

Computer Estimation of Dissociation Constants. Part IV.* Precision and Accuracy of Potentiometric Determinations

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Abstract. The protonation constants $\log K_{Hj}$ of the acid H_jL are determined by regression analysis of potentiometric titration data when *common* parameters ($\log K_{Hj}, j = 1, \dots, J$) and *group* parameters ($E^{0'}$, L_0 , H_T) are refined. Two kinds of systematic error have been investigated: the error from an uncertainty of group parameters and the error from a computational strategy of the minimization algorithm used. An analysis of variance of $\log K_{Hj}$ matrix was made for 6 reproduced titrations and 7 computational strategies of 6 various regression programs. It was concluded that the influence of the program used is negligible. From two ways of calibration of the glass electrode cell, *the internal calibration* (performed during titration) was slightly more accurate than *the external calibration* (done separately). Of programs tested, the ESAB and ACBA are most powerful because they permit refinement of group parameters and internal calibration. D-tartaric acid was chosen as model substance.

Key words: protonation constants, dissociation constants, reliability of regression estimation, estimation of group parameters, estimation of common parameters, internal and external calibration of glass electrode cell.

In the last three decades quite a large number of papers about a computer analysis of potentiometric titration data to estimate protonation (formation) constants [1–11] has been published and critical reviews are part of recent monographs [12–15]. The first attempt to use the nonlinear regression in refinement of both, protonation constants (denoted here as the common parameters) and analytical concentrations (the group parameters) was made by Sillén and Warnqvist [1].

Recently, nonlinear regression programs ESAB [16], ESAB2M [17], ACBA [18] and SUPERQUAD [19] were written for the evaluation of potentiometric titration data when both, the common and group parameters are estimated. *Com-*

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mon parameters are those that are the same for all experiments such as protonation constants. *Group* parameters are those that vary from one experiment to another, such as the standard potential E^0 , analytical concentrations, and non-Nernstian slope of electrode cell used, etc. In order to have a limited number of group parameters to deal with, the titrations must be carried out with each titration having its own set of group parameters. In selecting the group parameters to be refined one should keep those parameters constant which have little or no influence on the common parameters estimated. Group parameters are also termed dangerous parameters [19] as they are ill-conditioned and therefore contain compensating errors.

The influence of three kinds of error in protonation constants has been investigated recently [20], the error from a strategy of minimization algorithm, the error from uncertainty estimates of group parameters and random errors.

In this paper the reliability of protonation constants being affected by an algorithm used and by a choice of refined group parameters is examined. In order to have a well-known but not too trivial system, D-tartaric acid as a test substance of two close consecutive protonation equilibria of protonation constants [21], $\log K_{H1} = 3.95$, $\log K_{H2} = 2.82$ ($I = 0.1$, 298 K) was chosen. In the comparison presented below these values of consecutive protonation constants were formally taken as the “true” values.

Theoretical

An acid-base equilibrium is described in terms of protonation of the Broensted base L^{z-1}



characterized by the protonation constant

$$K_H = \frac{a_{HL^z}}{a_{L^{z-1}} a_{H^+}} = \frac{[HL^z]}{[L^{z-1}][H^+]} \cdot \frac{y_{HL^z}}{y_{L^{z-1}} \cdot y_{H^+}} \quad (2)$$

and in the case of a polyprotic species is protonated to yield a polyprotic acid $H_j L$:



The subscript to K_H indicates the ordinal number of the protonation step. Direct formation of each protonated species from the base L^{z-} can be expressed by the overall reaction



and by the overall constant

$$\beta_{Hj} = K_{H1} \cdot K_{H2} \cdots K_{Hj} \quad (5)$$

where j denotes the number of protons involved in the overall protonation.

For protonation reactions realized at constant ionic strength so called “mixed constants” are defined as

$$K_{Hj}^* = \frac{[H_j L]}{[H_{j-1} L] a_{H^+}} \quad (6)$$

These constants are found in experiments where pH values are measured with glass and reference electrodes, standardized with the practical $\text{pH}(S) = pa_{H^+}$ activity scale recommended internationally. The $\text{pH}(S) = p(a_H) = p(a_H)_c + \log \rho_s$ where index m means molal and c molar concentrations and ρ_s is the density of the solvent. For aqueous solutions and temperatures up to 35°C this correction is less than 0.003 pH unit. The value of $[H_jL]/[H_{j-1}L]$ is determined by some instrumental approach, for example, by a potentiometric titration.

