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A GENERALIZED APPROACH FOR THE CALCULATION AND AUTOMATION OF POTENTIOMETRIC TITRATIONS
Part 1. Acid-Base Titrations

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SUMMARY

Fast and accurate calculation procedures for pH and redox potentials are required for optimum control of automatic titrations. The procedure suggested is based on a three-dimensional titration curve $V = f(\text{pH, redox potential})$. All possible interactions between species in the solution, e.g., changes in activity coefficients and influence of redox potential on pH variations, are taken into account. The number of titrant additions can be reduced considerably without loss of precision, by using the fact that the pH of a protolyte or mixture of protolytes at some fraction titrated does not depend strongly on the actual concentration.

Although the number of direct instrumental methods of chemical analysis is continuously increasing, titrations are still important in routine practice in many laboratories. The reason may be that no direct instrumental methods with sufficient selectivity are available, but more probably that better precision is possible with titrations. Titrations done manually tend to be time-consuming and the results often depend on the skill of the technician. Both drawbacks can be largely overcome by automation; various automated titrators are commercially available. Many options are available to control the titration procedure, the addition of the titrant and the evaluation of the data. Table 1 presents a survey of the more important options. Reviews [1, 2] and a monograph [3] on automatic titrations are available. The whole subject can be subdivided into two parts: (i) control of the performance of the actual titration, and (ii) the calculation procedure(s) involved. The more recent literature on both subjects is summarized in Tables 2 and 3, respectively.

Especially for more complicated mixtures, existing automatic titration methods based on calculations with all data points are time-consuming and demand relatively large computing capacities; however, titrant delivery can be relatively simple, e.g., by the use of constant increments. Procedures in which the titration leads to an exact evaluation of the end-point generally force the use of more sophisticated control and delivery systems based on

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TABLE 1

Survey of automatic potentiometric titrations

Control mechanism
(1) Mechanical (2) Electronic (3) Computational (microprocessor)

Titrant addition
(1) Continuous
(a) Constant speed
(b) Decreasing speed
(2) Stepwise
(a) Equal volumes
(b) Decreasing volumes
(i) Mechanical control
(ii) Dynamic control with calculation from an empirical expression or system parameters

Method of obtaining end-point
(1) Addition of titrant is continued beyond the end-point; calculation based on several data points
(2) Addition of titrant stops at end-point; calculation based on one data point

Evaluation of end-point
(1) From inflection point of sigmoidal curve
(a) Biggest potential jump
(b) Steepest part of curve (tangential method)
(c) Intersecting with two midpoints of circles (Tubbs' method)
(d) Maximum of first derivative
(e) Zero of second derivative
(2) From linearized curve
(3) End-point potential
(a) Experimentally (by calibration titration)
(b) Calculated

on-line evaluation of the measurements. Mostly, this evaluation is based on a very simple model for the titration reaction, which does not take into account all the interactions that actually take place in the solution, such as protolytic side-reactions and electrostatic interactions as expressed by the respective activity coefficients of the species.

The object of the investigation presented here was to develop a calculation procedure that is fast enough to be used in an on-line control system for the titrant delivery but will still account for all possible interactions in the solution. As for the titration procedure itself, the number of additions of titrant has to be minimized, maintaining an acceptable level of precision in the determination of the end-point. Furthermore, the end-point found should be identical with the real equivalence point.

THEORY

In order to discuss the calculation procedure in a generalized form, the following symbols are adopted. The letter P is used for any protolyte, A for protolytic compounds that have no redox properties, and X for the set of redox substances; the suffix ox or red denotes the oxidation state if such

TABLE 2

A selected chronological survey of automatic potentiometric titration procedures

Ref.		Equipment computer	Titrant addn.	End-point evaluation	No. of points	Precision (%)
[4]	Empirical eqn. for calcn. of ΔV from preceding titration data points.	Radiometer system	Empirical formula	Inflexion point number.	12	0.6
[5]	Application of micropr. to control titration	INTEL 8001 CYBA-0	Constant rate	Max $\Delta pH/\Delta V$	—	0.3
[6]	Microcomp.-controlled automatic titrator with automatic sample processing.	Mettler system	No information		—	—
[7]	Autom. pot./photom. system, coulom. titrant generation; 3-dimensional plots.	PDP DEC-syst.-10	Constant rate	Overtitration, then calculation	—	
[8]	Versatile microcomp. contr. titrator for pot., photom., coulom., etc. titrations.	ADD 8080	Two different constant rates	Max $\Delta E/\Delta V$	200	0.1
[9]	Microcomp. contr. system for automatic pK determinations.	INTEL 8080	Simplified Christiansen method		50	0.04
[10]	Microproc. contr. automatic differential titr.	INTEL MCS-80	Constant ΔV	Max $\Delta E/\Delta V$	30	0.7
[11]	Microcomp. contr. automatic photometric syst.	INTEL 8080A	Constant	Break point of plot	500	0.6
[12]	Stepwise addition of equal volumes; also suitable for mixtures of polyprotic acids/bases	HP 9835/45	Constant ΔV	First deriv.	25	
[13]	Automatic microcomp. contr. potentiometric titrator for student demonstrations	ALTAIR 8800B	Two different constant rates	$\Delta E/\Delta V$ max.		0.1
[14]	Microcomp. contr. pot. analysis, describes a new computer language CONVERS.	IMSAI 8080	Christiansen method	Second deriv.	50	0.1—1.0
[15]	Learning method, for strong acids and bases.	JOLT system	Determination in learning mode		As manual	
[16]	Full automated computer-controlled system. ΔV approximated on the basis of constant ΔpH.	HP 9835/45	From preceding data	First deriv.	25	—
[17]	Computer contr. titration based on systems theory.	ZILOG 2.80 VARIAN V76	Preceding data, feedback factor	First and second deriv. hyperbolic function	50	0.05
[18]	Robotic sample preparation station. A high-class hardware system.	APPLE II	Constant rate	First deriv.	28	0.6
[19]	A microcomp. contr. system for pharmaceutical use (pK determ.).	IM-6100 m.p.	Constant rate	Second deriv. corrected	100	1.0

specification is necessary, and the suffix s or t refers to the solution titrated (sample) or the titrant, respectively. For example

in the solution $X_s \rightarrow X_{1s} \cdots X_{nxs}$

in the titrant $X_t \rightarrow X_{1t} \cdots X_{nxt}$

where $n$xs is the number of different redox substances in solution, and $n$xt is the number of different redox substances in the titrant; X_s can be present in the ox form, $X_{1sox} \cdots X_{nxsox}$; X_s can be present in the red form: $X_{1sred} \cdots X_{nxsred}$. If $C_{(i)}$ is the analytical concentration of substance i, and

