Available online at www.sciencedirect.com
SCIENCE DIRECT®
Talanta 65 (2005) 1221–1225
Talanta
www.elsevier.com/locate/talanta

Reflections on the calculation and publication of potentiometrically-determined formation constants

Montserrat Filella[a,*], Peter M. May[b]

[a] *Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva 4, Switzerland*
[b] *Chemistry, Division of Science and Engineering, Murdoch University, Murdoch, WA 6150, Australia*

Received 16 April 2004; received in revised form 8 August 2004; accepted 25 August 2004
Available online 1 October 2004

Abstract

Calculation and reporting procedures are described, which aim to improve the quality and comparability of published formation constant values obtained by glass-electrode potentiometry. Ways in which the processing of data by computer optimization programs can be standardized are the main concern, particularly in respect of improving the usefulness of equilibrium data through incorporation into large publically available databases. These recommendations may be particularly valuable to researchers beginning in this field as well as to those who determine formation constants only occasionally.

Keywords: Computer calculation; Equilibrium constants; Formation constants; Stability constants; Potentiometry

1. Introduction

The specific problem addressed in this paper is that many formation constants now being published in the literature are calculated and reported in disparate ways so that it is difficult to incorporate them into thermodynamic databases and to make valid comparisons between the results from different investigators. This can be troublesome enough for general readers who may not appreciate the implications of the various experimental and calculational procedures, but it is especially difficult for modellers with practical applications who must make critical assessments to identify the best equilibrium data available.

There are at least three reasons why this difficulty has become acute in recent years. First, there has been a proliferation of computer programs to determine formation constants (even though some of these codes contribute little, or nothing, new) [1–31]. Secondly, many possible methods of calculation, each capable of producing significantly different answers, have become readily available. The ease with which titration parameters other than formation constants (e.g. the analytical concentrations and electrode calibration parameters) can now be optimized simultaneously is responsible for much of this latter (calculational) diversity. Choices also have to be made, implicitly or explicitly, regarding the nature of the objective function (e.g. whether the residuals are expressed in terms of e.m.f., titre volumes, etc.) and what weighting of residuals is to be applied. Further variation occurs if corrections are made for the effects of changes in ionic strength, liquid junction potentials and/or ion selectivity of electrodes. Thirdly, and perhaps most importantly, formation-constant determination remains necessary but is less fashionable than it used to be. So, results are now often performed by researchers with less background and experience in this field. Available reference manuals are either old (e.g. [32]) and do not encompass the use of computer calculation-based approaches or are restricted to a particular calculation program [33].

Since it is unlikely that anything practical can, or even should, be done to limit the range of these computer programs, it seems that the only feasible way forward is to es-

* Corresponding author. Tel.: +41 22 3796 046; fax: +41 22 3796 069.
E-mail address: montserrat.filella@cabe.unige.ch (M. Filella).

0039-9140/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.talanta.2004.08.046

tablish some common ground between the various methods of calculation. Accordingly, our purpose here is to describe and justify a number of appropriate procedures and to detail the information required to make valid cross-comparisons between results. This establishes a minimum of information that ought to be included when formation constants optimized by computer program are reported. These recommendations are the outcome of our experiences (i) using ESTA [34] for the calculation of stability constants (e.g. [35–42]), (ii) building thermodynamically consistent stability constant databases [43,44] and (iii) refereeing stability constant papers. Since they are in part based on certain arbitrary decisions, there is of course no intention to restrict sensible alternative approaches; on the contrary, further investigation of these issues is only to be encouraged. We hope to complement the general recommendations that have been issued by IUPAC over the years [45–47].

2. Rationale

It is well known that the considerable discrepancies between values published for the same chemical system by various authors are a notorious feature of formation constant measurements [34,48]. To deal with the worst effects of this, those using results from different laboratories need sufficient information to judge the reliability of respective sets of formation constants. At present, this is often impossible because different calculational procedures and poorly specified experimental conditions do not allow like to be compared with like. The following reflections address this problem. They are divided into four sections, each concerned with stages of the overall procedure that are especially important to the outcome.

2.1. Data collection and evaluation

It seems trite to say that no method or amount of data analysis can overcome faulty data i.e. grossly mistaken values lying distinctly outside the experimentalist's ordinary error distribution. Nevertheless, the occurrence of such errors in titration data, which remain undetected before the data is processed by an optimizing computer program, is one of the commonest causes of the discrepancies between published sets of formation constants referred to above.