Since instrumental techniques as spectrophotometry, extraction and sometimes also potentiometry indicate concentration instead of activities, they allow determination of “concentration (stoichiometric) constants”. In order for a concentration constants to be actually constant, the activity coefficient term in Eq. (2) must be constant. One way to achieve this is to use an ionic medium of high concentration, consisting of ions that are expected not to interfere with the reaction of interest. If the protonation is studied at several ionic strengths or at low value of ionic strength, the thermodynamic protonation constant K_H can be obtained by extrapolating to zero ionic strength ($I = 0$), the reference state for the activity coefficient being an infinitely diluted solution.

(a) Regression Determination of Protonation Constants:

Potentiometric readings obtained with the proton-sensitive glass and reference electrodes cell can be described by the equation

$$\begin{aligned} E_{\text{cell}} &= E^0 + \frac{RT \ln 10}{F} \log a_{H^+} + j_a a_H - j_b K_w / a_H - E_{\text{ref}} \\ &= E^{0'} + S \log h \end{aligned} \quad (7)$$

where E^0 is the standard potential of a glass electrode cell plus other constants as the asymmetric potential, etc., and $a_H = [H^+] y_H = h y_H$, a liquid junction potential E_j is expressed by the term $j_a a_H - j_b K_w / a_H$, and $S = (RT \ln 10)/F$ is the slope of glass electrode for a Nernstian response. The term $E^{0'}$ expressed

$$E^{0'} = E^0 + S \log y_{H^+} + j_a h y_{H^+} - j_b K_w / (h y_{H^+}) - E_{\text{ref}} \quad (8)$$

with y_{H^+} the activity coefficient of proton. For a constant ionic strength the activity coefficient does not change and the term $E^{0'}$ in the pH range from 3 to 11 is practically constant.

An explicit equation for the titration curve under a constant ionic strength expresses a dependence between the volume of titrand added v_i and the monitored emf $E_{\text{cell},i}$ with the common parameters K_H and group parameters p ,

$$v_i = f(E_{\text{cell},i}; K_H, p) \quad (9)$$

Here the vector of common parameters $K_H = (K_{H1}, \dots, K_{Hm})$ contains the protonation constants of the acid H_jL while a vector of group parameters

$$p = (E^{0'}, S, K_w, j_a, j_b, L_0, L_T, H_0, H_T) \quad (10)$$

containing besides the constants of a Nernstian equation, $E^{0'}$ and S , the total ligand concentration L_0 , and hydrogen ion concentration H_0 in titrand, and the corresponding quantities in titrant L_T and H_T . Here, K_w is the operational ionic

product of water. In most cases all these group parameters can not be determined independently with sufficient accuracy. However, when working in high ionic media of constant ionic strength, both K_w and j_a (with j_b) may be determined by separate experiments.

Group parameters can be refined individually or with certain constraints introduced in the computation. In adjusting common and group parameters there are three different strategies of multiparametric refinement [1, 14–15]:

(i) *The first strategy* keeps all group parameters p constant and adjusts common parameters K_H by an analysis of all data. Then the common parameters K_H are kept constant and the group parameters adjusted for each group (titration). Then a refinement process is repeated adjusting first the common and then the group parameters. Two programs, MINQUAD [13, 22] (for common only) and MAGEC [13] (for group parameters) are combined usually.

(ii) *The second strategy* adjusts both parameters, K_H and p , simultaneously. Since each group parameter affects the part of residual sum of squares U that comes from a single group, a certain economy can be achieved in computations. This strategy is faster and often gives good minima. On the other hand, if some group parameter(s) are uncertain and do not affect the residual sum of squares U this uncertainty causes large standard deviations in other parameters. The programs ESAB [16–17] and ACBA [18] use this strategy.

(iii) *The third strategy* adjusts the common and group parameters at two different levels. For each set of common parameters the group parameters are adjusted at a lower level. By one or more minimizations on each group, the minimum contribution to U from that group is obtained giving the lowest value of U attainable with a given set of common parameters. These are now varied keeping the group parameters constant finding a new value of U . The process is repeated until no further improvement in U is obtained. This strategy is used in LETAGROP-ETITR [1] only.

In most regression programs for treating emf data the task is to find a model and to set up protonation constants that give the “best” fit to the experimental data. As primary data contains the total concentration H_T of proton from burette and the measured emf E_{cell} , one could either decide to trust added volumes $v_{\text{exp},i}$ and minimize the sum $(E_{\text{cell,exp}} - E_{\text{cell,calc}})^2$, or one could trust E_{cell} and minimize the residual sum of squares for $(v_{\text{exp}} - v_{\text{calc}})^2$ or some related quantity as the total concentrations of one or two components.