TABLE 3

A selected chronological survey of calculation methods for potentiometric titration curves

Ref.	Topic	Computer language	
[20]	General		End-point of potentiometric titn. at the steepest inflexion of titn. curve.
[21]	Redox, pH		Linearization of titn. curve. The most widely used method for detn. of end-point.
[22]	General		Graphical determination of end-point with the "circle method".
[23]	Redox		Exact numerical calculation of titn. curves with four equations. Definition of inhomogeneous redox systems.
[24]	General		Rigorous least-squares adjustment for calculation of non-linear eqns.
[25]	pH, redox	ALGOL	HALTAFALL program.
[26]	pH, redox	ALGOL	Computer calcn. of titn. curves in multicomponent systems.
[27]	pH, redox		Calcn. of redox titn. curves. Proved: equivalence point ≠ inflexion point.
[28]	pH	ALGOL	Improved linear titn. plots, with activity coefficients.
[29]	General		Numerical methods for data-fitting problems. Detailed review and comparison of methods.
[30]	pH		Learning machine method for calcn. of titn. curves by multiparametric curve-fitting.
[31]		FORTRAN	Non-linear least-squares approach. Simplified LETAGROP = ACBA.
[32]	pH		Calculation of pH titn. curves and end-points. Iterative method with interval halving.
[33]	pH		Unified calcn. of titn. curves (for limited number of components).
[34]	General		Multicomponent analysis computations using Kalman filtering.
[35]	pH, redox		Titration assisted by microcomputers. Electro-activity treated similarly to pH.
[36]	pH		Approximation formula for mixtures of acids and bases. Explicit formula for $[H^+]$ in simple cases.
[37]	General	FORTRAN	Resolution of overlapping electrochem. peaks with Kalman filtering.
[38]	pH	BASIC	TITFIT a comprehensive program, Newton—Gauss—Marquardt method.
[39]	pH		Calcn. using $[H^+]$ as independent and $[B^+]$ as dependent variable using pocket calculators.
[40]	pH	BASIC	Desk-computer program MINIPOT; utilisation of Gauss and Wentworth method.
[41]	pH		The limit of separation of two weak acids.
[42]	pH, redox		Titration in a mixture with resolution of difference u.v.-visible spectra.
[43]	pH	FORTRAN	Data analysis for up to nine components with TITAN program.
[44]	pH		Bjerrum plots for determination of systematic conc. errors.
[45]	pH, redox		Evaluation of digital potentiometric titns. by the Tubbs method.

[X] the actual concentration of species X, then $C(X_{is}) = C(X_{isox}) + C(X_{isred})$ and $C(X_{it}) = C(X_{itox}) + C(X_{itred})$.

For protolyte compounds that have no redox properties $A_s \rightarrow A_{1s} \cdots A_{nas}$ in solution and $A_t \rightarrow A_{1t} \cdots A_{nat}$ in the titrant, where $n$as is the number of protolytes without redox properties in solution, and $n$at is the number of protolytes without redox properties in the titrant.

For the initial analytical (formal) concentration in both solution and titrant, the symbol C ($C_{(i)}$ for the substance i) is used; concentrations in the solution during the titration are denoted by C'

$$C'_{(is)} = C_{(is)}V_0/(V_0 + V); \quad C'_{(it)} = C_{(it)}V/(V_0 + V) \tag{1}$$

Two further symbols will be used for characterization of the substances involved: taking the mostly deprotonated species of a substance as a Brønsted base, $N(i)$ is the maximum number of protons that can be accepted by this species and $g(i)$ is the charge of its totally deprotonated form: in general,

$g(i) \leqslant N(i)$. For example,

EDTA $N = 6; g = 4$
H_3PO_4 $N = 3; g = 3$
NH_3 $N = 1; g = 0$
Fe^{3+} $N = 3; g = 0$ $\{Fe^{3+}(H_2O)_6 + 3H_2O \rightarrow Fe(OH)_3(H_2O)_3 + 3H_3O^+\}$
Me^{2+} $N = 2; g = 0$ $\{Me^{2+} + 4H_2O \rightarrow Me(OH)_2 + 2H_3O^+\}$
K^+ $N = 1; g = 0$

The protonation constants for each species are subscripted with i, the subscript of the substance and j for its serial number. With charges omitted, $K_{i,1} = [HA]/[H][A]$, $K_{i,2} = [H_2A]/[H][HA]$, ... (charges omitted) $K_{i,j} = [H_jA]/[H][H_{j-1}A], \ldots, K_{i,N(i)} = [H_{N(i)}A]/[H][H_{N(i)-1}A]$.

For any protolyte, P, the analytical concentration can be written as

$$C(P) = \sum_{k=0}^{N(P)} [H_kP^{[k-g(P)]+}] \tag{2}$$

where P is X_{isox}, X_{isred}, A_{is} or X_{itox}, X_{itred}, A_{it}. Using the protonation constants, Eqn. (2) can be written as

$$C(P) = [P^{-g(P)}]\ \{1 + \beta_{P,1}[H^+] + \beta_{P,2}[H^+]^2 + \ldots + \beta_{P,N(P)}[H^+]^{N(P)}\} \tag{3}$$

where $\beta_{P,1} = K_{P,1}$; $\beta_{P,2} = K_{P,1}K_{P,2}$; $\ldots$ $\beta_{P,N(P)} = K_{P,1}K_{P,2} \ldots K_{P,N(P)}$ or generally $\beta_{P,k} = \Pi_{j=0}^{k} K_{P,j}$ with $\beta_{P,0} \equiv K_{P,0} = 1$. This yields

$$C_{(P)} = [P^{-g(P)}] \sum_{k=0}^{N(P)} [H^+] \prod_{j=0}^{k} K_{P,j} \equiv [P^{-g(P)}]\alpha_{P(H)} \tag{4}$$

where $\alpha_{P(H)}$ is Ringbom's side-reaction coefficient for the interaction of P with protons. So

$$[P^{-g(P)}] = C_{(P)}\alpha_{P(H)}^{-1} \tag{5}$$

$$\text{and } [H_kP] = C_{(P)}\alpha_{P(H)}^{-1}[H^+]^k \prod_{j=0}^{k} K_{P,j} \equiv C_{(P)}\alpha_{P(H)}^{-1}[H^+]^k\beta_{P,k} \tag{6}$$