This is because the effects of many kinds of analytical errors become obscured by correlations within the system [49] whenever formation constant values are optimized, especially, when this involves an unknown chemical species in the procedure to select a chemical model. As is well known, 'computer complexes' (artefacts of the least-squares calculation) frequently arise from poor experimentation. What it is less well appreciated, however, is that the nature of titrations (in which many observations are made at highly interdependent points) exacerbates this effect, and that matters can be made even worse if there is further inter-dependence between titrations. The latter arises especially from the use of stock solutions in common. This is because the so-called 'linkages of systematic errors' [49] make correlations with global parameters such as formation constants all the larger and often the more misleading.

It follows that before any data processing is commenced, considerable care must be taken to ensure that there are no gross errors in the titration data, and that there is as much independence between titrations as possible. Neither of these requirements is as easy to achieve as is often assumed. Ideally, the entire titration procedure should be replicated a number of times, absolutely independently and the results shown to be satisfactorily superimposable. This is simply not feasible in the strictest sense and, in any event, is far from practicable in the vast majority of formation constant determinations. Thus, individual workers must judge what is reasonable and report carefully what they do, so that their results can be assessed accordingly. It is doubtful that 'computer complexes' can be avoided unless the whole titration and calculation procedure, at least duplicated, gives the same result using independent stock solutions and two sets of electrodes.

2.2. Model selection

Model selection poses a formidable problem in the characterization of many equilibrium systems. In essence, the difficulty is to know when an optimized formation constant for a proposed species reflects a genuine reaction occurring in solution. All formation constant optimizations use a pre-defined set of species, which are supposed to exist in the solution, so the calculation is undermined if this *ab initio* assumption is untrue.

In practice, the inclusion of such non-existent species in the least-squares analysis often leads to a spurious improvement between observed and calculated data (as manifest, for example, in a lowered objective function value). This is because the optimization procedure can, in general, exploit the additional degree of freedom so as to reduce the effects of experimental errors that are always present in real titration data (i.e. even when there are no outliers). Hence, the question that always arises during model selection is whether or not the effect of including an additional species is 'significant enough' to establish that the species has a real existence. In other words, a decision must be made as to what precisely constitutes an effect that is 'significant enough' to permit the species to be characterized.

In principle, the answer to this question can be obtained by a Monte Carlo analysis [49]; simple statistics such as Student's *t*-test are not appropriate because of the systematic errors involved. However, in practice, model selection by Monte Carlo methods can be costly in terms of computer time and it has proved difficult to determine results unequivocally.

The traditional approach, taken by many working in this area (e.g. see reference [50]), has been to employ a variety of 'model selection criteria'. Foremost amongst these is to look for a substantial improvement in objective function (where, say, a reduction of 50% is regarded as impressive but 10% is

not). However, this criterion, by itself, is not sufficiently discriminating. For a minor species to be accepted as genuine, it should, when included in the model, also (i) lead to an improvement in internal consistency of the data as reflected by better calculated standard deviations of formation constants; improvements in respect to other (more major) species are especially encouraging, (ii) be calculated to occur at significant concentrations over a range of points in more than one titration-complexes not reaching 10% of the total metal ion concentration, say, should always be regarded as dubious and (iii) display a markedly better fit between observed and calculated data in graphical visualizations of the data such as given by the formation function, $\bar{Z}$.

One problem with these criteria, of course, is that they are inherently subjective. Another is that, unless applied with caution and knowledge of their limitations, they can be positively misleading. Each of these effects (supposedly indicating a genuine minor species) can equally well arise from removal of systematic experimental errors by the optimization process. This means that such criteria must be supplemented by chemical commonsense and judged overall, including some Monte Carlo analysis.

The number of possible complex stoichiometries that can in general be formed by binary metal-ligand co-ordination is large. Glass-electrode potentiometry is with few exceptions the only analytical technique capable of distinguishing between so many (labile) species. Nevertheless, it is common to find that the analytical information required to distinguish between models is close or below to the limit of analytical detection. Under these circumstances, it is impossible to distinguish between the effects of a small, but real interaction in solution and those of errors in (correlated) titration parameters. It then becomes preferable, for reasons discussed below, to exclude from the 'best model' the species in question. In other words, during model selection, it is always better to err on the side of too few species than too many.