The residual sum of squares U may be expressed by means of various types of variable y , (cf. ref. [14–15])

$$U = \sum_{i=1}^n w_i (y_{\text{exp},i} - y_{\text{calc},i})^2 = \sum_{i=1}^n w_i r_i^2 \quad (11)$$

where w_i is the statistical weight set equal to unity while in some programs it is expressed by

$$1/w_i = s_i^2 = s_E^2 + (dE_i/dv_i)^2 s_v^2 \quad (12)$$

with a good equipment, we have generally $s_E = 0.1 - 0.3$ and $s_v = 0.001 - 0.005$.

Type 1: The residual r is formulated with the volume of added titrant v from burette so that $r_i = (v_{\text{exp},i} - v_{\text{calc},i})$ and resulting residual sum of squares U is

denoted as U_v . This U_v is used in ESAB [16–17], ACBA [18] and PSEQUAD(v) [13] programs.

Type 2: The residual r is formulated with emf of glass electrode cell E_{cell} or with pH measured so that $r_i = (E_{\text{exp},i} - E_{\text{calc},i})$ or $r_i = (\text{pH}_{\text{exp},i} - \text{pH}_{\text{calc},i})$ and resulting U is denoted U_E or U_{pH} . This U_E being used in PSEQUAD(E) [13] and MAGEC(E) [13, 23] while U_{pH} is used in PKAS [24].

Type 3: The residual r is formulated with the total concentration of two components L and H so that $r_i = (C_{\text{exp},i} - C_{\text{calc},i})$ where C stands for H and L , and resulting U is denoted as U_c . This U_c is used in MINQUAD [13, 22].

Type 4: The orthogonal regression means that both U_v and U_E are used in U simultaneously. This type is used in PSEQUAD(v, E) [13].

(b) Accuracy of Protonation Constants:

The response of a certain protonation constant $\log K_H$ to a certain i th titration can be written

$$\log K_H(i) = \log K_H(t) + \varepsilon_{\text{cell}} + \varepsilon_{\text{conc}} + \varepsilon_{\text{alg}} + \varepsilon_i \quad (13)$$

where $\log K_H(t)$ is “true” value of protonation constant, $\varepsilon_{\text{cell}}$ is systematic error due to an imprecise estimate of group parameters, E^0 , S , j_a , j_b , and K_w . These parameters may be refined by calibration of the glass electrode; $\varepsilon_{\text{conc}}$ is the systematic error due to estimates of the group parameters L_0 , L_T , H_0 and H_T . They might be evaluated by an independent chemical analysis; ε_{alg} is the systematic error due to poor quality of a minimization process in the algorithm used, and ε_i is the unobservable (random) error in the i th titration.

The accuracy of $\log K_H(i)$ can be expressed by the systematic deviation $e(\log K_H)$ given by relation (14), (cf. ref. [20])

$$e(\log K_H) = \log K_{H,\text{true}} - \log K_{H,\text{exp}} \quad (14)$$

where for $\log K_{H,\text{true}}$ the “best” value for given experimental condition found in the literature may be approximated. In case of simulated data for $\log K_{H,\text{true}}$ the pre-selected value from which data have been generated is used.

(c) Precision of Protonation Constants:

The protonation constant K_H (i.e. one of the protonation constants of an acid H_jL) is affected by an error which is randomly distributed between the titrations performed rather than between individual titration points. Braibanti et al. [25] proved that σ_K^2 is nearly same as σ_{tit}^2 in relation

$$\sigma_K^2 = \sigma_i^2 + \sigma_{\text{tit}}^2 + \sigma_{\text{lab}}^2 \quad (15)$$

where σ_K is the standard deviation of $\log K_H$ being determined experimentally, σ_i is the intra-titration (from point-to-point) standard deviation, σ_{tit} is the inter-titration (from titration-to-titration) standard deviation, σ_{lab} is the intra-laboratory (from laboratory-to-laboratory) standard deviation.

Analysis of variance may examine:

(i) if the algorithm used has any influence on the common parameters (protonation constants) estimated;

(ii) if a certain number of group parameters (to be refined) has any influence on the common parameters (protonation constants) estimated.

Instead of σ_{lab}^2 in Braibanti's equation (15) the variance σ_{alg}^2 describing an influence of algorithm used may be introduced so that all sources of variance in protonation constants are separated

$$\sigma_K^2 = \sigma_i^2 + \sigma_{\text{tit}}^2 + \sigma_{\text{alg}}^2 \quad (16)$$

The precision of a protonation constant $\log K_H$ is expressed by the standard deviation $s(\log K_H)$ found by a regression algorithm used.