For the redox substances the following quantities are defined $E^0_{(i)}$ is the standard potential of substance i, and $z_{(i)}$ the number of electrons involved in the redox reaction; R, T and F have their usual meanings. The Nernst equation can be used to calculate the redox state of the substance at any stage of the titration. For this calculation, E^0 is chosen so that it applies to the most positively charged form of the oxidized species (i.e., $H_{N(Xiox)}X_{iox}$ with the positive valency of $[N_{(Xiox)} - g_{(Xiox)}]$) whereas for the reduced species, the most negatively charged form X_{ired} with the negative valency of $g_{(Xired)}$ is chosen. The Nernst equation then reads

$$E = E^0_{(X)} + (RT/z_{(X)}F) \ln \{[H_{N(Xox)}X_{ox}]/[X_{red}]\} \tag{7}$$

with $[H_{N(Xox)}X_{ox}] = C'_{(Xox)}\alpha^{-1}_{Xox(H)}[H^+]^{N(Xox)}\beta_{N(Xox)}$ and $[X_{red}] = C'_{(Xred)} \cdot \alpha^{-1}_{Xred(H)}$. Together with $[H^+] = 1$ (pH = 0), this reduces to

$$E = E^0_{(X)} + (RT/z_{(X)}F)\ln\{\alpha^*_{Xred(H)}\beta_{N(Xox)}/\alpha^*_{Xox(H)}\} + (RT/z_{(X)}F)\ln\{C'_{(Xox)}/C'_{(Xred)}\} \quad (8)$$

Here $\alpha^*_P = (\alpha_{P(H)})_{pH=0}$

The Nernst equation can now be rewritten as

$$E = E^{0*}_{(X)} + (RT/z_{(X)}F)\ln\{C'_{(Xox)}/C'_{(Xred)}\} \quad (9)$$

With $E^{0*}_{(X)} = E^0_{(X)} + (RT/z_{(X)}F)\ln\{\alpha^*_{Xred(H)}\beta_{N(Xox)}/\alpha^*_{Xox(H)}\}$ (10)

If $\Psi_{(X)}$ is defined as

$$\Psi_{(X)} = C'_{(Xox)}/C'_{(Xred)} \quad (11)$$

then $\Psi_{(X)}$ can be calculated from

$$\Psi_{(X)} = \exp\{(E - E^{0*}_{(X)})z_{(X)}F/RT\} \quad (12)$$

and because $C'_{(X)} = C'_{(Xox)} + C'_{(Xred)}$

$$C'_{(Xred)} = C'_{(X)}\{1 + \Psi_{(X)}\}^{-1} \quad (13)$$

$$C'_{(Xox)} = C'_{(X)}\Psi_{(X)}\ \{1 + \Psi_{(X)}\}^{-1} \quad (14)$$

Now two equations can be derived for the two unknown parameters E and pH in the titration mixture. The first equation uses the electron balance as a basis, i.e., the equivalents of reductant produced in the sample equals the equivalents of reductant consumed in the titrant. With Eqn. 13, the equilibrium concentration of the reduced species can be found from the analytical concentrations in the titration mixture, giving

$$\{V_0 + V\}\{\sum_{i=1}^{nxs} C'_{(Xis)}z_{(Xis)}(1 + \Psi_{(Xis)})^{-1}\} - V_0\{\sum_{i=1}^{nxs} C^0_{(Xis)}z_{(Xis)}\} = V\{\sum_{i=1}^{nts} C^0_{(Xit)}z_{(Xit)}\} - \{V_0 + V\}\{\sum_{i=1}^{nts} C'_{(Xit)}z_{(Xit)}(1 + \Psi_{(Xit)})^{-1}\} \quad (15)$$

Here $C^0_{(Xi)}$ represents the analytical concentration of substance X, originally present in the titrant or sample in reduced form.

With Eqn. 1 this balance can be rewritten as

$$V_0\{\sum_{i=1}^{nxs} C_{(Xis)}z_{(Xis)}\{1 + \Psi_{(Xis)}\}^{-1} - \sum_{i=1}^{nxs} C^0_{(Xis)}z_{(Xis)}\} + V\{\sum_{i=1}^{nxt} C_{(Xit)}z_{(Xit)}\{1 + \Psi_{(Xit)}\}^{-1} - \sum_{i=1}^{nxt} C^0_{(Xit)}z_{(Xit)}\} = 0 \quad (16)$$

or in simplified form

$$F_1 = V_0 P_{1(s)} + V P_{1(t)} = 0 \quad (17)$$

For the second expression, electroneutrality is taken as the starting point

$$\sum_{\substack{\text{all}\\ \text{substances}}} \sum_{k=0}^{N(i)} \{g(i) - k\} [H_k P_i] - [H^+] + [OH^-] = 0 \tag{18}$$

The symbol Q_i is now introduced

$$Q_i = C'_{Pi} \sum_{k=0}^{N(i)} \{g(i) - k\} [H_k P_i] = \sum_{k=0}^{N(i)} \{g(i) - k\} [H^+]^k \beta_{i,k} \alpha_i^{-1}(H) \tag{19}$$

Equations 2, 13 and 14, with the necessary transformations and simplifications, yield

$$V_0 \{[OH^-] - [H^+] + \sum_{i=1}^{nas} C_{(Ais)} Q_{(Ais)} + \sum_{i=1}^{nxs} C_{(Xis)} [Q_{(Xisox)} \Psi_{(Xis)} \{1 + \Psi_{(Xis)}\}^{-1} + Q_{(Xisred)} \{1 + \Psi_{(Xis)}\}^{-1}]\} + V\{[OH^-] - [H^+] + \sum_{i=1}^{nat} C_{(Ait)} Q_{(Ait)} + \sum_{i=1}^{nxt} C_{(Xit)} [Q_{(Xitox)} \Psi_{(Xit)} \{1 + \Psi_{(Xit)}\}^{-1} + Q_{(Xitred)} \{1 + \Psi_{(Xit)}\}^{-1}]\} = 0 \tag{20}$$

or in simplified form

$$F_2 = V_0 P_{2(s)} + V P_{2(t)} = 0 \tag{21}$$

Calculation procedure

For the numerical calculation of F_1 and F_2, the Newton—Raphson method was used. The advantage of this procedure is its fast convergence and the relatively small computer capacity needed. It has some disadvantages, however, for functions that do not show monotonous changes. In that case, large values of the derivatives can be obtained sometimes, which enhances the risk of ending up at a sub-minimum in an irrelevant region of the response plane. By setting appropriate limits of pH and V values and by limiting the allowable maximum and minimum step size, such pitfalls can be avoided. If intermediate results start to oscillate between the limiting pH and V values, one or both limits have to be changed.

