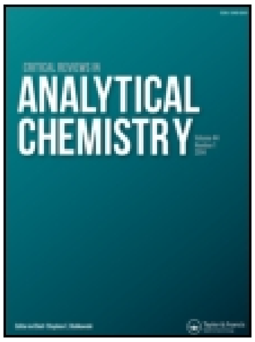

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Critical Reviews in Analytical Chemistry

ISSN: 1040-8347 (Print) 1547-6510 (Online) Journal homepage: http://www.tandfonline.com/loi/batc20

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To cite this article: Agustin G. Asuero & Tadeusz Michałowski (2011) Comprehensive Formulation of Titration Curves for Complex Acid-Base Systems and Its Analytical Implications, Critical Reviews in Analytical Chemistry, 41:2, 151-187, DOI: 10.1080/10408347.2011.559440

To link to this article: https://doi.org/10.1080/10408347.2011.559440

Critical Reviews in Analytical Chemistry, 41:151–187, 2011
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ISSN: 1040-8347 print / 1547-6510 online
DOI: 10.1080/10408347.2011.559440

Comprehensive Formulation of Titration Curves for Complex Acid-Base Systems and Its Analytical Implications

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This article provides extensive and exhaustive mathematical description of titration curves related to acid-base systems with mixtures of mono- and polyprotic acids and their salts and bases involved. The related curves are presented in compact forms facilitating further operations made for particular needs. Some derivative properties of the curves, such as buffer capacity and inflection points, are also discussed. The "windowed" (B_V) buffer capacity is interrelated with "dynamic" (β_V) buffer capacity, introduced for dynamic (titration) systems. The equations useful for searching the inflection points on titration curves are derived. A kind of "homogenization" of complex acid-base systems, with polyprotic acids with defined and/or undefined (e.g., fulvic acids) composition, with use of an approach based on Simms constants principle, has been considered in context with buffer capacity and alkalinity. The new concepts of total alkalinity (TAL) and total acidity (TAC), unlike ones considered hitherto, has been introduced. The TAL is determined according to curve–fitting method with use of iterative computer program, applied to nonlinear regression equation involving Simms or Hill constants. Searching the best fit of the related function is involved with addition of consecutive hyperbolic terms.

Keywords Acid-base equilibria, titration curves, bufer index, inflection point, Simms constants

INTRODUCTION

Reaction rate and mechanism, solubility, and partitioning of the species between different phases and other physicochemical properties are strongly influenced by some variables such as pH, ionic strength, and buffer concentration (Avdeef, 2007; Avdeef and Testa, 2002; Box et al., 2003). Equilibrium constants of acid-base equilibria and reaction rate constants are very useful parameters for various chemical, electrochemical, and technological applications (Asuero, 1989; Papanastasiou and Kokkinidis, 2003; Wiczling et al., 2008). Almost all chemical and biochemical processes are critically dependent on pH, and therefore the ability to control and measure the quantity is of paramount importance (McMillan and Cameron, 2004; Brown and Milton, 2003). Buffers play a central role in controlling the pH of solutions. A change of shift in pH of food would affect the rates of reactions, leading to a loss of shelf life. Therefore, the pH of the food is frequently controlled and monotorized (Chuy and Bell, 2009) in an attempt to limit chemical reactivity.

In laboratory practice, e.g., in electrophoretic and chromatographic techniques (Celentano et al., 1988; Righetti et al., 1988), it is often mandatory to ascertain pH, conductivity, or buffering action of complex mixtures. The analysis of acid-base reactions is important in the fields of chemistry, physiology, medicine (Nguyen et al., 2009; Wooten, 2004, 2010), and enology (Akin et al., 2008). Buffering is among the most important mechanisms that help to maintain homeostasis (Schmitt, 2005a, b) of various physiological parameters in living organisms. On the other hand, the speciation of polyprotic acids is a common problem (Szakács and Noszal, 1999; Szakács et al., 2005; Stoyanov and Righetti, 1999) in analytical and pharmaceutical chemistry. The pH control in electrolytic systems (McMillan and Cameron, 2004; Akin et al., 2008; Zaher and Vanrolleghem, 2006; Dougherty et al., 2006) and evaluation of acidity constants of natural or synthetic substances of therapeutical significance (Roda et al., 2010; Qiang and Adams, 2004) are also of paramount interest. For example, food systems are composed of multiple constituents that serve specific functions in the product, many of which directly or indirectly affect the pH value (Chuy and Bell, 2009).