Experimental

Materials

D-Tartaric acid, 0.030 mol. dm⁻³ was of analytical grade.

Sodium hydroxide, 1 mol. dm⁻³ was prepared from 50% solution of NaOH (equal weight of pellets and water) stored for several days in a polyethylene bottle. Then the clear supernatant solution was siphoned off and diluted with carbon dioxide-free water to obtain 1 mol. dm⁻³ NaOH. This solution was standardized against a solution of potassium hydrogen-phthalate using the Gran method in the MAGEC program [13, 23].

Perchloric acid, 1 mol. dm⁻³ was prepared by dilution of 70% HClO₄, p.a. quality with distilled water and standardized against HgO and KI with a reproducibility of $\pm 0.2\%$.

Twice-distilled water was used in preparation of all solutions.

Potentiometric Apparatus

The free hydrogen-ion concentration h was measured via emf (Eq. (7)) on a digital voltmeter OP-208/1 (Radelkis, Budapest) with a glass electrode G202B (Radiometer, Copenhagen) and a commercial SCE reference electrode OP-0830P (Radelkis, Budapest). Titrations were performed in a water-jacketed glass vessel of 100 cm³, closed with a Teflon bang containing the electrode, an argon inlet, a thermometer, a propeller stirrer and a capillary tip from a microburette. All emf measurements were carried out at 298.0 ± 0.1 K.

During the titrations a stream of argon was bubbled through the solution both for stirring and for maintaining an inert atmosphere. The argon was passed through pure ionic medium before entering the equilibrium solution.

The burettes used were home-made syringe microburette of 1250 μl capacity with a 25.00-mm micrometer screw. The polyethylene capillary tip of the microburette was immersed into solution when adding reagent but pulled out after each addition in order to avoid leakage of reagent during the pH reading. The microburettes were calibrated by weighing water on a Sartorius 1712 MP8 balance with a precision of $\pm 0.015\%$ in added volume over the whole volume range.

Calibration of Glass Electrode Cell

The potentiometric titrations of D-tartaric acid with sodium hydroxide were performed using a hydrogen concentration scale when the hydrogen ion concentration $[\text{H}^+] = h$ was known from a preparation of solution and the emf E_{cell} in mV was measured. Using a set of experimental data (E_{cell} , h) from a titration of perchloric acid of known concentration with standard sodium hydroxide unknown group parameters E^0 and S in Eq. (7) were evaluated.

Two calibration methods were used, internal and external, under which both a precision and accuracy of the protonation constants of D-tartaric acid were investigated. In case of an external calibration the actual values of the group parameters H_0 , H_T , E^0 , S and pK_w were estimated by the

MAGEC program on a separate acid-base titration. In case of the internal calibration the program ESAB estimated H_T , L_0 and $E^{0'}$ from an actual titration of a mixture of D-tartaric and perchloric acids with sodium hydroxide.

Some group parameters are given in the input data for ESAB such as the Nernstian slope and pK_w which both are accessible from literature. Group parameters can be estimated by a regression analysis of both benches of a titration curve or from the acid branch only because the basic side might contain some carbonate as well as silicate.

The program MAGEC offers a choice of group parameters to be estimated. The most accurate results were obtained by estimation of $E^{0'}$ and S only (Table 1). With ESAB three group parameters $E^{0'}$, L_0 and H_T were refined to give the best fit as may be examined by the goodness-of-fit criteria i.e. the Hamilton R -factor of relative fitness and the mean of absolute values of residuals (cf. p. 101 in ref.¹⁴), Table 2. Since $E^{0'}$ might slightly change from one titration to another because of a change of liquid-junction potential, the internal calibration seemed to be more accurate and therefore was here preferred.

Titration Procedure

An aqueous solution 20.00 cm³ containing 0.015 mol.dm⁻³ D-tartaric acid and 0.100 mol. dm⁻³ perchloric acid was titrated with standard 1.0 mol. dm⁻³ NaOH at 298 K and 30–40 titration points $\{v, E_{\text{cell}}\}$ were read.

