Pergamon

Talanta, Vol 41, No 3, pp 419–424, 1994
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0039-9140/94 $6 00 + 0 00

A PC PROGRAM FOR CALCULATION OF THE STABILITY CONSTANTS OF COMPLEXES $M_qL_pH_r$ FROM pH-METRIC MEASUREMENTS

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(*Received* 3 *May* 1993 *Revised* 5 *July* 1993 *Accepted* 2 *August* 1993)

Summary—A least-squares computer program MAXIPOT-F using the nonweighted residuals of emfs has been constructed for calculation of the optimum values of the cumulative stability constants of complexes $M_qL_pH_r$ and/or those of species H_rL_p or $H_{-r}M_q$ from pH-metric data The basic parameters (E^0, g, j_H, j_{OH} and K_s) necessary for evaluation can be obtained from blank titration curves These parameters and the total base concentration of the titrant are also treated as refinable group parameters

The programs, written in FORTRAN programming language, can be run on a PC and easily extended or connected to other programs

Small programs for species-distribution calculation under different experimental conditions are also reported

In previous papers[1,2] we introduced programs with low memory requirements for desk computers in BASIC programming language. One of them[1] was capable of calculating the cumulative stability constants of complexes of the type M_qL_p and H_rL_p from potentiometric measurements and the parameters of acid–base titration curves. The most frequent task in the examination of solution equilibria, however, is the determination of the stability constants of protonated $(+r)$ or deprotonated $(-r)$ complexes $M_qL_pH_r$. The solution of such problems from pH-metric data may require a rather long running time. However, we succeeded in decreasing the running time of our programs for the solution of such problems to such an extent that it is reasonable to use them with a PC. These BASIC programs[3,4] proved very useful because of their question and answer input system and the possibility of easy control of the values of the various variables during running. Their applicability was restricted, however, by the relatively low ability and primitive output system of the BASIC language. The present paper introduces the program MAXIPOT-F*, a developed version of MAXIPOT-B, written in FORTRAN. As "by-products" of MAXIPOT, four smaller programs capable of calculating species distributions under different conditions are also introduced.

BACKGROUND

When pH-metric titration is carried out, the total concentrations of the reactants (T_H, T_{OH}, T_M and T_L) and the emf of the hydrogen ion cell are available. The problem to be solved is the calculation of the cumulative stability constants ($\beta = [M_qL_pH_r] \times [M]^{-q} \times [L]^{-p} \times [H^+]^{-r}$) of the species $M_qL_pH_r$ formed. For an equilibrated solution, the following mass-balance equations hold·

$$T_H - T_{OH} = [H^+] - K_s/[H^+] + \sum_j j \times r_j \times c_j \quad (1)$$

$$T_M = [M] + \sum_j j + q_j \times c_j \quad (2)$$

$$T_L = [L] + \sum_j j \times p_j \times c_j \quad (3)$$

where $c_j = \beta_j \times [M]^{q_j} \times [L]^{p_j} \times [H^+]^{r_j}$. If the stoichiometric compositions (q, p and r) and the stability constants (β) of the complexes formed are assumed, the real roots $[M]_c$, $[L]_c$ and $[H^+]_c$ of equations (1)–(3) can be calculated, and this leads to the calculated emf (E_c)·

$$E_c = E^0 + g \times \log[H^+]_c \pm j_H \times [H^+]_c \pm j_{OH} \times K_s/[H^+]_c \quad (4)$$

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*Available from the authors upon request.