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Chemistry of electrolytic systems is a key consideration in nearly all microfluidic devices and techniques, and this is particularly true in the area of electrokinetic phenomena (Persat et al., 2009a, b).

The buffer capacity concept, as one of the distinguishing characteristics of buffer solutions (Schmitt, 2005a; Van Slyke, 1922; Fishtik, 1998; Opanasenko et al., 1978), is also a very important concept, which finds applications in a variety of disciplines (Urbansky and Schock, 2000), being applicable to natural (Totsche et al., 2006) and technical (Jung and Hur, 2000) systems. The buffering systems are of importance for environmental studies and treatment of acidic mining water (Totsche et al., 2006). In general, soils and water rich in humic substances are well buffered. Knowledge of the behavior of the interaction of proton and hydroxyl with humic acid is very important in the understanding of its physicochemical properties in soils and waters (Pertusatti and Prado, 2007). The processes occurring in cells, body fluids, and reaction vessels as well, may proceed normally at appropriate buffer capacity securing pH constancy (Rees et al., 1996; Fencl and Leith, 1993).

The previous work by Asuero (1992a) on the buffer index referred to monoprotic acids. However, numerous buffers utilized in daily laboratory practice, e.g., succinate, phosphate, or citrate buffers, are formed of polyprotic acids (Brooks and Storey, 1992; Good and Izawa, 1972). Citric acid is a natural component and common metabolite of plants and animals. It is the most versatile and widely used organic acid in foods, beverages, detergents, and pharmaceuticals because of its functionality and environmental acceptability, being also a source of energy for controlled bacterial metabolism (Akhond et al.; Lahav et al., 2005). Citric and phosphoric acids, as well as their salts, are commonly used in foods to (Chuy and Bell, 2009) to control pH and to modify tartness.

Though a number of articles (Waser, 1967; Olin and Wallen, 1978; de Levie, 1993; Maslarska et al., 2003) dealing with the titration of polyprotic acids have been published, only a few attempts to derive compact expressions for the buffer index, β (Perrin and Dempsey, 1979), and sharpness index, η (Butler and Cogley, 1999; Michalowski, 1981), of polyprotic acids have been made (Hesse and Olin, 1977; King and Kester, 1990). The general formulas derived in these articles are applicable to the buffer index of polyprotic acids but, except for the work of Michalowski (1981) and Michałowski and Parczewski (1978), the dilution effects were neglected in the calculations. The formation function $\bar{n} = \bar{n}(pH)$ and dissociation fractions (f_i) were incorporated by Michałowski (1981) and Michałowski and Parczewski (1978) and Asuero et al. (1986a), in the equations obtained on the basis of charge and concentration balances referred to polyprotic acids. In the related formulas, the mononuclear species participating in only acid–based equilibria (i.e. proton gain or loss) were taken into account.

In a later part of this article, the formulation of static buffer capacity (β) by Hesse and Olin (1977) is recalled in extended and modified form, with Simms constants involved. The buffer capacity concept has been lately considered in an extensive review paper by Asuero (2007), issued in this journal. In that article, the topic of interest was focused on properties of single mono- and polyprotic acids. Our present article refers to more complex acid-base systems.

The generalized buffer capacity (GBC) concept, introduced by Michałowski et al. (2005a), was also presented and referred to acid-base equilibria in the systems of different complexity. This possibility is offered by the generalized approach to electrolytic system (GATES), presented in Michałowski (2010) and Michałowski et al. (2010a) and in some references cited therein. In this article, the static (β), dynamic (β_V), and windowed (B_V) buffer capacities, with dilution effect involved, were referred to acid-base titrimetry and interrelated uniformly and consistently in the single relation for acid-base systems of different complexity. In this approach, any simpler system can be considered as a particular case of the complex system. It is an approach different from the common one provided by de Levie (1999a).