Calculations

Calculations relating to the determination of protonation constants were performed by regression analysis of titration curve. A set of reproduced titration curves was analyzed by eight regression methods, i.e. five programs in combination with MAGEC [13, 23] external calibration: PSEQUAD(v) [13], PSEQUAD (E) [13], MINQUAD [22], MIQUV [13], PKAS [24], and two programs with internal calibration ACBA [18], and ESAB [16–17]. Except for ANOVA having been applied from CHEMSTAT package [26–27] (Trilobyte, Prague) on IBM PC AT computer the rest of other computations were performed on the EC1033 computer at the Computing Centre of the University of Chemical Technology, CS-532 10 Pardubice, Czechoslovakia.

Results and Discussion

Six repeated titrations of a mixture of perchloric and D-tartaric acids with sodium hydroxide were analyzed. The data were treated with seven different programs. Besides two common parameters (protonation constants $\log K_{1H}$ and $\log K_{2H}$) also three group parameters (the concentration of D-tartaric acid L_0 , the concentration of sodium hydroxide in burette H_T , and the formal standard potential $E^{0'}$) were refined.

Table 1 gives the results of regression analysis of one particular titration with the use of the ESAB program. In part (a), besides the original data (v, E_{cell}) and $-\log h$, the statistical weight [cf. Eq. (12)], the Bjerrum protonation (formation) function (Z), the calculated ionic strength (I) at each point are given. Both common and group parameters are refined and best curve-fitting achieved is proved by low value of the mean of absolute values of residuals in a goodness-of-fit test.

Part (b) compares the influence of group parameters being refined on two protonation constants. Reliability of both protonation constants may be classified according to a goodness-of-fit achieved. As more group parameters are refined a

Table 1a. ESAB refinement of common and all group parameters

Common parameters: $\log K_{H1} = 3.919(4)$, $\log K_{H2} = 2.834(3)$. Group parameters: $H_0 = 0.9880(37)$ mol. dm ⁻³ , $L_0 = 0.01476(10)$ mol. dm ⁻³ , $H_T = 1.09309(409)$ mol. dm ⁻³ , $E^{0'} = 374.9(3)$ mV							
<i>i</i>	Volume [ml]	Residual [ml]	<i>E</i> _{cell} [mV]	−log <i>h</i>	Weight	Protonation function	Ionic strength
1	1.7400	−0.0001	244.00	2.213	0.84	1.80	0.094
2	1.7600	0.0000	240.80	2.267	0.87	1.78	0.095
3	1.7800	0.0000	237.40	2.324	0.90	1.75	0.095
4	1.8000	0.0001	233.80	2.385	0.92	1.72	0.095
5	1.8200	0.0003	230.00	2.450	0.94	1.69	0.096
6	1.8400	0.0001	226.10	2.515	0.96	1.65	0.096
7	1.8600	−0.0002	222.10	2.583	0.97	1.61	0.097
8	1.8800	0.0000	217.90	2.654	0.98	1.57	0.097
9	1.9000	−0.0007	213.80	2.723	0.98	1.52	0.098
10	1.9200	0.0001	209.30	2.799	0.99	1.47	0.099
11	1.9400	0.0001	204.90	2.874	0.99	1.41	0.099
12	1.9600	0.0004	200.40	2.950	1.00	1.35	0.100
13	1.9800	0.0000	196.00	3.024	1.00	1.29	0.101
14	2.0000	0.0002	191.40	3.102	1.01	1.23	0.102
15	2.0200	−0.0003	186.90	3.178	1.01	1.17	0.103
16	2.0400	−0.0002	182.20	3.258	1.01	1.10	0.104
17	2.0600	0.0001	177.40	3.339	1.02	1.03	0.106
18	2.0800	0.0001	172.60	3.420	1.02	0.96	0.107
19	2.1000	0.0001	167.70	3.503	1.03	0.89	0.108
20	2.1200	−0.0001	162.80	3.585	1.03	0.83	0.110
21	2.1400	0.0004	157.60	3.673	1.04	0.75	0.111
22	2.1600	0.0000	152.50	3.760	1.05	0.68	0.113
23	2.1800	−0.0002	147.20	3.849	1.06	0.61	0.114
24	2.2000	−0.0003	141.60	3.944	1.07	0.54	0.116
25	2.2200	0.0001	135.50	4.047	1.08	0.47	0.118
26	2.2400	−0.0002	129.10	4.155	1.10	0.40	0.119
27	2.2600	0.0002	121.70	4.280	1.12	0.32	0.121

Goodness-of-fit test
Mean of absolute values of residual, $|\bar{r}| = 0.2 \mu\text{l}$.