In equation (4), E^0 denotes the constant of the glass electrode, g is the Nernst factor (59.16 at 25°C), j_H and j_{OH} are factors for correction of the diffusion potentials in the acidic and alkaline region, respectively, and K_s is the ionic product of the solvent (water) under the experimental conditions. These five *basic parameters* can be obtained by the analysis of independent blank titration curves. Equation (4) allows a point by point comparison of measured emfs (E_m) with those calculated on the basis of the assumed model and stability constants, and the optimum constants resulting in the minimum value of $U = \Sigma(E_m - E_c)^2$ can also be calculated for the cumulative stability constants. For an assumed model, if satisfactory starting values are available for the cumulative stability constants, finding their optimum parameter values is a simple optimization task.[1,5] As a result of a refinement cycle, this program calculates a vector, the element of which contains the correction values of the parameters involved in the optimization. Thus, the solution of a pH-metric problem consists of two main steps: (1) finding the values of the five basic parameters by optimization from the data of independent blank titrations, and (2) guessing the model ($\vec{q}$, $\vec{p}$ and $\vec{r}$) and starting stability constant values ($\vec{\beta}$) for this, then calculating U, and refining the βs until U_{min} is reached. If U_{min} is not satisfactory, the whole procedure is repeated with a new model.

THE PROGRAM MAXIPOT-F AND ITS STRUCTURE

The principle, structure and usage of the present program have many similarities to those of MINIPOT[1] (and MINISPEF[2]) published in 1980. Some parts (*e.g.* the parameter search and refinement units) have not changed much. Numerous radical changes were necessary, however, and we had to construct new subroutines, too. Further, on the basis of experience acquired over more than 10 years, the values of some previously input variables are set up or calculated automatically, and the input is reduced to a minimum (Fig. 1).

MAXIPOT-F can execute two main tasks: (1) the refinement of one or (simultaneously) several parameters (JB = 0), and (2) the search for the approximate value of one of the parameters.

The program is capable of solving four chemical problems: calculation of (1) the basic parameters of blank titration curves, (2) the protonation constants of complexes H_rL_p, (3) the stability constants of species M_qL_p, and (4) the stability constants of $M_qL_pH_r$. Problem (4) includes the presence of complexes H_rL_p and/or M_qL_p and/or $H_{-r}M$ (hydroxo complexes) too.

The first part of the program serves for the input and pretreatment of measured data. There are two kinds of input, depending on the problem to be solved. The option depends on the variable number of complexes (*NK*); for $NK = 0$, a blank curve will be treated. If a complex-containing system is evaluated from pH-metric data, the number of base equivalents added (a) and the average number of protons bound ($Z_H = (T_H - [H^+] - T_{OH} + (K_s/[H^+]))/T_L$) are calculated and output.

With the parameter-search unit, starting parameter values for refinement can be obtained. Until U_{min} is reached, this program part changes the value of the parameter to be searched stepwise (TB) between the lower (TA) and upper (TC) limits, which are either input ($JB = 1$) or generated by multiplication ($JB = 2$) from the already existing parameter value.[1] A significant decrease in running time can be achieved when the search interval and search step are calculated by multiplication factors from a roughly-searched parameter value.[1]

The parameter-refinement part calculates the correction vector $\mathbf{h} = (\mathbf{G}^T . \mathbf{G})^{-1} . \mathbf{d}$; here, $\mathbf{d}$ is the difference vector, the elements of which are the differences between emfs measured (E_m) and calculated from the starting parameter values (E_c°). The elements g_{ij} of matrix $\mathbf{G}$ can be calculated by numeric differentiation via the formula $g_{ij} = (E_m - E_c^{\prime})/\Delta k_j$, where $E_c^{\prime}$ is the emf calculated on increasing the jth parameter by Δk_j. However, the parameters are usually not actually corrected by the correction vector itself, but by its value multiplied by a scalar resulting in the maximum decrease in U.[6,5] The errors in parameters are calculated with the formula $\sigma(\beta_j) = \sqrt{|c_{jj}^{inv}| . U_j^{\prime}/(n - 1 - \mathrm{NPF}})$, where c_{jj}^{inv} denotes the diagonal elements of $(\mathbf{G}^T . \mathbf{G})^{-1}$, NPF is the number of parameters refined simultaneously, n is the number experimental points involved in the calculation, and $U_j^{\prime}$ is the sum of the square of residuals of points where the formation of the jth complex reaches a reasonable limit (*e.g.* 1%).[5] On the basis of literature data[7,8] and our own observations, the 3σ values are output as estimated errors in parameters.

The subroutine EQUSOL calculates the real roots of equations (1)–(3). The solution of the equation is attempted first by the Newton–Raphson iteration method, but if this fails, the algorithm turns to another iteration procedure which iterates by systematically modified increments and is always successful.