The equations derived in this article enable calculating, as a function of pH, the degree of protolysis of each acid species, the formation function, the slope of the titration curve, and the buffer and sharpness indexes. A simplifying assumption put in the related formulas is involved with an assumption that all the equilibrium constants involved in the formulas are constant during the dynamic process exemplified by an acid-base titration. This assumption is involved with stability of all activity coefficients during the titration. This requirement is approximately valid in the presence of a sufficient amount of a neutral (basal) salt added during preparation of D and T, as one exemplified in the series of articles by Michałowski and coworkers (Michałowski, 1988a, 1990, 1992; Michałowski et al., 1987, 1988, 1989, 1994, 1995; Michałowski and Gibas, 1994; Janecki et al., 1999a, b, 2000a, b; Janecki and Michałowski, 1999), where a more advanced approach to the isomolarity condition was presented. The latter approach is based, among others, on addition of a sample tested on the step of D and T preparation. The pH changes are affected there by the presence of an excessive amount of acid or base in one of the solutions considered, and basal electrolyte MB is present in D and T in the quantities securing the related isomolarity condition.

The chemical equilibria are an essential part of the chemical knowledge. The detailed and thorough presentation of this problem in the present article offers extremely detailed coverage. The generalized approach is applied to acid-base systems of different degrees of complexity. The concept of the fraction titrated (Φ) (Butler and Cogley, 1999; Butler, 1964), titration error, buffering effects, and equivalence point/end point discrepancies, are all touched upon. The titration curves, pH, and buffer topics are important enough to deserve a systematic and detailed treatment, which is the aim of this article. The importance of pH, titration curves, and buffers topics is highlighted in Tables 1, 2, and 3. Table 1 describes some selected articles concerning pH calculations, paying special attention to complex systems. Only articles not included in the review of Frison and Calatroni (n. d.) are considered. In Tables 2 and 3 are described some selected articles published in the past decade, dealing with titration curves and buffer capacity, respectively, of complex systems.

Titrimetry is one of the oldest analytical methods, and is still developing; it plays an important role in various analytical fields as well as routine studies (Zhang and Narusawa, 1997), and it is often applied in analytical chemistry, for its superior speed and simplicity, with little sacrifice in accuracy and precision (Zhan et al., 2004), offering the possibility of simultaneous measurements (Van Hulle et al., 2009) at low cost of several (buffering) components. Methods and applications based on pH titrations are used in a variety of fields (aerobic, anaerobic and physicochemical wastewater treatment, food and feed applications, soil science, microbiology, aquatic chemistry, etc.) (Van de Steene et al., 2002; Van Vooren et al., 2001). The potentiometric method with a glass electrode is preferably used in analytical laboratories for the quantitative determination of substances (Fang et al., 2009) with acid-base properties. Potentiometric titration is the method of choice for measuring equilibrium, proton-binding constants in colloids and materials surface science, biology, and biochemistry. In environmental science, the titration method is commonly used to characterize acid-base properties of natural organic matter (NOM) (Lenoir and Manceau, 2010).

To present an all-encompassing theory requires consistent application of many symbols—alone or with some subscripts and/or superscripts. For this purpose, the symbols applied and some elementary relationships between equilibrium constants and some particular variables, useful in different parts of the present article, are specified in introductory sections.

BASIC CONSIDERATIONS

Titration and Titration Curves: Introductory Remarks

A titration is considered as a kind of dynamic process, in which a properly chosen titrant (T) is added in consecutive portions into V_0 mL of the solution titrated (titrand, D) (Michałowski et al., 2010a; Beck, 1997; Felber et al., 2003; King, 1997). The volume of T added to a given moment of titration is denoted by V [mL]. Under the assumption of additivity in the volumes, V_0+V mL of D+T mixture is thus obtained at a particular moment of titration stage. For modeling purposes it is assumed that the titration is carried out in *quasi-static* manner, under isothermal conditions. The same requirements are also tacitly put in place with simulated titrations. When ionic strength (I) and dielectric constant (ε) of the mixture do not vary distinctly during the titration, all the equilibrium constant values related to a system in question can be assumed constant.

In a common acid-base titration, the points $\{(V_j, pH_j)| j = 1,\ldots,N\}$, registered after consecutive portions of T added, form a continuous plot named the pH titration curve, pH = pH(V). The titration curve can also be obtained in a simulated manner, with the use of an Excel spreadsheet applied to the related function, V = V(pH), which can be accounted for as the reverse function against pH = pH(V) (Billo, 2001; Guenther, 1991; Freiser, 1992; de Levie, 2001c). In other words, V = V(pH) and pH = pH(V) are a pair of bijective (mutually interchangeable) functions, i.e., with one-to-one correspondence property (Bijective Function, 2011). This property is very important in light of fact that the relationship V = V(pH) can be formulated in a simple and uniform functional manner, even for complicated acid-base systems—contrary to the relationships pH = pH(V) that assume more complex form even for simple acid-base systems (see, e.g., Janecki et al. (1999a, b, 2000b), Michałowski et al. (2000)) or do not exist at all. Note that the non-monotonic pH versus V relationships were also stated in pH titrations made in some binary-solvent media (Pilarski et al., 2010; Michałowski et al., 2010b) and in some redox systems, see, e.g., Michałowski (2010).