Table 4 summarizes the expressions to be calculated. It can be seen that the mathematical expressions of the derivatives to be used in the Jacobian are very similar to the original functions. Hence, this calculation can be easily performed simultaneously with the calculation of the function itself.

In order to reach a precision of 1 in 10^6, generally, 5—6 iterations are necessary, provided that the starting conditions were chosen properly. When no such conditions are available, the arbitrarily chosen values pH = 7, E = 0.5 are used.

TABLE 4

Survey of the equations used for the calculation of the three-dimensional titration curve
(Indices, charges and [ ] are omitted where possible. For explanation of the symbols, see text.)

$D_1 = \frac{\delta F_1}{\delta E} \cdot \frac{\delta F_2}{\delta H} - \frac{\delta F_1}{\delta H}\frac{\delta F_2}{\delta E}$	$\Delta E = \left(-F_1\frac{\delta F_2}{\delta H} + F_2\frac{\delta F_1}{\delta H}\right)/D$	$\Delta H = \left(F_1\frac{\delta F_2}{\delta E} - F_2\frac{\delta F_1}{\delta E}\right)/D$
$F_1 = V_0 P_{1(s)} + V P_{1(t)}$	$\frac{\delta F_1}{\delta E} = V_0\frac{\delta P_{1(s)}}{\delta E} + V\frac{\delta P_{1(t)}}{\delta E}$	$\frac{\delta F_1}{\delta H} = V_0\frac{\delta P_{1(s)}}{\delta H} + V\frac{\delta P_{1(t)}}{\delta H}$
$F_2 = V_0 P_{2(s)} + V P_{2(t)}$	$\frac{\delta F_2}{\delta E} = V_0\frac{\delta P_{2(s)}}{\delta E} + V\frac{\delta P_{2(t)}}{\delta E}$	$\frac{\delta F_2}{\delta H} = V_0\frac{\delta P_{2(s)}}{\delta H} + V\frac{\delta P_{2(t)}}{\delta H}$
$P_1 = \sum_1^{nx} C_{(X)} z S - \sum_1^{nx} C^0_{(X)} z$	$\frac{\delta P_1}{\delta E} = \sum_1^{nx} C_{(X)} z \frac{\delta S}{\delta E}$	$\frac{\delta P_1}{\delta H} = \sum_1^{nx} C_{(X)} z \frac{\delta S}{\delta H}$
$P_2 = \frac{K_W}{H} - H + \sum_1^{na} C_{(A)} Q_{(A)} + \sum_1^{nx} C_{(X)}[(1-S)Q_{(Xox)} + S Q_{(Xred)}]$	$\frac{\delta P_2}{\delta E} = \sum_1^{nx} C_{(X)}(Q_{(Xred)} - Q_{(Xox)})\frac{\delta S}{\delta E}$	$\frac{\delta P_2}{\delta H} = \frac{-K_W}{\delta H^2} - 1 + \sum_1^{na} C_{(A)}\frac{\delta Q_{(A)}}{\delta H} + \sum_1^{nx} C_{(X)}[(1-S)\frac{\delta Q_{(Xox)}}{\delta H} + S\frac{\delta Q_{(Xred)}}{\delta H} + \frac{\delta S}{\delta H}(Q_{(Xred)} - Q_{(Xox)})]$
$S = (1+\phi)^{-1}$	$\frac{\delta S}{\delta E} = -\frac{\delta \phi}{\delta E}(1-\phi)^{-2}$	$\frac{\delta S}{\delta H} = -\frac{\delta \phi}{\delta H}(1-\phi)^{-2}$
$\phi = \frac{M_{(ox)}}{M_{(red)}} \exp\frac{zF}{RT}(E - E^{0*})$	$\frac{\delta \phi}{\delta E} = \frac{zF\, M_{(ox)}}{RT M_{(red)}} \exp\frac{zF}{RT}(E - E^{0*})$	$\frac{\delta \phi}{\delta H} = \left(\frac{\delta M_{(ox)}}{\delta H} M_{(red)} - M_{(ox)}\frac{\delta M_{(red)}}{\delta H}\right)(M_{(red)})^{-2} \exp\frac{zF}{RT}(E - E^{0*})$
$M_{(ox)} = \alpha_{(ox)} H^{-N(ox)}$		$\frac{\delta M_{(ox)}}{\delta H} = \frac{\delta \alpha_{(ox)}}{\delta H} H^{-N(ox)} - \alpha_{(ox)} N_{(ox)} H^{-(N_{(ox)}+1)}$
$M_{(red)} = \alpha_{(red)} \beta^{-1}_{N(red)}$	$E^{0*} = E^0_k + \frac{RT}{zF}\ln\frac{\alpha^*_{(red)}\beta_{N(ox)}}{\alpha^*_{(ox)}}$	$\frac{\delta M_{(red)}}{\delta H} = \frac{\delta \alpha_{(red)}}{\delta H}\beta^{-1}_{N(red)}$
	$\alpha^* = \sum_{k=0}^{N} \beta_k$	
$Q = L/\alpha$		$\frac{\delta Q}{\delta H} = \left(\frac{\delta L}{\delta H}\alpha - \frac{\delta \alpha}{\delta H} L\right)\alpha^{-2}$

$$L = \sum_{k=0}^{N} (g-k)H^k\beta_k$$

$$\alpha = \sum_{k=0}^{N} H^k\beta_k$$

$$\beta_k = \prod_{j=0}^{k} K_j/\gamma_k (K_0 = 1')$$

$$\gamma_k = \exp\left[-(g-k)^2 0.509 \left\{\sqrt{I}\,(1+\sqrt{I})^{-1} + BI\right\}\right]$$

$$I = 1/2\,[10^{-pH}\cdot\gamma_H^{-1} + K_w(10^{-pH}\cdot\gamma_{OH})^{-1}\cdot\Sigma C \sum_{k=0}^{N} (g-k)^2 H^k\beta_k\alpha^{-1}]$$

$$\frac{\delta L}{\delta H} = \sum_{k=0}^{N} k(g-k)H^{k-1}\beta_k$$

$$\frac{\delta \alpha}{\delta H} = \sum_{k=0}^{N} kH^{k-1}\beta_k$$

In Eqns. 3, 4 and 6, stability constants were used based on concentrations. If thermodynamic constants are used, concentrations must be replaced by activities. In that case, activity coefficients for each individual species (γ_{H_kP}) must be calculated. Apart from H_3O^+ and OH^-, the Davies equation was adopted for all species

$$-\log \gamma_{H_kP} = \{g(P) - k\}^2 A \{I^{1/2}(1 + I^{1/2})^{-1} + BI\} \quad (22)$$

where A and B are constants (for aqueous solutions at 25°C, $A = 0.509$ and $B = 0.2$). The ionic strength is calculated from the formula

$$I = 0.5 \left[10^{-pH}\gamma_H^{-1} + K_w(10^{-pH}\gamma_{OH})^{-1} + \sum_{\substack{all \\ P}} C(P) \sum_{k=0}^{N(P)} \{\{g(P) - k\}^2 \cdot [H^+]^k \beta_k \alpha_{P(H)}^{-1}\}\right] \quad (23)$$