When the values of basic parameters describing the blank curves are calculated, the $[H^+]_c$ values before and after the equivalence point are calculated via the formulas $[H^+]_c = \frac{1}{2} \cdot [(T_H - T_{OH}) + \sqrt{(T_H - T_{OH})^2 + 4 . K_s}]$, and $[H^+]_c = 2 . K_s/[|(T_H - T_{OH})| + \sqrt{(T_H - T_{OH})^2 + 4 . K_s}]$, respectively.

The subroutine PARMOD calculates the optimum values of the five basic parameters, and subroutine TOTOHCH that of the base concentration in the titrant. Subroutine PRINT serves for the output of results of evaluation. The extent of the output depends on the value of variable PR; the most detailed output can be obtained with PR = 6. An illustrative output is given in the Appendix.

THE MAIN CHARACTERISTICS OF THE PROGRAM

The program is constructed for the simultaneous refinement of a maximum of four parameters. The parameters are stored in an array and can be treated by serial number. The parameters that can be refined are as follows: log βs, E^0, g, log j_H, log j_{OH}, log K_s and the base concentration of the titrant. The serial numbers of the last six parameters (E^0, g, *etc.*) are NK + 1, NK + 2, . . ., NK + 6, where NK denotes the number of complexes. If no blank titration is treated, these parameters are stored automatically from the input data. When more than one point group is calculated, only the parameters of the last point group will be printed.

The program is dimensioned for 200 experimental points and 18 complexes, but it can easily be extended. It can treat any point groups, because each experimental point has individual basic parameters stored in proper arrays. The experimental points to be involved in calculations can be given by input, allowing a decrease in running time or treatment of individual point groups. Following a minor alteration, the program allows the simultaneous treatment of measurements made with three electrodes.

The input of the program with the names of variables can be seen in Table 1. It is important to note that the program always executes only one task (refinement of parameter-search) and then returns to a program point determined by the value of variable *W*.

SMALL PROGRAMS FOR CALCULATION OF SPECIES DISTRIBUTION

MAXIPOT-F calculates and outputs the percentage distribution of total metal ion or total ligand in different species. However, it is often necessary to calculate the species distribution under different experimental conditions. We have therefore written a few small programs for different purposes. These programs use the original or simplified EQUSOL subroutine. They are very simple and require only input of the data of the given chemical problem. One of these programs (DIST-QP) is capable of calculating the distribution of T_M and T_L in the complexes M_qL_p as a function of ligand equivalents at constant T_M, another program (DIST-PH) calculates that of complexes $M_qL_pH_r$ as a function of pH, and a third program (BASEQU) solves the previous problem, but as a function of base equivalents added. A fourth program, TITSIM, can simulate a pH-metric titration with species distribution as output.

