefficients of multiply charged ions up to ionic strengths of about 0.2 mol dm^{-3} to within ± 1%. A complete discussion of this and other equations can be found elsewhere (11-14). In the presence of relatively large concentrations of "neutral" or inert electrolytes which are assumed not to form complexes with the reacting species, the activity coefficients can be taken as constant. Concentrations are then calculated from the experimental measurements leading to constants of the form:

$$\beta_{M_iH_jL_k} = \frac{[M_iH_jL_k]}{[M]^i[H]^j[L]^k} \tag{3}$$

In Equation (3) and in the remainder of this Chapter, charges will be omitted for clarity. These concentration constants are valid only at or near the conditions at which they were determined whereas thermodynamic constants are dependent only upon temperature and pressure. The thermodynamic constants are, therefore, a property of the isolated species in water and are of fundamental interest for the understanding of ionic interactions which take place in electrolyte solutions. It should be stressed, however, that the constants at known ionic strengths are equally valid as thermodynamic equilibrium constants provided that the background salt solution is defined as the standard state (15). They are often used to calculate the concentrations of species in specific cases such as serum or concentrated solutions encountered in natural water systems and marine chemistry because the functional form of the activity coefficient is not known over the wide range of conditions of interest.

In addition, for metal-ligand systems where it is not always clear which complex species have to be taken into account, preliminary work at constant ionic strength can help to identify the important components by eliminating uncertainties in activity coefficient estimations.

Potentiometry: The most frequently studied ion association reaction is that between a metal ion M^{m+} and an anion of a weak acid $H_\ell L$. In the application of the potentiometric method, the problem is to determine the nature and concentrations of all the species present in the solutions from the measured pH($= -\log \{H^+\}$) of buffer solutions containing the acid $H_\ell L$, the base (e.g. NaOH or KOH, generalized as BOH) and the metal ion (usually added as the perchlorate salt $M(ClO_4)_m$ generalized as MX_m). It should be noted that if two or more solution species have identical charges and the same number of metal ions and ligand molecules, only the sum of the concentrations can be determined potentiometrically (16). Thus the two forms of glycine $NH_3^+CH_2COO^-$ and NH_2CH_2COOH, complex species such as $[FeEDTA]^{-1}$ and $[Fe(OH)(H.EDTA)]^{-1}$, configurational and conformational isomers and inner- and outer-sphere complexes are indistinguishable. Other methods such as spectrophotometry may be more suitable in these cases.

   In order to calculate the stability constants from potentiometric pH titration data, two more types of equations are needed; the mass balance and charge balance conditions. The total concentration of the metal ion may be written:-

$$T_M = [M] + \sum_{\substack{\text{all species} \\ \text{containing M}}} i[M_iH_jL_k] \tag{4}$$

and the total ligand concentration

$$T_L = [L] + \sum_{\substack{\text{all species} \\ \text{containing L}}} k[M_iH_jL_k] \tag{5}$$

A charge balance or electroneutrality condition expresses the fact that the solution-containing ions must be electrically neutral and, dropping the ionic charges for the sake of convenience, this can be expressed by Equation (6).

$$[H] + [B] + m[M] - [X] - [OH] - \ell[L] + \sum_{\substack{\text{all complex} \\ \text{species}}} (im+j-k\ell)[M_iH_jL_k] = 0 \tag{6}$$

Substituting for each complex species from Equation 3 into Equation 4-6:

$$T_M = [M] + \sum_{\substack{\text{all species} \\ \text{containing M}}} i\ \beta_{M_iH_jL_k}[M]^i[H]^j[L]^k \tag{7}$$

$$T_L = [L] + \sum_{\substack{\text{all species} \\ \text{containing L}}} k \, \beta_{M_i H_j L_k} [M]^i [H]^j [L]^k \tag{8}$$

$$[B] + [H] + m[M] - [X] - [OH] - \ell[L] + \sum (im+j-k\ell)\beta_{M_i H_j L_k} [M]^i [H]^j [L]^k = 0 \tag{9}$$