This Davies equation has the advantage of being applicable to solutions with a widely variable ionic strength while no specific information about the substance is required. Therefore, it can be easily incorporated in the program. For H_3O^+ and OH^-, the extended Debye—Hückel equations are used

$$-\log \gamma = 0.5085\, I^{1/2}(1 + 0.328\sigma I^{1/2})^{-1} \quad (H^+ : \sigma = 3 \text{ and } OH^- : \sigma = 9) \quad (24)$$

Titration procedure

The concept of optimized titrant delivery is based on the fact that the difference in the shape of titration curves of two systems of similar qualitative composition, but different in concentration, is very small, even in the region of the equivalence point. This allows the use of an "indicator curve" calculated with a concentration of the compound to be determined that is definitely smaller than the guessed concentration for controlling the titrant delivery. The titration can then be done with a small number of arbitrarily chosen steps until the pH of the indicator curve at the end-point is reached. Overtitration is thus avoided. At this stage it is possible to calculate a fairly accurate estimate of the unknown concentration based on the actually measured data pairs of pH and volume of titrant. With this estimate, a new value of the pH of the expected equivalence point can be calculated. Now a maximum change in the pH (ΔpH) per titration step can be found from the required precision of the titration and the titration can be completed by titrant addition steps corresponding to this ΔpH value. After each of these steps, the estimate of the unknown concentration is updated and the titration is finished when the last calculated equivalence point pH is reached.

The final correct concentration can be calculated with the use of all the titration data, but the equivalence volume found in the procedure described above also gives the wanted information with the required accuracy.

In practice, the control of the first stage of the titration is based on an indicator titration curve calculated with a concentration of the component

to be determined equal to one half of the guessed concentration. An example is given in Fig. 1 and Table 5. First the pH_{ind} values on the indicator curve are calculated at titration fractions of 0.5, 0.9, 0.99, 0.999 and 1.0. This indicator curve is based on a concentration $C = C_{guess}/2$. The values are tabulated in the first column of Table 5 and correspond to the points △1, △2, etc. in Fig. 1. Subsequently, the titrant volumes needed to reach these pH_{ind} values are calculated for the guessed concentration (second column, Table 5; points □1, □2, etc. in Fig. 1). The first increment, $\triangle V_1$, is added and the actual pH is measured (point ○2). This pH corresponds to a volume on the guessed curve which in this case is smaller than V_1. In Table 5 this volume is denoted as V_{old} (third column). The second increment $\triangle V_2$ is obtained as the difference between V_{guess} (second column) and V_{old} (third column). After addition of this increment, the actual pH (○3 in Fig. 1) is measured and the corresponding V_{old} is calculated. This procedure is repeated 5 times.

TABLE 5

The first five titration points calculated for the titration of sodium acetate (0.01 M) with NaOH (1.0 M) with the fractions titrated (fr): (1) 0.5; (2) 0.9; (3) 0.99; (4) 0.999; (5) 1.0 for different first guessed concentrations ($C_{(g)}$). V_0 = 100.0 ml, pK = 4.76, pH_{ep} = 3.3891

	pH_{ind}	V_{guess}	V_{old}	$\triangle V$	V_{added}	$pH_{measured}$
Calc. with	$C_{guess}/2$ $V = V_{ep}$. fr	C_{guess} pH_{ind}	C_{guess} $pH_{m\ old}$	V_{guess} $-V_{old}$	$\Sigma \triangle V$	C_{real} V_{added}
	$C_{guess} = 0.008\ M$					
	4.7386	0.3930	0.0	0.3930	0.3930	4.9061
	3.9410	0.6982	0.3165	0.3817	0.7747	4.1957
	3.6268	0.7660	0.6225	0.1434	0.9181	3.7642
	3.5970	0.7715	0.7398	0.0317	0.9498	3.6290
	3.5937	0.7721	0.7650	0.0071	0.9569	3.6023
	$C_{guess} = 0.010\ M$					
	4.7338	0.4911	0.0	0.4911	0.4911	4.7338
	3.8919	0.8834	0.4911	0.3923	0.8834	3.8918
	3.5801	0.9607	0.8834	0.0773	0.9607	3.5801
	3.5403	0.9677	0.9607	0.0070	0.9677	3.5473
	3.5437	0.9683	0.9677	0.0006	0.9683	3.5437
	$C_{guess} = 0.016\ M$					
	4.7235	0.7848	0.0	0.7848	0.7848	4.1717
	3.8506	1.4195	1.2449	0.1746	0.9594	3.5862
	3.4834	1.5464	1.5161	0.0303	0.9897	3.4399
	3.4432	1.5576	1.5585	neg.	0.9897	3.4399
	3.4387	1.5598	1.5585	0.0003	0.9900	3.4384
	$C_{guess} = 0.020\ M$					
	4.7185	0.9800	0.0	0.9800	0.9800	3.4875
	3.8335	1.7770	1.9215	neg.	0.98	3.4875
	3.4384	1.9377	1.9215	0.0162	0.9962	3.4078
	3.3940	1.9518	1.9518	0.0	0.9962	3.4078
	3.3891	1.9534	1.9518	0.0016	0.9978	3.3999