Equations for titration curves are the basis for quantitative inferences in titrimetry (Michałowski, 2001; de Levie, 1997a; Harris, 2010; Skoog et al., 2003). For a defined electrolytic system, all attainable physicochemical information (equilibrium constant values) is involved therein. In the case of acid-base systems, the equilibrium constants involved in the related acid-base reactions are applied. The choice of the equilibrium constants resulted from practical needs (Poncelet et al., 1985; Kankare, 1972; Nurchi and Crisponi, 1989; Ure and Davidson, 2002; Asuero et al., 1986b), namely: (a) simplicity of notation of the related formulas, where the equilibrium constants are involved, (b) usefulness of the equilibrium constants for immediate application, and (c) accessibility of particular kinds of equilibrium constants in the related tables of equilibrium data, such as dissociation constants, protonation constants, and successive protonation constants. Knowledge of the relationships between the equilibrium constants appears then to be useful for particular purposes.

Equilibrium Constants Applied in Acid-Base Systems

Equilibrium constants referring to an acid-base system can be formulated in different ways. For this purpose, let us assume the protonation of a basic form L^{-n} of an acid H_nL involved with formation of the species:

$$HL^{+1-n}, H_2L^{+2-n}, \ldots, H_qL^{+q-n}$$

where $q \geq n$ for weak acids and $q < n$ for strong acids.

Notation of the species can be made differently; the (non-obligatory) choice is involved mainly with the simplest indexing of the related equilibrium constants. Two kinds of equilibrium constants involved with these species and applied in this article are related to:

TABLE 1
Selected papers on pH calculation in complex systems.

Content	Reference
Formulation and solutions for general mixtures involving acid-base reactions and salts. The root of the polynomial in C^H can be computed directly by solving for the eigenvalues of the companion matriz (roots command in MATLAB).	Persat et al., 2009a
Many of the traditional equilibrium problems from acid-base chemistry can be conveniently expressed in matrix formalism by the use of the extent of reaction.	Birk, 2009
A new mathematical model that accurately predicts quantitatively the partitioning of H^+ among various monoprotic buffer pairs in aqueous solution, and the equilibrium H^+ based on the pre-equilibrium reactant concentrations in a multiple buffered solution.	Nguyen at al., 2009; Wooten, 2010; Corey, 2010; Ring, 2010
A model is proposed to predict accurately pH evolution during alcoholic fermentation of must by *Saccharomyces cerevisiae*, validated in synthetic media and grape must without tartaric acid.	Akin et al., 2008
pH and titratable acidity are calculated by rigorous treatment as a multi-composed acid-base system from proton dissociation equation, mass balance equations, and electroneutrality condition.	Lang and Meier, 2007
A simple procedure useful for generalizing the pH calculation for any pH-dependent model is developed to evaluate numerically the total equivalents introduced by any buffer component in solution.	Zafer and Vanrolleghem, 2006
Calculation of pH of arbitrary Bronsted acid-base mixtures in aqueous medium through the application of the proton function shows it is a monotonic decreasing function in the pH interval and there is only one equilibrium condition.	Frison and Calatroni, 2006
The pH of the root of the general expression for the porton function for any mixture of acids, bases, and salts is found either by bisection or by using the Newton-Raphson or Levenberg-Marquardt algorithms, which are easily implemented on a spreadsheet.	de Levie et al., 2003
Three "easy-to-use solvers" for the approximation of pH and the concentration of protolytic species in marine aqueous systems, based on the conservation of alkalinity, the progress of a chemical reaction, and charge balance, respectively, each in FORTRAN and MATLAB.	Luff et al., 2001
A mathematical model for acid-base reactions describing the pH and concentration of various protolytes from material balance electroneutrality condition, treating features as precipitation and formation of complexes in solution.	Gustafsson et al., 1995
A new methodology of pH-metric data treatment allows the stoichiometric and association constants to be determined in those cases in which the guest is a participant in an acid-base equilibrium.	Boudeville and Burgot, 1995
A simple mathematical model is developed to calculate the pH values in acidic mineral waters, which can depict a general picture to show how acid precipitation influences the pH value of surface water.	Bi, 1995
A mathematical model based on theoretical considerations allows the interpretation of equilibrium and performs accurate calculations of ingredients for preparation of permanent wave solutions satisfying special conditions.	Chiodi, 1989
A comment to a previously article dealing with the pH calculation value of a mixture of acids and bases, calling attention to the chemical point of view.	Guiñon, 1987
A general method for calculating the pH of complex mixtures of acids, bases, and ampholytes is derived and a FORTRAN program implemented.	Cutler, 1986
Generic equations and algorithms transformed into computer programs have been developed in order to compute pH and other parameters in complex systems and to simulate titration of a complex system, taking ionic strength into consideration.	Poncelet et al., 1985
A new method for determination of the pH of mixtures of acids and bases is developed, which uses a "golden section" optimization technique, implemented on a real-time processing computer controlling a neutralization process.	Pons et al., 1983
An approach to acid-base that revolutionizes our ability to understand, predict, and control what happens to hydrogen ions in living systems.	Stewart, 1983