At each point in a potentiometric titration experiment, T_M, T_L, [B] and [X] are known and the equations 7-9 have three unknowns [M], [H], and [L] which can be calculated provided that values for the stability constants are available. If one of the stability constants is not known, it may be calculated provided that either the free metal [M], free ligand [L] or pH is measured. Normally the hydrogen ion activity is determined, and, for a given titration point, equations 7-9 can be reduced to an equation with one unknown:

$$\beta = \text{function } ([M], [L], 10^{-pH})$$

This computational method and its subsequent application is usually unnecessarily tedious. Rather, the digital computer can be used to perform an iterative solution. Then if two or more stability constants are unknown, two or more data points can be used to solve the equations for the unknown constants. More titration points are always determined than there are unknown constants, so that a set of average stability constants which best describe the data can be calculated by a non-linear least squares procedure. If the sum of the squared residuals, s, is defined as $\sum [\text{Titer-titer(calculated)}]^2$, the mathematical problem is that of finding the numerical values of the stability constants which will minimize s subject to the constraints imposed by equations 7-9 for each titration point. This is a standard minimization problem and can be solved by the method of Lagrangian multipliers (17-19). From a knowledge of the stability constants together with [H], [L] or [M], the concentrations of all other ionic species in the solution can be calculated for each point from equations 7-9. If activity coefficient corrections are to be made, the ionic strength can also be calculated from the species concentrations using equation 2 at each titration point. The minimization procedure, can also be performed using a total concentration or the pH.

Other Methods

The computational methods outlined above are based on the assumption that the concentration or activity of a single component in the solution, free hydrogen ion, free metal ion or free ligand can be measured. The ready availability of glass electrodes for the determination of hydrogen ion activity makes this one of the prime methods for determining stability constants and the design of experiments based on this method will be discussed later in this report. Two other methods involving different approaches are based

upon the measurement of conductance and UV or visible spectra. Some of the problems
involved in determining stability constants using these approaches will be briefly outlined.

Conductance Method

The measurement of conductivity of solutions of symmetrical electrolytes provides a
valuable method for studying the formation of uncharged ion-pairs. It is assumed that
these species will not contribute to the conductivity of the solution and that the free
ions obey the equations which have been established for the dependence of equivalent con-
ductance upon concentration (13,20). This method has been used extensively for the study of
complex formation in 1 - 1 electrolyte solutions and has also been applied to 2 - 2 and
some 3 - 3 salts (12). In the case of the higher charge-type electrolytes one of the
greatest difficulties is that no information is available as to how the salt would behave
if it were completely dissociated. The calculated stability constant depends to some extent
upon the arbitrary selection of a curve to represent the conductance of the free ions. With
unsymmetrical electrolytes the position is more complicated since the metal complex is
itself charged and contributes to the measured conductivity. The calculation of stability
constants in these systems has been discussed extensively by Davies (12) and by Monk and
his co-workers (21).

One of the strengths of the conductance method is that measurements can be made
with great precision and designs of both cells and measuring equipment have been well
established. Although the conductance method cannot be used to study multiply charged
ions or solutions of high ionic strength, the method may find application in a limited
number of systems in which complex formation takes place between ions of the same charge
type and in relatively dilute solution.

Spectrophotometric Method

Spectrophotometric methods depend upon the fact that when complex formation takes
place, the absorption of the new species formed may be considerably different from that of
the reactants. In favorable cases, therefore, the measurement of UV and visible spectra
enables a direct calculation to be made of the concentration, c, of the new species. The
method is based on the Beer-Lambert Law

$$\log (I_0/I) = \varepsilon c d$$

where I_0/I is the ratio of incident to transmitted light, c is the molar concentration of
the absorbing solute, d is the light path length in centimeters and ε is the absorptivity.
Although the measurement of absorbance is both easy and rapid, for the work of the highest
precision, it has been recommended that cells should be filled and emptied without removal

from the cell holder in order to prevent contamination of the solutions and the cell faces. In addition, the spectrophotometer should be used to measure only small differences in optical density for which inaccuracies in the absorbance scale of the instrument are of little importance and the errors caused by stray light are minimal (13,22).

When only two species are present such as the ionization of monobasic acids, a direct approach of measuring the absorbance as a function of wavelength at various pH values can be used to calculate the equilibrium constant (23). This may be useful for compounds whose solubility is too small to allow direct titration since absorptivities are often large enough to allow 10^{-5} mol dm^{-3} solutions to be studied (23). The Job method of continuous variation can yield both the stability constants and stoichiometry of the species without explicit determination of the absorptivities of the complexes. Unfortunately, if the complex is too stable or too weak ($1 > K > 10^6$) the K value cannot be determined spectro-photometrically. In addition, if the ligand or metal absorb at the chosen wavelength, the measured absorbances must be corrected.