(a) The regression analysis of an emf-titration curve of a mixture of perchloric and tartaric acids with NaOH, and (b) an effect of choice of group parameters refined on accuracy and precision of two common parameters $\log K_{H1}$ and $\log K_{H2}$. Experimental conditions: 25°C, $pK_w = 13.78$, $V_0 = 2.00$ ml, $\sigma(v) = 0.001$ ml, $\sigma(E) = 0.1$ mV, $I = 0.1$ (NaClO₄), the initial guess of group parameters: $\log K_{H1} = 3.918$, $\log K_{H2} = 2.834$, $H_0 = 0.09868$ mol. dm⁻³, $L_0 = 0.01478$ mol. dm⁻³, $H_T = 1.09420$ mol. dm⁻³, $E^{0'} = 375.74$ mV, $j_a = 0.0$, $j_b = 0.0$. Standard deviation of parameter estimate in last valid digits are in brackets.

Table 1b. Choice of group parameters to be refined

To be refined	$\log K_{H1}$	$\log K_{H2}$	$E^{0'}$ [mV]	L_0 [mol. dm ⁻³]	$-H_T$ [mol. dm ⁻³]	$ \bar{r} $ [μl]
<i>For initial guess of group parameters the rounded values are used</i>						
Common only	3.977(2)	2.860(2)	375.0	0.01500	1.0900	0.9
Common + $E^{0'}$	3.970(2)	2.842(5)	374.4(1)	0.01500	1.0900	0.6
Common + L_0	3.912(6)	2.850(1)	375.0	0.01459(3)	1.0900	0.4
Common + H_T	3.943(4)	2.827(3)	375.0	0.01500	1.0935(3)	0.4
<i>For initial guess of group parameters the best estimates are used</i>						
Common only	3.927(0)	2.826(0)	375.74	0.01499	1.09593	0.2
Common + $E^{0'}$	3.917(0)	2.833(0)	374.8(0)	0.01499	1.09593	0.2
C. + H_0 + L_0	3.947(4)	2.836(2)	374.8(0)	0.01494(3)	1.09593	0.2
C. + group p.	3.919(4)	2.834(3)	374.9(3)	0.01476(10)	1.0931(41)	0.2

better fit is achieved and therefore more reliable estimates of protonation constants result. In the last row besides two common parameters also four group parameters ($E^{0'}$, L_0 , H_T , and H_0) were refined and therefore these protonation constants can be considered as final results.

Table 2 brings an influence of the regression program used on accuracy and precision of two estimated protonated constants. An accuracy is expressed by the systematic deviation in $\log K_{Hj}$ related to the “best literature value for given experimental conditions used”. All 42 values of protonation constants lead to the mean $\log K_{H1} = 3.941$ and $\log K_{H2} = 2.799$, and the estimate of a systematic deviation $e(\log K_H)$ given by Eq. (6) is $e(\log K_{H1}) = -0.009$ and $e(\log K_{H2}) = -0.021$. It is obvious that the error from various computational strategies of 6 different regression programs is much smaller than the error from experimental reproducibility, and therefore it may be concluded that the regression program has no significant effect on both protonation constants. Both external and internal calibrations of glass electrode cell lead to the same results.

A quite sensitive criterion of reliability of protonation constants estimates in a goodness-of-fit test are the Hamilton R -factor of relative fitness and the mean of absolute values of residuals $|\bar{r}|$. Comparing residuals with the instrumental noise $s_{\text{inst}}(y)$ represented here by either $s(v) = 0.001$ ml or $s(E) = 0.1$ mV, an excellent fit is considered when $|\bar{r}|$ is of the same magnitude as $s_{\text{inst}}(y)$. From that point of view, the internal calibration of glass electrode cell and an application of ACBA and ESAB lead to best and most reliable estimates of $\log K_{H1}$ and $\log K_{H2}$. As a general criterion, the Hamilton R -factor may be used for objective comparison of regression programs based on various types of formulation of a residual sum of squares. The lowest value of R -factor i.e. the best fit was achieved by ACBA and ESAB.

Table 3 brings a response of a reproducibility on accuracy and precision of two protonation constants when three group parameters H_T , L_0 and $E^{0'}$ also are refined by ESAB. All six reproduced titration curves were perfectly fitted as $|\bar{r}| \sim 0.24 \mu\text{l}$ is much smaller than the instrumental noise $s(v) = 1 \mu\text{l}$. Systematic error expressed by deviation from “true” value, $e(\log K_{H1}) = 3.93 - \log K_{H1,\text{true}} = 0.020$ and

Table 2.