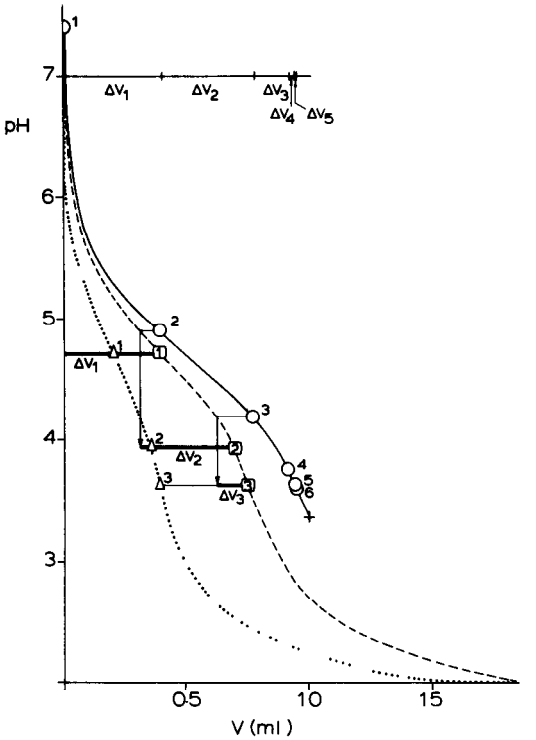

Fig. 1. Titration curves for the system given in Table 5: (—) titration curve; (- - -) first guess curve; (· · ·) indicator curve. (○) Measurement points; (□) indicator values; (△) guessed values; (+) equivalence point. ΔV is the difference of projected pH values on the guessed curve: $\Delta V = V_{(\text{pH ind})} - V_{(\text{pH measured})}$.

EXPERIMENTAL

Chemicals

Stock solutions of boric, phosphoric and oxalic acid, sodium acetate and potassium hydrogenphthalate were prepared from analytical-grade reagents (Merck). Solutions with known proportions of substances were made by mixing the stock solutions. Sodium acetate was dried at 105°C for 2 h. Phosphoric acid solution was made by diluting the 85% reagent solution and its concentration was checked by titration with sodium hydroxide. Titrant solutions of sodium hydroxide and hydrochloric acid were prepared by diluting Merck ampoules with carbon dioxide-free, double-distilled water and standardized against potassium hydrogenphthalate and also checked against Tris.

Apparatus

Titrations were done in a Metrohm titration vessel thermostated at 22.0 ± 0.05°C (Lauda, Klixon MX-125 thermostat) and equipped with a combined glass/reference electrode (Metrohm EA 121), an inlet tube for nitrogen and a

magnetic stirring bar. The combined glass electrode was calibrated by using at least 5 buffer systems (Merck standard buffer solutions) over a range covering the whole pH domain of the titration.

The titration equipment was constructed from a Heathkit H11 computer with a microprocessor (Digital Equipment Corp. LSI-11A) with 24 kbyte of memory and two H11-2 parallel I/O interfaces. A digital voltmeter (Tekelec Airtronic TE-350-F + s-BCD coded output; 4 digits) was connected to one H11-2 interface. The output of a Knick industrial pH meter (type DIN) was connected to the digital voltmeter. A piston buret (Mettler DV 11) was driven from one TTL signal line from the second H11-2 computer interface on its pulse input terminal. The total volume of the buret was 10.0 ml and its accuracy was 0.001 ml.

Computer program

The programs were written in FORTRAN-10. The operator/program interface is menu-driven and constitutes the main routine of the program. From the choice offered (Table 6), the operator picks the subroutine that performs the requested task (e.g., experimental parameter input). The titration and calculation subroutines offer further options for how the task requested is to be done (Tables 7 and 8). This set offers a very flexible operator/program interaction ranging from full automatic titration and calculation with a minimum of data input for the titration parameters to a very detailed access to specific calculation steps and "manual" control of the titration.

The program is designed in such a way that the values of the different parameters are retained from one experiment to another, so for a new run only the parameters different from the old conditions have to be changed. Most of the options are self-explanatory; only the titration options (Table 7) will be explained in detail as a guide in the choice of the appropriate parameters for a given titration problem.

These titration options offer possibilities to try and compare all the different methods, which are to be used in control of the automatic potentiometric titration. Thus it can be used with fixed volume increments, with fixed pH increments, and with the optimized titrant delivery method.

TABLE 6

Initial choice in program (menu I)

DO YOU WANT: 1. TO INPUT THE CONSTANTS OF SUBSTANCES
2. TO CHANGE THE CONSTANTS OF SUBSTANCES STORED
3. TO LIST THE CONSTANTS
4. TO TITRATE
5. TO MAKE CALCULATIONS
6. TO CHECK AND CHANGE STORED VARIABLES AND CONSTANTS
7. TO TYPE IN TITRATION POINTS
TYPE THE NUMBER OF TASK

TABLE 7

Titration options

```
DO YOU WANT: 1. TO INPUT OR CHANGE PARAMETERS
             2. TO CALCULATE THE PARAMETERS
             3. TO CALIBRATE THE GLASS ELECTRODE
             4. TO PERFORM A FIXED VOLUME TITRATION
             5. TO PERFORM A FIXED DELTA PH TITR.
             6. TO PERFORM AN OPTIMIZED TITRATION
             7. TO PERFORM A SINGLE PH MEASUREMENT
             8. TO OPERATE THE BURET
             9. TO RETURN TO MENU I
TYPE THE NUMBER OF TASK
```

TABLE 8

Calculation options

```
DO YOU WANT TO CALCULATE:
1. THE WHOLE TITRATION CURVE?
2. THE PH FOR A GIVEN VOLUME ADDED?
3. THE VOLUME ADDED FOR A GIVEN PH?
4. THE CONCENTRATION FROM TITRATION DATA?
5. THE PK FROM TITRATION DATA?
6. TO RETURN TO MENU I?
TYPE THE NUMBER OF TASK
```

(1) The parameters VEVP, PHSTART, PHEVP and DELTA(PH) control the titration. In this step they are calculated from the input data of the constants of the substances given and the estimated concentration of the compound to be determined. DELTA(PH) is the maximum change in pH allowed for a titrant addition step and is calculated from the given required precision of the titration. If another equivalence point is wanted in a multi-step titration, it has to be stated here.

(2) PHMETER-ERROR and WAITING TIME are the parameters for the pH measurement and should be given values that match the performance of the pH-meter/glass electrode combination with respect to accuracy and response time. The latter should also allow for the mixing behaviour of the titration vessel. For special purposes the parameters calculated in (1) can be changed in this step.

(3) This step provides the glass electrode calibration. It allows the use of more than two buffers and calculates the calibration constants via least-squares regression.

(4) For pK determinations, the titration is best conducted with the use of fixed titrant additions. The fixed titrant addition per step and the maximum volume of titrant to be delivered should be given as parameters.