Polarographic Method

Polarographic methods to determine stability constants consist of measurements of changes in the half wave potentials, $\Delta E_{1/2}$, in solutions of various total ligand concentrations, T_L, relative to the half wave potential for the same solution in the absence of ligand. It can be shown (24) that

$$\Delta E_{1/2} = -\frac{RT}{nF} \ln \left[\left(\frac{D_C}{D_M} \right)^{1/2} \sum_{0}^{m} \beta_j [L]^j \right] \qquad (10)$$

$$\text{and} \quad T_L = \sum_{0}^{m} j\beta_j [L]^j \qquad (11)$$

where D_C and D_M are the diffusion coefficients of the complex and free metal ion respectively, R is the gas constant (8.314 J $°K^{-1}$ $mole^{-1}$), T is in $°K$, F is the Faraday (96487 C equiv. $^{-1}$), and $\Delta E_{1/2}$ is expressed in volts. If the ratio D_C/D_M is taken as unity, the more typical expression proposed by Ringbom and Eriksson for the determination of stability constants is obtained (A. Ringbom and L. Eriksson, Acta Chem. Scand., 7, 1105 (1953).) The free ligand concentration [L] in Equation 10 is, formally, the ligand activity at the mercury electrode surface {L⁻}. However, at the very low concentrations involved, this is assumed to be the same as the bulk solution concentration, requiring the kinetics of association and dissociation to be fast compared to diffusion. By measurements of $\Delta E_{1/2}$ at various T_L values it is possible to calculate the stability constants β_j by a least squares

procedure similar to that herein described to calculate stability constants from potentio-metric data.

To suppress undesired current-voltage maxima, sufficient gelatin to prepare a 0.005 percent solution is generally added. Other nonionic maxima suppressors such as Triton X-100 or methyl cellulose are sometimes used. An indifferent or neutral electrolyte (e.g. 0.1 to 1.0 mol dm^{-3} KCl) is generally added to assure that the total current at the working elec-trode surface is due to diffusion of the metal ion under study. The electroactive proper-ties of oxygen, makes it necessary to remove all traces. This is generally done by bubbling oxygen-free nitrogen or hydrogen through the cell for 15 to 20 minutes prior to, but not during, polarographic measurements.

To test for reversibility, the "polarographic equation" (12) which describes the potential versus current character of the dropping mercury electrode, (dme) during reduction can be used

$$E_{dme} = E_{1/2} + \frac{RT}{nF} \ln \left(\frac{id - i}{i} \right) \qquad (12)$$

where E_{dme} is the dropping mercury electrode potential at current i, and i_d is the diffusion current for a particular solution. A plot of E_{dme} versus ln $(i_d-i/i)/I$ should be a straight line of Nernstian slope, RT/nF, and intercept $E_{1/2}$ (characteristic of the metal and inde-pendent of the particular solution under study). Although many metals and nonmetals may be studied polarographically, this condition of electrode reversibility limits its application to the determination of stability constants to systems readily electroactive (or some indirect method) such as Pb^{2+}, Tl^+, Cd^{2+}, Cu^{2+}, $Fe^{2+,3+}$, In^{3+}, Mn^{2+}, Ni^{2+}, Sb^{3+}, $Sn^{2+,4+}$, and Zn^{2+}. Of these ions the Cd^{2+}, Pb^{2+}, and Cu^{2+} systems have been most thoroughly studied.

Polarography is often used to determine the maximum coordination number (p) for a metal in the presence of an excess of ligand by use of equation (13), (ref. 14):

$$\Delta E_{1/2} = \frac{-RT}{nF} (\ln \beta_p + p \ln (L)) \qquad (13)$$

A review of the major polarographic and related volammetric techniques in use today is beyond the scope of the present article. The papers by H. W. Nurnberg should be con-sulted for state-of-the-art electronics used in ultra-trace level metal analyses in natural waters as well as physiological fluids. For the determination of stability constants, a paper such as that by DeFord and Hume (25) on the $Cd(CNS)_{1-4}$ system or the text by Nancollas (14) and references therein should be consulted.