CONCLUSIONS

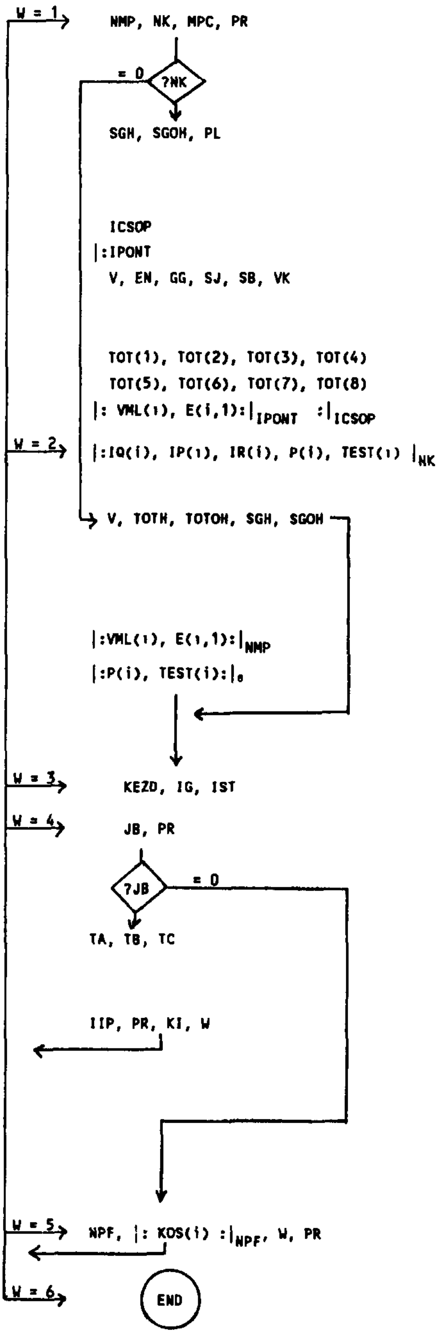
In spite of its simplicity, the present program MAXIPOT-F is capable of solving even the most complicated systems, such as the evaluation of the protonation and zinc complex formation constants of the insulin molecule, which has 16 functional groups,[9] or the silver iodide system in DMSO with (1,1), (6,8), (5,7), (4,6), (2,4) and (1,2) (q,p) complexes,[10] or the calculation of the protonation and complex formation constants of species HL, HL_2, ML, ML_2, MLH_{-1}, and MLH_{-2} of HIDA and its derivatives.[11] It is a short program, consisting of about 800 FORTRAN lines. The input system has been simplified to a maximum and usage of the program does not demand any special knowledge. Although the program has been elaborated to treat the data of the most frequently used pH-metric technique, it can easily be adapted to data originating from other types of measurement.

Both the parameter search and refinement are generally programmed and can be used for any measurement resulting in data that can be treated by unique weighting factors. Even when starting from rough parameter values, the parameter refinement procedure converges well and the parameter-search procedure perfectly substitutes the application of any numeric or graphic method. The minimization of the non-weighted residuals of emfs has proved to be correct,[8] and the stability constants calculated in this way are in good agreement with those in the literature. The particular advantage of the use of emf is that these are the primary readings and the convergence is stable and especially fast.

Through the treatment of parameters by serial number, our main goal was to allow the applicability of evaluation strategies based on chemical considerations. It is well known that, if the constancy of the Nernst factor (g) is assumed, for example, then of the basic parameters of the blank curves, only E^0 and K_s are determining; the correction of diffusion potentials has only a minor influence on the fit. The simultaneous refinement of all four parameters would not be reasonable, because this would result in U_{min} with totally unrealistic j_H and j_{OH} A good strategy, therefore, is as follows.

Table 1

The input scheme of the program MAXIPOT-F
(For further details, see also Ref 1)



NMP, NK, MPC, PR	Number of measured points, Number of complexes, Percentage distribution of complex species related to T_M or T_L (1 or 2, respectively), Print-out of measured data (0 or 1)
SGH, SGOH, PL	Sign of corrections for diffusion potentials in acidic and alkaline region (+1 or -1, respectively), Number of protons capable of dissociation from ligand
ICSOP	Number of point groups to be input
|:IPONT	Number of measured points in the subgroup
V, EN, GG, SJ, SB, VK	Initial volume of titrant, Nernst constant, Nernst factor (59.16 mV at 25 °C), log of correction factor for diffusion potential in acidic and alkaline region, respectively, log K of solvent
TOT(1), TOT(2), TOT(3), TOT(4)	C_H, C_{OH}, C_M, C_L in titrand
TOT(5), TOT(6), TOT(7), TOT(8)	C_H, C_{OH}, C_M, C_L, in titrant
|: VML(i), E(i,1):|$_{IPONT}$:|$_{ICSOP}$	Volume of titrant, Measured emf
|:IQ(i), IP(i), IR(i), P(i), TEST(i) |$_{NK}$	Stoichiometric q, p, and r coefficients of species, log ß of species, its increment
V, TOTH, TOTOH, SGH, SGOH	Initial volume of titrand, C_H in titrand, C_{OH} in titrant, sign of corrections for diffusion potentials in acidic and alkaline region, respectively (+1.0 or -1.0)
|:VML(i), E(i,1):|$_{NMP}$	Volume of titrant, measured emf.
|:P(i), TEST(i):|$_6$	Nernst constant, its increment (e.g. 0.3), Nernst factor, its increment (e.g. 0.2), log of correction factor for diffusion potential in acidic region, its increment (e.g. 0.2), that in alkaline region, its increment (e.g. 0.2), log K_s of solvent, its increment (e.g. 0.03)
KEZD, IG, IST	First and Last experimental points involved in the calculation, the Step between them
JB, PR	Task to be executed (0 or 1 or 2), print format (0 - 6)
TA, TB, TC	If F1 = 1, then starting value, step and upper limit for parameter value search; if F1 = 2, then factors to generate these values
IIP, PR, KI, W	Serial number of parameter to be searched for, Print format, Number of steps after U-minimum. Where to go after executing current task
NPF, |: KOS(i) :|$_{NPF}$, W, PR	Number of parameters to be refined (max. 4). Serial number of parameter(s) to be refined, Where to go after executing current task (1 - 6), Print format (0 - 6)