TABLE 2
Selected papers on titration curves in (main) complex systems.

Content	Reference
Different methods of using computer acquisition and modeling to examine acid-base titrations are reviewed, showing that a versatile, integrated computer learning environment can be successfully applied to this end.	Heck et al., 2009
A simple way of treating the general equation for acid-base titrations based on the degree of dissociation is presented; a new spreadsheet approach for simulating the titration of mixtures of polyprotic acids (both in MS Excel and Visual-Basic-for-Excel) is also proposed.	Oliveira et al., 2007
The methods published in the past four decades concerning on-site titration measurement of volatile fatty acids (VFA) and carbonate alkalinity concentrations are reviewed in connection with anaerobic treatment systems.	Lahav and Morgan, 2004
A formula giving explicitly the relation V = f(pH) is derived that includes mono- and polyfunctional protolytes and their mixtures, applied to the simplest case, the analysis of one monofunctional protolyte.	Maslarska et al., 2003
Ii is possible for simple titration reactions to derive expressions in terms of inverse hyperbolic or trigonometric functions, the general expressions so obtained being used to model more complicated titrations.	Morales, 2002
An alternative method is presented for modeling and graphic presentation of titration curves based on titration degree as a function of pH closed formula.	Heil and Schäfer, 2002
The pH of any solution, the buffer strength, and the titration of any acid or mixture of acids with a base or mixtures of bases (or its inverse) may be given as a function of the proton function ^{H}C in each case; the approach may be extended to complexation, titration, and redox equilibria.	de Levie, 2001a
The dependence of various concentrations on the progress of an acid-base titration can be visualized in the form of linear graphs.	de Levie, 2001b
The general equation for the acid-base titration curve can be written in the form of the general equation for additive properties and may be used to derive an iterative procedure for extracting: pKa's, the relative activity coefficients of the ionic species and the concentration of analyte, as well as calculating the error in each parameter.	Jano et al., 2002

Successive deprotonation (dissociation)

$$H_{q+1-i}L^{+\mathrm{q+1-i-n}} = H^+ + H_{q-i}L^{+\mathrm{q-i-n}}$$

$$K_i = \frac{[H^+][H_{q-i}L^{+\mathrm{q-i-n}}]}{[H_{q+1-i}L^{+\mathrm{q+1-i}}]} \quad (i = 1, \ldots, q) \; [1]$$

Cumulative (overall) proto-complex formation

$$iH^+ + L^{-\mathrm{n}} = H_iL^{+i-n} \;\; K_i^H = \frac{[H_iL^{+i-n}]}{[H^{+1}]^i[L^{-\mathrm{n}}]} \; (i = 1, \ldots, q), \quad K_0^H = 1 \qquad [2]$$

The following interrelations are valid:

$$K_i = \frac{K_{q-i}^H}{K_{q+1-i}^H}; \quad K_i^H = \frac{1}{\prod_{\mathrm{j=1}}^{i} K_{q+1-j}} = \frac{1}{\prod_{\mathrm{j=q+1-i}}^{q} K_j} \qquad [3]$$

In more complex acid-base systems, the equilibrium constants K_{ik}^H, defined by relation

$$[H_iL_{(k)}^{+l-n_k}] = K_{ik}^H \cdot [H^+]^i \cdot [L_{(k)}^{-\mathrm{n_k}}] \; (i = 0, \ldots, q_k; k = 1, \ldots, P) \qquad [4]$$

will be applied; P is number of acid-base systems, and $K_{0k}^H = 1$.