Experimental Design

Only those aspects of error analysis of importance in stability constant determina-tions will be discussed here. For detailed discussions of error analysis and statistics the reader is referred to treatises by Laitinen and Harris (26), Shoemaker and Garland (27) and Benson (28). Before carrying out experimental work for the determination of stability constants in a specific system it is recommended that the effect of typical errors in the

independent experimental measurements upon the calculated stability constants be examined. In order to calculate expected errors in specific systems, an approximate stability constant for the metal complex of interest may be taken from the same system under slightly different medium conditions or from similar metals and/or ligands. Such calculations are readily performed by numerical differentiations (29) by increasing the independent variables by the expected error and recalculating the stability constants. This approximate error analysis will save much experimental work. As an example, for a model system such as calcium acetate with the acid stability constant of $10^5 dm^3 mol^{-1}$, metal acetate stability constant of $10 \, dm^3 mol^{-1}$, and with $T_M = 0.01$ mol dm^{-3} and $T_L = 0.01$ mol dm^{-3}, to calculate the metal acetate K value to within 1% would require a pH precision of $\pm$ 0.00002 or better. This is clearly impossible and to attempt to achieve it a waste of effort. Yet for a similar system with a metal complex stability constant of $10^4 \, dm^3 mol^{-1}$, a precision of $\pm$ 0.003 in pH is sufficient to obtain the constant to within 1%. Although this degree of precision in pH measurements requires considerable experimental effort, it is at least attainable. Similarly, if in the same system, the stability constant is $10^9 dm^3 mol^{-1}$, to determine the value to 1% would require $\pm$ 0.0004 in pH. This again is clearly beyond present day experimental precision. The larger values of K can often be measured potentiometrically by using a competition method involving two complexing systems. Thus the stability constants of some rare earth EDTA complexes, LnEDTA, have been determined by competition with $CuEDTA^{2-}$ and Ln^{3+} in the presence of a second ligand 2,2',2"-triaminoethylamine (30).

In practice the experimental uncertainties in the total concentrations of metal, ligand and base should be less than 0.1%, and the pH should be determined to within $\pm$ 0.003. The uncertainty in y_1, the activity coefficient of a univalent ion will be 1 - 2%. All these uncertainties are experimentally feasible.

Experimental Procedure

In this section the precautions which should be observed for precise determination of pH will be discussed. Although the use of the hydrogen electrode cell (20) has obvious advantages with regard to the interpretation of the electromotive force data and the elimination of liquid junction potentials, most measurements are made much more conveniently with a glass electrode incorporated in cells of the type

glass electrodes/solution under study/satd.KCl/Hg_2Cl_2,Hg
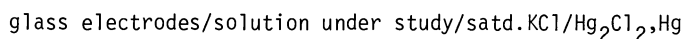
In making the experiment, all chemicals should be reagent grade or better, water from multiple distillations should be conductivity quality or better (specific conductance $<10^{-6} \Omega^{-1} cm^{-1}$). Glassware should be of Pyrex or possess similar inertness and of grade A quality where volumetric work is contemplated. Temperatures should be controlled to $< (\pm)$ 0.05°C which can be achieved with any of the numerous mercury contact thermo-regulators and circulators.
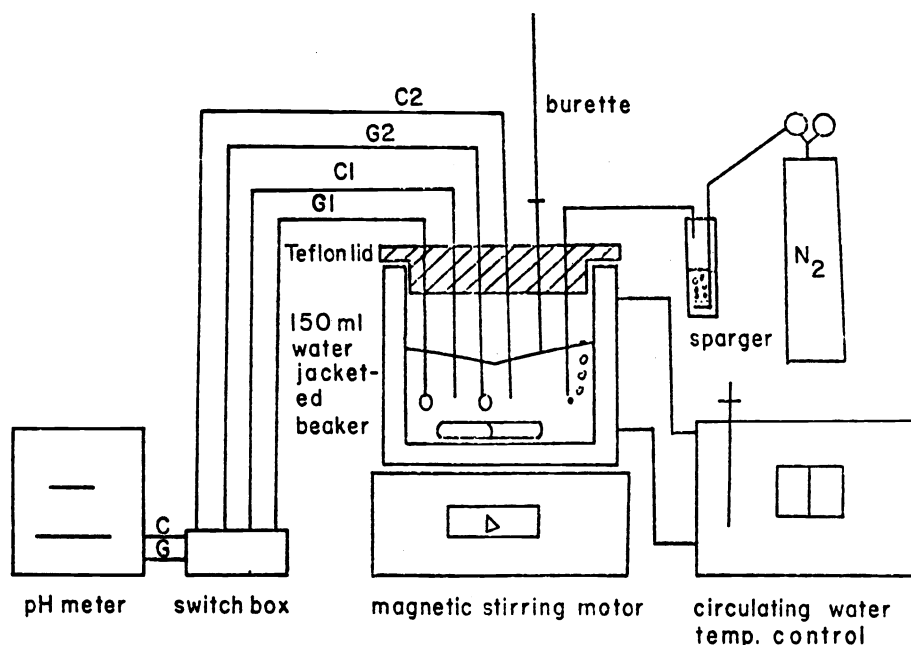
Fig. 1