Program	Reproduced titrations						Mean
	1	2	3	4	5	6	
log K_{H_2}							
1	2.753(6)	2.761(7)	2.803(3)	2.833(2)	2.876(3)	2.758(2)	2.797(2)
2	2.760(4)	2.769(5)	2.805(2)	2.832(1)	2.872(3)	2.760(2)	2.800(1)
3	2.758(5)	2.768(6)	2.804(2)	2.832(1)	2.872(3)	2.760(2)	2.799(1)
4	2.759(2)	2.769(2)	2.804(1)	2.831(1)	2.872(2)	2.759(1)	2.799(1)
5	2.572(5)	2.761(7)	2.802(7)	2.833(1)	2.875(3)	2.758(2)	2.797(2)
6	2.765(10)	2.776(13)	2.808(6)	2.827(4)	2.866(6)	2.762(4)	2.801(3)
7	2.752(5)	2.761(7)	2.802(3)	2.833(1)	2.875(3)	2.758(2)	2.797(2)
log K_{H_1}							
1	3.903(6)	3.927(8)	3.963(3)	3.927(2)	3.994(3)	3.937(2)	3.942(2)
2	3.897(4)	3.921(4)	3.962(2)	3.928(1)	3.998(3)	3.936(2)	3.940(1)
3	3.897(4)	3.921(5)	3.962(2)	3.928(1)	3.997(3)	3.935(2)	3.940(1)
4	3.897(2)	3.921(2)	3.962(1)	3.928(1)	3.997(2)	3.936(1)	3.940(1)
5	3.902(6)	3.927(8)	3.963(3)	3.927(2)	3.994(3)	3.937(2)	3.942(2)
6	3.892(2)	3.915(2)	3.960(2)	3.930(2)	4.002(7)	3.934(2)	3.939(1)
7	3.902(6)	3.927(8)	3.963(3)	3.927(2)	3.994(3)	3.937(2)	3.942(2)
Hamilton R -factor [%]							
1	—	—	—	—	—	—	—
2	—	—	—	—	—	—	—
3	0.312	0.389	0.160	0.090	0.190	0.127	0.211
4	2.246	2.801	1.186	0.693	1.486	0.967	1.563
5	0.135	0.173	0.073	0.036	0.068	0.052	0.090
6	0.201	0.272	0.118	0.084	0.157	0.089	0.154
7	0.134	0.173	0.073	0.037	0.068	0.052	0.089
Mean of absolute values of residuals, $ \bar{r} $							
1	—	—	—	—	—	—	—
2	—	—	—	—	—	—	—
3	4.05	4.65	1.76	1.16	2.44	1.72	2.63
4 [mV]	3.59	4.08	1.56	1.06	2.29	1.58	2.35
5 [μ l]	0.22	0.26	0.10	0.06	0.01	0.09	0.12
6	3.9	4.5	2.0	1.9	3.6	2.1	3.0
7 [μ l]	0.22	0.26	0.10	0.06	0.11	0.09	0.14

Response of chosen regression program and reproducibility on accuracy and precision of protonation constants log K_{H_1} and log K_{H_2} of D-tartaric acid in analysis of potentiometric titration of a mixture of perchloric acid and D-tartaric acid with NaOH: Programs in rows: (1) PSEQUAD(v) with MAGEC, (2) PSEQUAD(E) with MAGEC, (3) MINQUAD with MAGEC, (4) MIQUV with MAGEC, (5) ACBA, (6) PKAS with MAGEC, (7) ESAB. Standard deviations in last valid digits are in brackets. Initial guess of group parameters: $L_0^{(0)} = 0.01505$ mol. dm⁻³, $H_T^{(0)} = -1.0927$ mol. dm⁻³, $H_0 = 0.09868$ mol. dm⁻³ (HClO₄), $E^{0'}$ = 374.8 mV, $S^{(0)} = 58.55$ mV/pH, $pK_w = 13.78$ at $I = 0.10$ (NaClO₄) and 298 K, $V_0 = 20.0$ cm³. Statistic $|\bar{r}|$ is for (3) in 10⁵ mol. dm⁻³ while for (6) in 10³ pH units.

Table 3.