In all aqueous media, and acid-base systems in particular, the relation for ionic product (K_W) of water

$$[\mathrm{H^+}][\mathrm{OH^-}] = \mathrm{K_W} \qquad [5]$$

is valid.

Among the equilibrium constants, one can distinguish (a) concentration, (b) hybrid, and (c) thermodynamic constants (Irving et al., 1955; Connors and Mecozzi, 2010; Zevatskii et al., 2009). Denoting by [X] and {X} the concentration and activity of the species X, respectively, and $\gamma = \{\mathrm{H^+}\}/[\mathrm{H^+}]$ as the activity coefficient for $\mathrm{X} = \mathrm{H^+}$. In particular, referring to the dissociation reaction $\mathrm{HL} = \mathrm{H^+} + \mathrm{L^-}$, we have:

$$\text{(a) } \mathrm{K_1} = [\mathrm{H^+}][\mathrm{L^-}]/[\mathrm{HL}],$$

$$\text{(b) } \mathrm{K_1^*} = \{\mathrm{H^+}\}[\mathrm{L^-}]/[\mathrm{HL}], \quad \text{(c) } \mathrm{K_{1a}} = \{\mathrm{H^+}\}\{\mathrm{L^-}\}/\{\mathrm{HL}\} \qquad [6]$$

For brevity, one can write $\{\mathrm{H^+}\} = \mathrm{h} = \gamma \cdot [\mathrm{H^+}]$, where γ is the activity coefficient of hydrogen ions. The γ-value is a function of temperature (T), ionic strength (I), and dielectric permittivity (dielectric constant, ε) values, $\gamma = \gamma(\mathrm{T, I}, \varepsilon)$. One can note that $\varepsilon = \varepsilon(\mathrm{I})$ (Conway, 1952).

TABLE 3
Selected papers on buffer capacity in complex systems

Content	Reference
The acid concentration and pK_a parameter are estimated from the buffer capacity curve (calculated from the titration curve) by using an algorithm developed in MS Excel using the Solver function, the minimum value found using the generalized reduced nonlinear algorithm.	Van Hulle et al., 2009
From the general equation of Asuero (2007) a program created by using REAL Basic 2007 Release 4 for Mac OS X (Version 10.5) has the ability to calculate and view the buffering environment with and without correction of ionic strength.	Ranaghan, n.d.
Simple expressions for the buffer capacity and its first derivative are devised, which may be easily extended to a mixture of acids, and methods to evaluate strong and moderate overlapping pK_a's are suggested and applied to literature data.	Asuero, 2007
The buffer acidity of humic acid to strong acid is low, but shows excellent buffer capacity to base addition and resists pH changes in a range between pH 5.5 and 8.	Pertusatti and Prado, 2007
A general formula and efficient algorithms implemented in a free software package pH-Tools for use in MATLAB are given for predicting the pH, titration, ionic species concentration, buffer capacity, and ionic strength of buffer solutions contaminated with defined and undefined compounds.	Dougherty et al., 2006
The buffer capacity of a chemical species in a multiple chemical reaction system is discussed in terms of a special class of stoichiometrically unique reactions using a response reaction (REPs) approach, which provides a simple algorithm for computer generation of the buffer capacity in complex systems.	Fishtik and Povar, 2006
Titration curves were shown to be a versatile tool for assessing the acidity of acidic mining waters, providing information about the strength of the buffer system present.	Totsche et al., 2006
An optimization procedure is devised to fit the model of the buffer components to the titration data and to determine accurately the buffer concentration and pKa values, implemented in a software layer and integrated to a buffer capacity sensor.	Zaher and Vanrolleghem, 2005
A general derivation is given for the isohydric theorem of Arrhenius, and its consequences for some aspects of buffer pH are considered.	de Levie, 2005
The buffer capacity of an arbitrary salt is given by the sum of cation + anion acid + anion base + water, the expressions computed by means of the Hesse and Olin (1977) formula.	Frison and Calatroni, 2005
The set of means of distributions of molar fractions in a system M, ML,. . . ML_n corresponds to the average ligand number ñ, and the set of variances of the same distributions is related to the intrinsic buffer capacity of the system.	Moya-Hernández et al., 2002
A general model for calculating electron buffer capacity is derived and applied to the generation of $p\varepsilon$-pH diagrams, extensively used in geochemistry and environmental chemistry.	King, 2002
A generalized buffer capacity model building algorithm applicable for advanced interpretation of a wide variety of titration curves is derived and evaluated and applied to a variety of experimental data.	Van de Steene et al., 2002
Buffer capacity profiles are used in the framework of automatic monitoring of water quality, with the aim of automatically and stepwise building buffer capacity models.	Van Vooren et al., 2001
An overview of the definition of pH and buffer capacity is given; the computation, numerical approximation, extrema, and applications of buffer capacity are also taken into consideration.	Urbansky and Schock, 2000
Aqueous and hydroalcoholic (11% v/v) model solutions of some organic acids of grape or formed during primary fermentation are used to determine the influence of organic acids on the buffering capacity of musts and wines.	Dartignenave et al., 2000
A software sensor was developed for the measurement of buffer capacity and alkali consumption rate from the pH response signals generated by an automatic pH controller.	Jung and Hur, 2000