A convenient potentiometric apparatus shown in Fig. 1, consists of a double-walled glass vessel with thermostated water circulating in the space between the walls. The use of a good quality research-type pH meter enables the emf's to be measured to $\pm$ 0.1mV and each cell should incorporate a pair of glass and a pair of reference electrodes of similar type so that any irregularity in their behavior can be immediately revealed (31). Due to assymmetry potentials, the emf's of different glass electrodes with the same reference will not be closer than 2-5 mv. Nitrogen, presaturated at the temperature of measurement, should be passed through the cell during the potentiometric titrations. Stirring can be achieved by use of a magnetic stirrer. For measurements at relatively low ionic strength, it is important to standardize the electrode systems both before and after each experiment using at least two primary standard buffers (32). For standard buffers such as 4.01 and 9.18, the Nerstian slope, k $[= (E_{4.01}-E_{9.18})/(9.18-4.01)]$, for each electrode combination can be calculated from the measured emf values $E_{4.01}$ and $E_{9.18}$ at the two pH values. The value of k will normally be slightly less than the theoretical value, 0.05916 volts (at 25°C), and a value in the range $0.0586 < k < 0.05916$, represents an acceptable pair of electrodes.

In studies at constant ionic strength, calibration of the glass electrode as a hydrogen ion concentration probe, p[H] $(= -\log[H^+])$ should be made by titration of a strong acid with a strong base under the same conditions. (32,33). The difference between p[H] and the reading of the pH meter, standardized with primary buffers, can then be calculated. This difference may be regarded as a correction term to convert experimental pH

values into hydrogen ion concentrations in the particular ionic medium (32).

Glass electrodes should be handled with great care and stored in buffer solution or deionized water when not in use. Frequently, electrode problems can be traced to the liquid junction of the reference electrode if the flow of salt bridge solution is interrupted. Possible changes of ionic strength caused by diffusion of solution from the salt bridge may also have to be taken into account. An intermediate salt bridge using a solution of composition close to that under study may be necessary in order to achieve the desired precision. Where measurements are contemplated over a range of temperature, calomel and similar secondary reference electrodes should be maintained at each temperature for several hours before any measurements are attempted. Potentiometric titrations may be made using either a volumetric buret (eg. precision piston-type) or by making additions from a weight buret. The solutions should be allowed sufficient time to come to equilibrium after each addition of titrant.

Model Systems

Probably the most useful procedure when contemplating the determination of a stability constant is to make preliminary measurements with a system for which the data have already been established. Well characterized simple systems are available (3,4) and should be used to test the overall analysis and experimental procedures. If the results of your experiments do not agree with the established methods to within $\pm$ (your standard deviation) then some problem should be suspected. An example of the satisfactory agreement which can be obtained when the same activity coefficient equation is used to analyze electromotive force data involving quinhydrone, glass and hydrogen electrodes is shown in Table 1.

Table 1

Dissociation constant for 1,2,3,4,5,6-Benzenehexacarboxylic Acid (Recalculated using Equation 2, Ionic Strength $\rightarrow$ 0).

Method	pK_1	pK_2	pK_3	pK_4	pK_5	pK6
Quinhydrone electrode (35)	1.31	2.39	3.57	5.08	6.31	7.46
Glass electrode (34)	1.21	2.19	3.53	5.09	6.31	7.45
Hydrogen electrode (34)	0.68	2.21	3.52	5.09	6.32	7.49

If uncertainties of 0.1% in analytical concentrations and 0.6% in hydrogen ion activity are assumed and a propagation of error analysis performed, the differences in Table 1 are well within predicted error limits for each ionization constant. It is interesting to note that the quinhydrone electrode data were obtained by Maxwell and Partington in 1949 and were recalculated using the Davies equation for activity coefficients, for the purpose of

comparison.