(5) In the "extra-fast" titration mode, titrant is delivered in constant pH increments. For the calculation of the appropriate volume to be added

(in contrast to the methods commonly used which are based on an empirical equation), the system parameters for the theoretical titration curve are used. Calculations operate with a ΔV calculated from $V_{(\text{pH measured} + \Delta\text{pH})} - V_{(\text{pH measured})}$. The estimated concentration is not updated during the titration process.

(6) In the "fast" titration mode, titrant is delivered according to the algorithm described under optimized titrant delivery, with updating of the estimated concentration during titration. There are two options: first, the estimated concentration during the titration can be updated as many times as the user wants; secondly, besides the "standard" fractions described, other combinations of titration fractions can also be used.

(7) and (8) these options offer the possibility of a "manual" titration.

All calculations were done with the use of a small set of subroutines. In all calculating subroutines, the option of using concentrations or activities is offered. The calculation with concentrations, although less exact, avoids numerous iteration processes and is therefore definitely faster. CAVAPD is the main calculating subroutine of the program. It calculates for a given pH value simultaneously all values of P and their derivatives (Eqns. 17 and 21, Table 4) and gives as a result V(act) and V(conc). In the case of activity calculations the subroutine CARIS is used to obtain the ionic strength. This needs the value of V for the calculation of the actual concentrations. The final value is obtained by iteration; the starting value of V is the calculated V(conc). Thus, if the CAVAPD program calculates with activities, it works in a loop, calculating first in a short-cut way the V(conc) and repeating the process for calculation of V(act).

CAPHA calculates the pH for a given titrant volume added (V). For calculation of the function $V = f(pH)$, Eqn. 21 is solved with the Newton–Raphson iteration process. The method is the same as described earlier. In the calculation with activities, one simplifying step is performed, namely in the differential quotient the activity factor is kept constant. For this reason, one or two more iterations may be necessary, but it simplifies the program greatly.

The CADAT subroutine, using a brute force method, calculates from titration data (the starting and terminating number of which can be given) the concentration or pK value. The number of digits calculated can be stated in advance, to regulate the speed of the process. From the same data set, several concentrations and/or pK values can be calculated.

RESULTS AND DISCUSSION

The examples given for acid-base titrations are selected to demonstrate the different capabilities of the above system. The real three-dimensional character of the procedure ($V = f(pH, E)$) will be more extensively illustrated in a subsequent paper which will deal with redox titrations accompanied with pH changes.

As a first example, the titration of the half-neutralized salt of a relatively strong acid, sodium hydrogenphthalate, is presented. The three samples were titrated with different first-guess concentrations, one close to, and the others lower and higher than, the real value. For better comparison, the same indicator curve was chosen. The results obtained are presented in Table 9.

Titrations of boric acid and sodium acetate are normally impossible without the use of complexing agents, because the sharpness index [3] is below 10. However, the boric acid could be titrated with the present procedure with a sufficient precision in 8—9 steps (Table 10) and so was sodium acetate (Table 11). For comparison, the results produced by another system (the Metrohm automatic titration) are also shown in the Tables.

Although the determination of the separate members of a multicomponent system was not the aim of this work, it can be shown that even in a mixture of weak acids (Table 12) not only the sum of all components but also one

TABLE 9

Titration of potassium hydrogenphthalate with sodium hydroxide
(V_0 = 50.0 ml, Conc. (NaOH) = 0.1 M. Input values: accuracy = 0.1%; first-guess concentration = 0.01 M; conc. for indicator curve = 0.005 M; for phthalic acid, log K_1 = 5.41 and log K_2 = 2.95. For pH measurement: pH stable to 0.001 for at least 3 s. Calculated values: $pH_{(start)}$ = 4.115; $pH_{(ep)}$ = 8.5422; $V_{(ep)}$ = 5.0 ml; $\triangle$pH = 0.458)

Given (M)	Found[a] (M)	$C_{(guess)}$ (M)
0.01	0.010050	0.010
	0.010052	0.015
	0.010048	0.008

[a]Eight points in each case.

TABLE 10

Titration of boric acid with sodium hydroxide
(V_0 = 50.0 ml, Conc. (NaOH) = 0.9940 M. Input values: accuracy = 0.1%; first-guess concentration = 0.01 M; conc. for indicator curve = 0.005 M; for boric acid, log K_1 = 9.23. For pH measurement: pH stable to 0.001 for at least 3 s. Calculated values: $pH_{(start)}$ = 5.5997; $pH_{(ep)}$ = 10.5265; $V_{(ep)}$ = 4.97; $\triangle$pH = 0.0054)

Given (M)	Found (M)	No. of points	First guess (M)	Metrohm titrator (M)
0.01	0.009950	8	0.01	0.01001
	0.009948	9	0.01	
	0.009950	7	0.01	
	0.009906	8	0.01	
	0.009926	8	0.01	
	0.009944	8	0.01	
	0.01005	7	0.001	

TABLE 11

Titration of sodium acetate with hydrochloric acid
(V_0 = 50.0 ml, Conc. (HCl) = 0.10028 M. Input values: accuracy = 0.1%; first-guess concentration = 0.01 M; Conc. for indicator curve = 0.005 M; for acetic acid, log K_1 = 4.76. For pH measurement: pH stable to 0.001 for at least 3 s. Calculated values: $pH_{(start)}$ = 8.3346; $pH_{(ep)}$ = 3.4083; $V_{(ep)}$ = 5.014 ml; $\triangle$pH = 0.0040)

Given (M)	Found (M)	First guess	No. of points	Metrohm titrator (M)
0.01	0.009982	0.01	9	0.00996
	0.009988	0.01	9	
	0.010006	0.01	10	
	0.010016	0.01	10	
	0.010046	0.012	10	
	0.010044	0.080	9	

TABLE 12

Titration of boric acid in a mixture of phosphoric acid (0.001998 M), phthalic acid (0.003018 M), oxalic acid (0.000502 M) and potassium hydroxide (0.003018 M)
(Titrant: sodium hydroxide. V_0 = 50.0 ml, Conc. (NaOH) = 0.09940 M. Input values: accuracy = 0.1%, first-guess concentration = 0.004 M; Conc. for indicator curve = 0.002 M. For phosphoric acid, log K_1 = 12.36, log K_2 = 7.20, log K_3 = 2.12; for phthalic acid, log K_1 = 5.41, log K_2 = 2.95; for oxalic acid, log K_1 = 4.27, log K_2 = 1.25. For pH measurement: pH stable to 0.001 for at least 3 s. Calculated values: $pH_{(start)}$ = 3.0266; $pH_{(ep)}$ = 10.3032; $V_{(ep)}$ = 6.009 ml; $\triangle$pH = 0.0104)

Given (M)	Found (M)	No. of points	$C_{(guess)}$
0.004	0.004039	7	0.004
	0.004045	9	
	0.004025	7	

particular component can be determined, even if there is no sharp potential jump between the components. The sharpness index between the last components is below 1.0 (about 0.25) and the last end-point is also not suitable for common titrations as shown above. In this mixture, boric acid has such a low concentration (0.004 M) that its sharpness index was only 3.38. The results (Table 12) show that all the results are somewhat high. This probably arose from the carbonate concentration of the titrant, which when calculated from the titration data points, accounted exactly for the deviation observed.