The measured pH value is principally related to the activity of hydrogen ions. In order to distinguish the pH values involved with concentration and activity of hydrogen ions, one can write:

$$\mathrm{pH} = -\log[\mathrm{H}^+],\ \mathrm{ph} = -\log \mathrm{h} \qquad [7]$$

and then

$$[H^+] = 10^{-\mathrm{pH}}, \quad h = 10^{-\mathrm{ph}} \qquad [8]$$

For modeling purposes, it is assumed that the titration is made in a *quasi-static* manner under isothermal conditions in the system separated from its environment by diathermal walls and that ionic strength (I) and dielectric constant (ε) values are kept constant (Meloun et al., 1988).

Further Terms Involved with Acid-Base Titration Curves

In a simple titration, V_0 mL of titrand (D), containing the analyte A of unknown (in principle) concentration C_0 mol/L, is titrated with V mL of titrant (T) containing the reagent B (C mol/L). The degree of advancement of the reaction between B and A is the fraction titrated, Φ (Butler and Cogley, 1999; Butler, 1964; Freiser, 1970; Michałowski, 1983; Kościelniak and Michałowski, 1986) (named also as degree of titration (Waser, 1967)), expressed as the quotient $\Phi = n_B/n_A$ of the numbers of mmoles: $n_B = C{\cdot}V$ of B and $n_A = C_0{\cdot}V_0$ of A, i.e.,

$$\Phi = \frac{C \cdot V}{C_0 \cdot V_0} \quad [9]$$

The Φ versus pH relationships, $\Phi = \Phi(\mathrm{pH})$, refer only to acid-base systems with only one analyte A in D and only one reagent B in T. In a more general case of acid-base systems, the V = V(pH) functions are considered. Another formulation of equations for titration curves, such as the one presented in Campbell and Meites (1974), is not necessary and leads to ambiguities.

The Φ parameter (Equation [9]) plays a central role in the generalized equivalence mass (GEM) concept (Michałowski et al., 2010a).

Note that Φ, the molar ratio of reagents can take any positive value, $\Phi \geq 0$, and monotonically increases upon addition of titrant (Vershinin and Kukin, 2004; Vershinin, 2003; Gonzalez et al., 1990). The degree of completeness or extent of reaction (i.e., the fraction HL converted in L^- in the case of a monoprotic acid) depends on the equilibrium constant and varies in the process of titration depending on Φ (Vershinin and Kukin, 2004; Vershinin, 2003; Gonzalez et al., 1990).

In acid-base systems, with mono- and polyprotic acids H_nL involved, it is convenient to use the formation function, termed also Bjerrum's function, $\bar{n}$; see e.g., Beck (1970), Birnbaum and Walker (1987), Golonanov (2006), and Dimitrov and Kamenski 1997). When referring to acid-base systems, it expresses the mean number of protons attached to the basic form L^{-n} (Michalowski, 1981; Michałowski and Parczewski, 1978; Michałowski et al., 2010a; Asuero, 1992b, 1993) and depends immediately on pH value, $\bar{n} = \bar{n}(pH)$, i.e.,