Computational Procedure

The computational method* can be used in two basic modes: (1) to calculate stability constants from potentiometric data and (2) to calculate solution species concentrations when the stability constants are known. The method of calculation is a nonlinear least squares procedure. Initial guesses (eg. K'_1 and K'_2) of the various stability constants are made. From these guesses the amount of titer required to obtain the reported pH at each point, k, is calculated ($CTIT_k$), and compared with the experimentally determined titer, $DTIT_k$, to obtain the residual, $R_k = CTIT_k - DTIT_k$. The amount by which each estimated constant must be changed, (a "shift" of Δ'_1 and Δ'_2) in order to minimize the sum of the squared residuals, s, is calculated

$$s = \sum_{\substack{\text{all} \\ \text{data} \\ \text{points}}} (CTIT-DTIT)^2$$

by a standard numerical partial derivative method. These calculated shifts are applied to the guessed constants to obtain a second set of improved constants.

$$K''_1 = K'_1 + \Delta'_1$$

$$K''_2 = K'_2 + \Delta'_2$$

These improved constants are then used to calculate the titer at each point and, hence, the cycle is repeated. This cycling with progressively improved estimates of the stability constants is repeated typically 10 times before the final values are printed.

ACKNOWLEDGMENTS

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* Details of the computer programme listed in Appendix B may be obtained from
   Pergamon Press Ltd., Headington Hill Hall, Oxford, OX3 OBW, U.K.

List of Symbols

β_Z^{th} Thermodynamic association (stability) constant for the formation

of species Z from uncomplexed ionic components.

$\{Z\}$ Activity of species Z

$[Z]$ Molar concentration of species Z

y_z Activity coefficient of a $\pm z$ charged species

K_z Concentration stability constant of species z

i,j,k The number of atoms of metal, protons and ligands in a given complex

m,ℓ Charge on the uncomplexed metal and ligand, respectively

K_w^{th} Activity product of water $(= \{H^+\}\{OH^-\})$

A Constant in the Debye-Hückel activity coefficient expression

I Molar ionic strength $(= 1/2 \sum\limits_{\substack{\text{all species} \\ \text{in solution}}} z^2[Z])$

BOH Base added in a potentiometric pH titration, eg. KOH

References

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Appendix A

Converting from normally reported acid dissociation constants and complex stability constants to association constants

Citric acid will serve as an example of the conversion procedure. We will neglect activity coefficients for clarity . The dissociation constants, K_i^d, of citric acid at 25°C from R. Bates, J. Amer. Chem. Soc., 71, 1274 (1949) are:

$$K_1^d = 7.447 \times 10^{-4} \, mol \, dm^{-3} = \frac{\{H^+\} \, \{H_2Cit^-\}}{\{H_3Cit\}} \quad or \quad pK_1 = 3.128$$

$$K_2^d = 1.734 \times 10^{-5} \, mol \, dm^{-3} = \frac{\{H^+\} \, \{HCit^{2-}\}}{\{H_2Cit^-\}} \quad or \quad pK_2 = 4.761$$

$$K_3^d = 4.018 \times 10^{-7} \, mol \, dm^{-3} = \frac{\{H^+\} \, \{Cit^{3-}\}}{\{HCit^{2-}\}} \quad or \quad pK_3 = 6.396$$

From these dissociation constants the association or stability constants are obtained:

$$\beta_{HC} = \frac{\{HCit^{2-}\}}{\{H^+\}\{Cit^{3-}\}} = \frac{1}{K_3^d} = 2.489 \times 10^6 \quad or \quad \log_{10}\beta_{HC} = 6.396$$

$$\beta_{H_2C} = \frac{\{H_2Cit^-\}}{\{H^+\}^2\{Cit^{3-}\}} = \frac{1}{K_2^d K_3^d} = 1.435 \times 10^{11} \quad or \quad \log_{10}\beta_{H_2C} = 11.157$$

$$\beta_{H_3C} = \frac{\{H_3Cit\}}{\{H^+\}^3\{Cit^{3-}\}} = \frac{1}{K_1^d K_2^d K_3^d} = 1.927 \times 10^{-4} \quad or \quad \log_{10}\beta_{H_3C} = 14.285$$