refinement of E^0 and $\log K_s$ twice, then search for $\log j_H$, then for $\log j_{OH}$, and finally refinement of E^0 and $\log K_s$. This can be achieved with the following input: 0,6,// 2, 1,5, 5,2,// 2, 1,5, 4,2,// 1,4,// −3.0, 0.1, 3.0,// 3,2,2,4,// 1,4,// −3.0, 0.1, 3.0,// 4,2,2,4,// 0,4,// 2, 1,5, 6,6, (// denotes new line). A similar situation can arise when the log βs of minor complexes are refined On this basis, the simultaneous refinement of a maximum of four parameters does not restrict the applicability of the program. On the other hand, a multiparametric problem can also be solved by successive refinement.

The calculation of errors in parameters, which takes into account only experimental points which influence the value of a parameter,[5,8] reflects the reliability of stability constants much better. This is especially important in the case of complicated systems where, as a result of successive complex formation, some complexes can be present only in narrow pH ranges

With a Microsoft 5.1 compiler, the running time of this program is favourable even with an IBM 286 PC. A further advantage of this program is that its structure allows it to be connected to automatic measuring systems or it can yield data for other, e.g. plotter programs. It is also very useful for teaching pH-metric evaluations.

Acknowledgement—This work was supported by the Hungarian Academy of Science, Project OTKA 1305/1991

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APPENDIX

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             OUTPUT OF MAXIPOT - F,  PROTONATION OF ETHANE - TRICARBOX.  ACID, # 630


          V,ML        TOT H        TOT OH        TOT M         TOT L      E,MSD     A        Z       PH
   .
   .
   .
  20     4.000    .22863E-01   .72590E-02   .92593E-19   .45737E-02   179.60  -.4116   2.4139  2.3407
  21     4.200    .22778E-01   .75939E-02   .92251E-19   .45569E-02   177.70  -.3323   2.4023  2.3729
  22     4.400    .22695E-01   .79262E-02   .91912E-19   .45401E-02   175.90  -.2529   2.3827  2.4033
  23     4.600    .22612E-01   .82562E-02   .91575E-19   .45235E-02   173.70  -.1736   2.3727  2.4410
  24     4.800    .22529E-01   .85837E-02   .91241E-19   .45070E-02   172.00  -.0942   2.3419  2.4697
  25     5.000    .22447E-01   .89088E-02   .90909E-19   .44906E-02   169.50  -.0148   2.3298  2.5120
  26     5.200    .22366E-01   .92316E-02   .90580E-19   .44743E-02   167.20   .0645   2.3068  2.5508
  27     5.400    .22285E-01   .95521E-02   .90253E-19   .44581E-02   164.60   .1439   2.2859  2.5948
  28     5.600    .22205E-01   .98702E-02   .89928E-19   .44421E-02   161.90   .2232   2.2616  2.6404
  29     5.800    .22125E-01   .10186E-01   .89606E-19   .44262E-02   159.20   .3026   2.2319  2.6861
  30     6.000    .22046E-01   .10500E-01   .89286E-19   .44104E-02   156.10   .3819   2.2040  2.7385
   .
   .
   .