With regard to the time needed for the titration, the preliminary calculations for pH(start), pH(ep) and $\triangle$pH need 120 s, and the calculation of indicator pH values takes about 30 s per value. The titration is done with a delivery of 1.0 ml per 30 s; stabilization of pH at the start and near the end-point may take 3 s to 3.0 min, depending on the system, with intermediate waiting times of 3—6 s. Calculation of $\triangle V$ values takes 1—2 s. The calculation time

for concentration can be estimated by means of the expression $TK \times$ data points $\times$ digits calculated; TK = 30 s or 8 s when activity or concentration, respectively, is used for calculation. When the same titration is repeated, the preliminary calculation, which takes about 4.5 min, can be omitted. In that case, a titration with a total titrant consumption of 5.0 ml will take only 5.0 min if the updating calculation is based on concentrations and 8.5 min if the calculation is based on activities.

REFERENCES

1 T. W. Hunter, I. T. Sinnamon and G. H. Hieftje, Anal. Chem., 47 (1975) 497.
2 S. Ebel, Chem. Ing. Tech., 46 (1974) 811.
3 G. Svehla, Automatic Potentiometric Titrations, Pergamon, Oxford, 1978.
4 T. F. Christiansen, J. E. Busch and S. C. Krogh, Anal. Chem., 48 (1976) 1051.
5 D. Betteridge, E. L. Dagless, P. David, D. R. Deans, G. E. Penketh and P. Shawcross, Analyst, 101 (1976) 409.
6 P. V. Früh, L. Meier and H. Rutishauser, Anal. Chim. Acta, 95 (1977) 97.
7 R. W. Hendler, D. Songco and T. R. Clem, Anal. Chem., 49 (1977) 1908, 1914.
8 A. A. B. Wu and H. V. Malmstadt, Anal. Chem., 50 (1976) 2090.
9 D. J. Legget, Anal. Chem., 50 (1978) 718.
10 N. Busch, P. Freyer and H. Szamelt, Anal. Chem., 50 (1978) 2166.
11 L. Andersson, A. Granéli and M. Strandberg, Anal. Chim. Acta, 103 (1978) 489.
12 L. Pehrsson, F. Ingman and S. Johansson, Talanta, 23 (1976) 769, 781; 24 (1977) 79.
13 L. M. Doane, J. T. Stock and J. D. Stuart, Anal. Chem., 56 (1979) 415.
14 Ch. R. Martin and H. Freiser, Anal. Chem., 51 (1979) 803.
15 T. Nishikawa, I. Ogasawara and T. Harada, Anal. Chim. Acta, 133 (1981) 463.
16 S. Ebel, J. Hocke and B. Reyer, Fresenius Z. Anal. Chem., 308 (1980) 437; 312 (1982) 346.
17 J. C. Smit and H. C. Smit, Anal. Chim. Acta, 143 (1982) 45.
18 G. D. Owens and R. J. Eckstein, Anal. Chem., 54 (1982) 2347.
19 J. Boelema, Ph.D. Thesis, University of Groningen, 1982.
20 F. L. Hahn and G. Weiler, Fresenius Z. Anal. Chem., 69 (1926) 417.
21 G. Gran, Acta Chem. Scand., 4 (1950) 559; Analyst, 77 (1952) 661.
22 G. F. Tubbs, Anal. Chem., 26 (1954) 1670.
23 E. Bishop, Anal. Chim. Acta, 26 (1962) 397; 27 (1962) 253.
24 W. E. Wentworth, J. Chem. Educ., 42 (1965) 96.
25 N. Ingri, W. Kakołowicz, L. G. Sillen and B. Warnqvist, Talanta, 14 (1967) 1261.
26 D. Dyrssen, D. Jagner and F. Wengelin, Computer Calculations of Ionic Equilibria and Titration Procedures, Almqvist and Wiksel, Stockholm, 1968.
27 J. A. Goldman and L. Meites, J. Electroanal. Chem., 14 (1967) 373; 16 (1968) 47; 18 (1968) 41; 19 (1968) 204; Anal. Chim. Acta, 28 (1963) 472.
28 D. Midgley and C. McCallum, Talanta, 21 (1974) 723.
29 P. Gans, Coord. Chem. Rev., 19 (1976) 99.
30 M. Bos, Anal. Chim. Acta, 81 (1976) 21; 90 (1977) 61; 122 (1980) 193.
31 G. Arena, E. Rizzarelli, S. Sammartano and C. Rigano, Talanta, 26 (1979) 1.
32 Å. Olin and B. Wallén, Talanta, 25 (1978) 720.
33 R. A. Stairs, J. Chem. Educ., 55 (1978) 99.
34 H. N. J. Poulisse, Anal. Chim. Acta, 112 (1979) 361.
35 R. Rosset, D. Bauer and J. Desbarres, Labo-Pharma, 303 (1980) 833; Chimie Analytique des Solutions et Micro-informatique, Masson, Paris, 1979.
36 H. Narasaki, Talanta, 27 (1980) 409.
37 T. F. Brown and S. D. Brown, Anal. Chem., 53 (1981) 1410.

38 A. D. Zuberbühler and T. A. Kaden, Talanta, 29 (1982) 201.
39 Ch. Willis, J. Chem. Educ., 58 (1981) 659.
40 F. Gaizer and A. Puskás, Talanta, 28 (1981) 565.
41 L. Meites, Anal. Lett., 15 (1982) 507.
42 R. T. Shrager and R. W. Hendler, Anal. Chem., 54 (1982) 1147.
43 W. E. Gordon, J. Phys. Chem., 83 (1979) 1365; Anal. Chem., 54 (1982) 1595.
44 A. Avdeef, D. L. Kearney, J. A. Brown and A. R. Chemotti, Jr., Anal. Chem., 54 (1982) 2322.
45 S. Ebel, E. Glaser, R. Kantelberg and B. Reyer, Fresenius Z. Anal. Chem., 312 (1982) 604.