The implication is that species should only be selected when their effect on titration behaviour is clearly beyond any other reasonable explanation. This principle underpins the thrust of recommendation 2a (see Section 2.3); it is important to perform the model selection stage only using titration parameter values that have been determined independently. Simultaneous optimization of titration parameters other than the formation constants being determined precludes a verdict 'beyond reasonable doubt'. It is important to note that this requirement for independently determined values of titration parameters arises out of the need to maximize the information content of the titrations for the purpose of model selection and not because optimization of titration parameters is in some sense 'improper'. For example, simultaneous refinement of titration parameters and formation constants has proved generally advantageous [35–40,51] as long as the chemical species in solution are well established.

There is another practical advantage of using total concentrations (or titre volumes). As the dependent variable, these quantities permit optimization with unit-weighted residuals. The (absolute) objective function values thus obtained are directly comparable between chemical systems in a way that weighted objective functions, depending on estimates of errors and how the weighting is done, are not.

2.3. Assessment of the effects of ionic strength corrections and of weighting

Neither corrections for changes in ionic strength nor the choices made regarding weighting should significantly alter the formation constant values obtained. However, in practice, both produce differences which, depending on the system and the ranges over which data have been collected, can sometimes be too large to be ignored. The aim of recommendations 3a and 3b is thus to ensure that investigators do not overlook this issue and, if necessary, provide sufficient information for its effects on their final 'best values' to be assessed.

Introducing a correction for changes in ionic strength should only have a marginal influence on the objective function value because experimental conditions should be chosen so as to minimize such changes. However, the ionic strength must vary to some extent over the course of a titration and it may sometimes do so quite markedly (e.g. when the concentration of one ion from the background electrolyte is maintained constant at relatively low concentrations, say 100 mM). Under such circumstances, the chief consequence of applying activity coefficient corrections in programs that allow it (such as ESTA) is to improve the internal consistency between data points and to ensure that all refer precisely to the same reference ionic strength. This can sometimes alter the formation constant values significantly. If it does, the experiment needs to be re-designed.

Similarly, the use of corrections for changes in liquid junction potential or ion selectivity of electrodes should not be regarded as means by which formation constant determinations can be improved. It seems most unlikely at the present time that these effects can usefully be modelled due to poorly developed theory and the lack of suitable parameter values in the literature. Rather, they can be used to test the sensitivity of results with respect to such effects so that unstable formation constant values are identified.

Exact comparability between different optimization programs and between different objective functions is not possible as far as weighting is concerned. This is because the coded methods used for weighting differ at a very fundamental level and because there must always be some inherent dependence of estimates of error that are specific to individual users [52]. Provided the experimental data are not too badly affected by systematic errors, however, the effect of such differences on the final, published formation constants obtained can be restricted.

2.4. Refinement of values

Refinement of the formation constant values by simultaneously optimizing other titration parameters generally yields

better values than are obtained otherwise, as is discussed in detail in [49]. This is because the effects of (unavoidable) systematic errors, from whatever source, are at least partially adsorbed into the additional refinable parameters. This is beneficial because the latter are not relevant to the result of primary interest, namely the formation constants to be published. Note, for example, that the ill effects of omitting a genuine minor species from the model are likely to be reduced by simultaneous refinement of an appropriate titration parameter whereas, if an extra (incorrect) species is included, its effects on the formation constants being optimized can only be harmful.

To achieve this potential improvement in formation constant values, it is necessary to find a suitable set of titration parameters for simultaneous optimization. Clearly, these should be such that correlations with the formation constants being determined are minimized whereas correlations with parameters likely to introduce the most harmful systematic errors (when held constant) are maximized. This optimum set of parameters to optimize can be found using a Monte Carlo analysis of error propagation, as described in [49].

Thus, for the chosen model, those optimized values of the formation constants should be regarded as 'best' i.e. approximating the true values most closely. These are the data, which should be used by others, e.g. in speciation calculations. Accordingly, they should be clearly identified as the final result and distinguished as such from the other, intermediate sets of constants.