SERIAL NUMBER OF PARAMETERS TO BE REFINED:   1    2    3

      *** REFINED PARAMETERS: ***


COMP. OF CPXES, Q,P,R:   0  1  1   0  1  2   0  1  3
LOG BETAS:                 5.7387   9.9020   12.1316
                        EO:  318.108 G:  59.160 LOG J/H, J/OH:   1.2000  1.7000 LOG KS: -13.6430 TOH:   .097997

SQUARE OF RESIDUALS:   141.24570000 FROM    90 POINTS
STANDARD DEVIATION:      1.281558

REFD. VAL. OF PAR. #:  1    5.7387   ERROR:   .0141  FROM    41  POINTS
REFD. VAL. OF PAR. #:  2    9.9020   ERROR:   .0119  FROM    57  POINTS
REFD. VAL. OF PAR. #:  3   12.1316   ERROR:   .0118  FROM    42  POINTS
```

```
                    CONCENTRATIONS IN MMOL
      V, ML     TOT H     TOT OH      TOT M      TOT L   E,MSD  E,CALC   DTA E    LOG M      LOG L  PH,MSD  PH,CLD    DF H   DF O
  .
  .
  .
 20  4.000   22.8629    7.2590      .0000     4.5737  179.60  179.56    -.04  -19.0334   -7.7973   2.341   2.341   -.072    .00
 21  4.200   22.7785    7.5939      .0000     4.5569  177.70  177.52    -.18  -19.0350   -7.7116   2.373   2.375   -.067    .00
 22  4.400   22.6948    7.9262      .0000     4.5401  175.90  175.95     .05  -19.0366   -7.6523   2.403   2.402   -.063    .00
 23  4.600   22.6116    8.2562      .0000     4.5235  173.70  174.19     .49  -19.0382   -7.5833   2.441   2.432   -.059    .00
 24  4.800   22.5291    8.5837      .0000     4.5070  172.00  171.79    -.21  -19.0398   -7.4862   2.470   2.472   -.053    .00
 25  5.000   22.4472    8.9088      .0000     4.4906  169.50  169.69     .19  -19.0414   -7.4052   2.512   2.508   -.049    .00
 26  5.200   22.3658    9.2316      .0000     4.4743  167.20  167.32     .12  -19.0430   -7.3136   2.551   2.548   -.045    .00
 27  5.400   22.2851    9.5521      .0000     4.4581  164.60  164.77     .17  -19.0445   -7.2148   2.595   2.591   -.041    .00
 28  5.600   22.2049    9.8702      .0000     4.4421  161.90  161.77    -.13  -19.0461   -7.1024   2.640   2.642   -.036    .00
 29  5.800   22.1254   10.1861      .0000     4.4262  159.20  159.42     .22  -19.0477   -7.0144   2.686   2.682   -.033    .00
 30  6.000   22.0463   10.4997      .0000     4.4104  156.10  156.43     .33  -19.0492   -6.9060   2.738   2.732   -.029    .00
  .
  .
  .


                                   PERCENTAGE DISTRIBUTION OF TOTAL L IN CPXES


COMPOSITION OF SPECIES:   0  1  1   0  1  2   0  1  3   1  0  0   0  1  0
         DTA E   PH,C
  .
  .
  .
 20      -.038   2.34       .86     55.10     43.67      0.00      0.00
 21      -.184   2.38       .97     57.41     42.01      0.00      0.00
 22       .049   2.40      1.05     58.46     40.24      0.00      0.00
 23       .495   2.43      1.16     59.98     38.56      0.00      0.00
 24      -.207   2.47      1.32     62.42     36.54      0.00      0.00
 25       .194   2.51      1.47     64.09     34.56      0.00      0.00
 26       .118   2.55      1.66     65.99     32.44      0.00      0.00
 27       .167   2.59      1.90     68.15     30.33      0.00      0.00
 28      -.131   2.64      2.20     70.14     27.77      0.00      0.00
 29       .222   2.68      2.46     71.78     25.94      0.00      0.00
 30       .333   2.73      2.82     73.25     23.56      0.00      0.00
  .
  .
  .
```