The calcium-citrate complex stability constants at 25° from: C. W. Davies and B. E. Hoyle, J. Chem. Soc., 4134 (1953) are:

$$K_{CaCit}^{Davies} = \frac{\{CaCit^-\}}{\{Ca^{2+}\}\{Cit^{3-}\}} = 7.943 \times 10^4 \, dm^3 mol^{-1} \quad or \quad \log_{10}K_{CaCit}^{Davies} = 4.90$$

$$K_{CaHCit}^{Davies} = \frac{\{CaHCit\}}{\{Ca^{2+}\}\{HCit^{2-}\}} = 1.122 \times 10^3 dm^3 mol^{-1} \quad or \quad \log_{10}K_{CaHC}^{Davies} = 3.05$$

$$K_{CaH_2Cit}^{Davies} = \frac{\{CaH_2Cit^+\}}{\{Ca^{2+}\}\{H_2Cit^-\}} = 1.413 \times 10^1 dm^3 mol^{-1} \quad or \quad \log_{10}K_{CaH_2C}^{Davies} = 1.15$$

The association constants from the free metal, Ca^{2+}, free ligand, Cit^{3-} and acid, H^+, to be used in the program are:

$$\beta_{CaCit}^{assoc.} = \frac{\{CaCit^-\}}{\{Ca^{2+}\}\{Cit^{3-}\}} = K_{CaCit}^{Davies} = 7.943 \times 10^4 dm^3 mol^{-1} \quad or \quad \log_{10}\beta_{CaCit}^{assoc} = 4.90$$

$$\beta_{CaHCit}^{assoc} = \frac{\{CaHCit\}}{\{Ca^{2+}\}\{H^+\}\{Cit^{3-}\}} = \frac{K_{CaHC}^{Davies}}{K_3^d} = 2.793 \times 10^9 (dm^3 mol^{-1})^2 \quad or \quad \log_{10}\beta_{CaHC}^{assoc} = 9.45$$

$$\beta_{CaH_2Cit}^{assoc} = \frac{\{CaH_2Cit^+\}}{\{Ca^{2+}\}\{H^+\}^2\{Cit^{2-}\}} = \frac{K_{CaH_2C}^{Davies}}{K_2^d K_3^d} = 2.028 \times 10^{12} (dm^3 mol^{-1})^3 \quad or \quad \log_{10}\beta_{CaH_2Cit}^{assoc} = 12.31$$

In the papers by Bates and Davies activities were used. The program here can be used with or without activity coefficients; the notation K^{Davies} implies that the Davies equation (2) has been used to calculate the activity coefficient terms.

APPENDIX B

```
                      START
                        │
                        ▼
              ┌─────────────────────┐
              │   INPUT DATA        │
              │  (SEE "INPUT")      │
              └─────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │   OUTPUT DATA           │
           │  JUST AS WAS INPUT      │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │        K = 1            │
           │     (POINT #)           │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │        J=0              │
           │ (SPECIES BEING VARIED)  │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │        M=0              │
           │ (DIFFERENTIATION INDEX) │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │  UX = 10^(-PH)          │
           │  VX = FREE METAL        │
           │       GUESS = TOTAL     │
           │  TX = FREE LIGAND       │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │    CALL COGSNR          │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │  CALCULATE TITER        │
           │  FROM RESULTS OF COGSNR │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │   R = DTIT - CTIT       │
           │  RESIDUAL AS MEASURED   │
           │  MINUS CALC. TITER      │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │  APPLY SHIFT TO CONSTANT│
           │  FOR NUMERICAL DIFFER.  │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │ CALCULATE DIFFERENTIAL  │
           │ TERM FOR ALL J-SPECIES  │
           │ AT POINT - K.           │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │ SET UP TERMS OF COFACTOR│
           │ MATRIX, C(II, JJ),      │
           │ FOR POINT - K.          │
           └─────────────────────────┘
                        │
                        ▼
           ┌─────────────────────────┐
           │ OBTAIN SHIFT AND APPLY  │
           │ TO VARIOUS CONSTANTS    │
           │ FOR CYCLE.              │
           └─────────────────────────┘
```

For differentiation of constant JJ at Point K

For All Constants at Pt. K.

Repeat for all K- Points

Repeat for Desired Number of Cycles