Estimation of the standard deviations associated with these 'best' values is accomplished directly during the Monte Carlo procedure. There is no doubt that these estimates represent a much more realistic assessment of error than the so-called 'conventional standard deviations' mentioned in 2b (see reference [49]). Authors are therefore strongly encouraged to report the uncertainties determined by Monte Carlo methods.

Even more important, however, alongside their 'best' set of formation constants authors should report for comparison the corresponding values obtained when only the formation constants themselves are optimized (i.e. no simultaneous refinement of titration parameters). Here again, any substantive difference between the two sets is indicative of calculation instability (typically arising through the correlation of parameters), which can only be addressed by covering a better range of titration conditions.

3. Recommendation checklist

The following procedures would help to ensure that publications of formation constants determined potentiometrically have, at least, some well-defined points of reference in common. The rationale behind the recommended procedures is to be found in the corresponding parts of Section 2. The same headings have been used in both sections to help cross-referencing. Examples of equilibrium constant determinations that closely follow the philosophy and general guidelines explained in this paper can be found in references [39,42].

3.1. Data collection and evaluation

1a) Report the number of titrations, the number of data points in each, and the titrant and titrand concentrations.
1b) Report the degree of independence between titrations, especially regarding stock solutions and sets of electrodes.
1c) Report precisely the measures taken to ensure reproducibility of the measured data.

3.2. Model selection

2a) Optimize the sets of formation constants under investigation on their own i.e. using externally determined values for all other parameters. Employ an objective function based on unit-weighted residuals in total analytical concentrations (or, with some programs, the equivalent titre volumes). Do not use program-applied corrections for changes in ionic strength, liquid junction potential or ion selectivity of electrodes.
2b) Report, for the 'best model' and any other model considered appropriate, the optimized formation-constant values, corresponding standard deviations, objective function values and the Hamilton R-factor.

3.3. Assessment of the effects of ionic strength corrections and of weighting

3a) Optimize as in 2a but with an objective function based on weighted residuals in e.m.f. Apply ionic strength corrections, if necessary.
3b) Report the optimized formation constants and the associated standard deviations obtained at this stage.

3.4. Refinement of values

4a) Optimize, simultaneously with the formation constant values, those titration parameters, which have been selected as most appropriate, using the same objective function, weighting and correction methods as in 3a above.
4b) Report the formation constants produced at this stage as the 'best' values.

References

[1] J.P. Chandler, R.E. Thompson, H.O. Spivey, E.L.-F. Li, Anal. Chim. Acta 162 (1984) 399.
[2] P. Gans, A. Sabatini, A. Vacca, J. Chem. Soc. Dalton Trans. (1985) 1195.
[3] D.J. Leggett (Ed.), Computational Methods for the Determination of Formation Constants, Plenum Press, New York, 1985.