Group parameter	Reproduced titrations						Mean
	1	2	3	4	5	6	
H_T	1.075(1)	1.091(3)	1.104(4)	1.075(3)	1.079(2)	1.066(2)	1.082(1)
$E^{0'}$	377.6(3)	381.4(6)	380.1(9)	375.0(5)	375.2(3)	374.6(4)	377.3(2)
$10^2 \cdot L_0$	1.47(1)	1.56(2)	1.59(3)	1.46(2)	1.44(1)	1.40(1)	1.487(7)
$\log K_{H1}$	3.918(5)	3.963(6)	3.975(7)	3.895(8)	3.924(4)	3.902(6)	3.930(3)
$\log K_{H2}$	2.828(5)	2.821(6)	2.797(9)	2.822(6)	2.840(4)	2.812(6)	2.820(3)
$R, [\%]$	0.011	0.015	0.018	0.020	0.011	0.015	0.015
$ \bar{r} , [\mu\text{l}]$	0.19	0.24	0.31	0.32	0.18	0.23	0.24

Response of a reproducibility on accuracy and precision of protonation constants $\log K_{H1}$ and $\log K_{H2}$ of D-tartaric acid and three group parameters H_T , L_0 and $E^{0'}$ in the ESAB-regression analysis of potentiometric titration curve of a mixture of perchloric and D-tartaric acids with sodium hydroxide. Standard deviation of parameters estimate in last valid digits are in brackets. Experimental conditions as in Table 1. Concentrations are expressed in mol. dm⁻³ and $E^{0'}$ in mV.

$e(\log K_{H2}) = 2.820 - \log K_{H2, \text{true}} = 0.000$ proves a quite good agreement with the value from literature.

Analysis of variance, ANOVA, decomposes a total variability σ_K^2 of protonation constants into a variance coming from reproducibility “ $\sigma_i^2 + \sigma_{\text{tit}}^2$ ” and a variance coming from the algorithm used σ_{alg}^2 . The systematic error caused by the regression program used (effect α_i) is larger than error caused by reproducibility, (Table 4). The F -test proved that a variability caused by seven different regression algorithms is negligible in comparison with the variability caused by the reproducibility of potentiometric titration, $\sigma_{\text{alg}}^2 \ll (\sigma_i^2 + \sigma_{\text{tit}}^2)$. It means that both techniques of external or internal calibration of a glass electrode cell lead to a correct values of group parameters and the term ($\varepsilon_{\text{cell}} + \varepsilon_{\text{conc}}$) in Eq. (13) is negligible. The main part of variability in $s^2(\log K_H)$ comes from a reproducibility of potentiometric titration.

Conclusion

Three kinds of errors in protonation constants, two systematic and one random error have been investigated in this study: systematic error coming from uncertain group parameters and systematic error from a minimization strategy and random error. Advanced regression programs ESAB and ACBA removed uncertainty of group parameters and therefore this systematic error in $\log K_H$ is negligible. From group parameters the formal standard potential $E^{0'}$ has a strong effect and one should always try to refine it together with protonation constants in spite of fact that it might be ill-conditioned in the model. Influence of algorithm used on $\log K_H$ is also negligible. The main source of variability in protonation constants is from experimental reproducibility of potentiometric titration σ_{tit}^2 . Of the programs tested, ESAB and ACBA are the most rigorous and powerful, because they permit refinement of the group parameters.

Table 4. One-way analysis of variance in two consecutive protonation constants of D-tartaric acid. The effect α (influence of algorithm used), in comparison with reproducibility; $F_{\text{crit}}(0.95, 6, 35) = 2.372$

$$\log K_{H1,i} = 3.941 + \alpha_i + \varepsilon_i$$

<i>i</i>	The <i>i</i> th algorithm	$\log K_{H1,i}$	Effect α_i
1	PSEQUAD(v)	3.942	0.001
2	PSEQUAD(E)	3.940	0.000
3	MINIQUAD	3.940	-0.001
4	MIQUV	3.940	0.000
5	ACBA	3.942	0.001
6	PKAS	3.939	-0.002
7	ESAB	3.942	0.001

$$H_0: \alpha_i = 0, i = 1, \dots, 7. F_{\text{exp}} = 0.006 < F_{\text{crit}} = 2.372.$$

Conclusion: H_0 is accepted.

$$\log K_{H2,i} = 2.799 + \alpha_i + \varepsilon_i$$

<i>i</i>	The <i>i</i> th algorithm	$\log K_{H2,i}$	Effect α_i
1	PSEQUAD(v)	2.797	-0.001
2	PSEQUAD(E)	2.800	0.001
3	MINIQUAD	2.799	0.000
4	MIQUV	2.799	0.000
5	ACBA	2.797	-0.002
6	PKAS	2.800	0.002
7	ESAB	2.797	-0.002

$$H_0: \alpha_i = 0, i = 1, \dots, 7. F_{\text{exp}} = 0.006 < F_{\text{crit}} = 2.372.$$

Conclusion: H_0 is accepted.

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