[4] J. Havel, M. Meloun, Talanta 33 (1986) 525.
[5] A. Izquierdo, J.L. Beltrán, Anal. Chim. Acta 181 (1986) 87.
[6] P. Decock, B. Sarker, Can. J. Chem. 65 (1987) 2798.
[7] C. De Stefano, P. Princi, C. Rigano, S. Sammartano, Ann. Chim. (Rome) 77 (1987) 643.
[8] R. Fournaise, C. Petitfaux, Talanta 34 (1987) 385.
[9] Y.L. Sidrak, A. Aboul-Seoud, J. Comput. Chem. 8 (1987) 575.
[10] J.J. Baeza, G. Ramis, C. Mongay, J. Chemom. 3 (Suppl A) (1988) 223.
[11] E. Bottari, T. Coccitto, G. Curzio, M.R. Festa, R. Jasionowska, Ann. Chim. (Rome) 78 (1988) 635.
[12] V. Cerdá, J. Maimo, J.M. Estela, A. Salva, J. Ramis, Talanta 35 (1988) 667.
[13] M. Meloun, J. Havel, E. Högfeldt, Computation of Solution Equilibria: A Guide to Methods in Potentiometry, Extraction and Spectrophotometry, Ellis Horwood, Chichester, 1988.
[14] P.D. Taylor, I.E.G. Morrison, R.C. Hider, Talanta 35 (1988) 507.
[15] V. Gadjokov, Kh. Mihailova, Comput. Chem. 13 (1989) 325.
[16] A. Poznajilo, J. Radioanal. Nucl. Chem. 134 (1989) 97.
[17] R. Fournaise, C. Petitfaux, Analusis 18 (1990) 242.
[18] M. Meloun, M. Javúrek, J. Militký, Mikrochim. Acta 109 (1992) 221.
[19] T. Michalowski, Talanta 39 (1992) 1127.
[20] A. Sabatini, A. Vacca, P. Gans, Coord. Chem. Rev. 120 (1992) 389.
[21] C. De Stefano, P. Mineo, C. Rigano, S. Sammartano, Ann. Chim. (Rome) 83 (1993) 243.
[22] F. Gaizer, I.I. Kiss, Talanta 41 (1994) 419.
[23] V.I. Vetrogon, N.G. Lukynenko, M.-J. Schwing-Weill, F. Arnaud-Neu, Talanta 41 (1994) 2105.
[24] J. Barbosa, D. Barrón, J.-L. Beltrán, V. Sanz-Nebot, Anal. Chim. Acta 317 (1995) 75.
[25] G. Papanastasiou, I. Ziogas, Talanta 42 (1995) 827.
[26] M.P. García Armada, Comput. Chem. 19 (1995) 137.
[27] C. De Stefano, C. Foti, O. Giuffrè, P. Mineo, C. Rigano, S. Sammartano, Ann. Chim. (Rome) 86 (1996) 257.
[28] P. Gans, A. Sabatini, A. Vacca, Talanta 43 (1996) 1739.
[29] I. Ingri, I. Andersson, L. Petersson, A. Yagasaki, L. Andersson, K. Holmström, Acta Chem. Scand. 50 (1996) 717.
[30] M.P. García Armada, Comput. Chem. 20 (1996) 385.
[31] L. Alderighi, P. Gans P, A. Ienco, D. Peters, A. Sabatini, A. Vacca, Coord. Chem. Rev. 184 (1999) 311.
[32] H. Rossotti, The Study of Ionic Equilibria: An Introduction, Longman, New York, 1978.
[33] A.E. Martell, R.J. Motekaitis, Determination and Use of Stability Constants, second ed., VCH, 1992.
[34] P.M. May, K. Murray, D.R. Williams, Talanta 35 (1988) 825.
[35] M. Filella, D.R. Williams, Inorg. Chim. Acta 106 (1985) 49.
[36] M. Filella, A. Izquierdo, E. Casassas, J. Inorg. Biochem. 28 (1986) 1.
[37] M. Filella, E. Casassas, D.R. Williams, Inorg. Chim. Acta 136 (1987) 177.
[38] M. García Bugarín, J.S. Casas, J. Sordo, M. Filella, J. Inorg. Biochem. 35 (1989) 95.
[39] M. García Bugarín, M. Filella, J. Inorg. Biochem. 73 (1999) 17.
[40] M. Filella, R.M. Town, M. García, Bugarín, J. Chem. Eng. Data 44 (1999) 1009.
[41] L.-C. Königsberger, E. Königsberger, P.M. May, G.T. Hefter, J. Inorg. Biochem. 78 (2000) 155.
[42] M. Filella, M. García Bugarín, P.M. May, Analyst 126 (2001) 2093.
[43] P.M. May, K. Murray, J. Chem. Eng. Data 46 (2001) 1035.
[44] M. Filella, P.M. May, Geochim. Cosmochim. Acta 67 (2003) 4013.
[45] G.H. Nancollas, M.B. Tomson, Pure Appl. Chem. 54 (1982) 2657.
[46] A. Braibanti, G. Ostacoli, P. Paoletti, L.D. Pettit, S. Sammartano, Pure Appl. Chem. 59 (1987) 1721.
[47] D.G. Tuck, Pure Appl. Chem. 61 (1989) 1161.
[48] L.D. Pettit, K.J. Powell, SC-Database, IUPAC and Academic Software, 1993–2001.
[49] P.M. May, K. Murray, Talanta 35 (1988) 933.
[50] G. Berthon, P.M. May, D.R. Williams, J. Chem. Soc. Dalton Trans. (1978) 1433.
[51] P.M. May, D.R. Williams, P.W. Linder, R.G. Torrington, Talanta 29 (1982) 249.
[52] P.M. May, K. Murray, Talanta 35 (1988) 927.