$$\bar{n} = \frac{\sum_{i=1}^{q} i \cdot [H_iL^{+i-n}]}{\sum_{j=0}^{q} [H_jL^{+j-n}]} = \frac{\sum_{i=1}^{q} i \cdot 10^{\log K_i^H - i \cdot pH}}{\sum_{j=0}^{q} 10^{\log K_j^H - j \cdot pH}} \quad [10]$$

where K_i^H is as in Equation [2], and $K_0^H = 1$. The relative contents of the species H_iL^{+i-n} is expressed by the mole fraction (Asuero et al., 1986a, 2007; Asuero, 1993; de Levie, 1999b):

$$f_j = \frac{[H_jL]}{\sum_{i=0}^{q} [H_iL]} \quad [11]$$

In particular, at j = 0, we have

$$f_0 = \frac{1}{\sum_{i=0}^{q} K_i^H \cdot [H^+]^i} \quad [12]$$

i.e.,

$$f_i = K_i^H \cdot [H^+]^i \cdot f_0 \quad [13]$$

From Equations [10] and [11] we get

$$\bar{n} = \sum_{i=0}^{q} i \cdot f_i = \sum_{i=1}^{q} i \cdot f_i \quad [14]$$

Applying the notations:

$$y_i = K_i^H \cdot [H^+]^i, \quad y_{ik} = K_{ik}^H \cdot [H^+]^i, \quad y_0 = y_{0k} = 1 \quad [15]$$

where k = 1,...,P refers to acid-base system of k-th kind, we get:

$$[H^+] \cdot \frac{dy_i}{d[H^+]} = i \cdot y_i, \quad [H^+] \cdot \frac{dy_{ik}}{d[H^+]} = i \cdot y_{ik} \quad [16]$$

$$f_i = y_i \Big/ \sum_{j=0}^{q} y_j, \quad f_{ik} = y_{ik} \Big/ \sum_{j=0}^{q_k} y_{jk} \quad [17]$$

$$\bar{n}_k = \sum_{i=0}^{q_k} i \cdot f_{ik} \quad [18]$$

Equation [13], in its logarithmic form, $\log f_i = \log K_i^H - i \cdot pH + \log f_0$, is applicable for construction of logarithmic speciation diagrams (Wänninen, 1980; Johansson, 1973.

In all equations for acid-base systems considered in this article, the ubiquitous symbol

$$\alpha = [H^+] - [OH^-] = 10^{-\mathrm{pH}} - 10^{pH - pK_w} \quad [19]$$

originating from charge balance and termed proton excess (de Levie, 2001b; Ricci, 1952) is used.

FORMULATION OF EQUATIONS FOR ACID-BASE TITRATION CURVES

Acid-base titration curves are formulated on the basis of charge and concentration balances. This principle can be illustrated by the following examples.

Simple Acid-Base Systems: Examples

Titration of V_0 mL of C_0 mol/L HB with V mL of C mol/L MOH

From charge and concentration balances (de Levie, 1997a; Harris, 2010):

$$\alpha + [M^+] - [B^-] = 0, \quad [B^-] = \frac{C_0V_0}{V_0 + V}, \quad [M^+] = \frac{CV}{V_0 + V}$$

we have

$$V = V_0 \cdot \frac{C_0 - \alpha}{C + \alpha} \quad [20]$$

Titration of V_0 mL of C_0 mol/L MOH with V mL of C mol/L HB

From charge and concentration balances:

$$\alpha+[M^+]-[B^-]=0,\quad [M^+]=\frac{C_0V_0}{V_0+V},\quad [B^-]=\frac{CV}{V_0+V}$$

we have

$$V=V_0\cdot\frac{C_0+\alpha}{C-\alpha} \qquad [21]$$

Titration of V_0 mL of C_0 mol/L H_n L with V mL of C mol/L MOH

From (Olin and Wallen, 1978; Hesse and Olin, 1977):

$$\alpha+[M^+]+\sum_{i=0}^{q}(i-n)[H_iL^{+i-n}]=0,$$

$$\sum_{i=0}^{q}[H_iL^{+i-n}]=\frac{C_0V_0}{V_0+V},\quad [M^+]=\frac{CV}{V_0+V} \qquad [22]$$

we have

$$\alpha+[M^+]+\sum_{i=0}^{q}i\cdot[H_iL^{+i-n}]-n\cdot\sum_{i=0}^{q}[H_iL^{+i-n}]=0 \qquad [23]$$

Applying Equations [10] and [19] in [23] and rearranging the terms, we have

$$V=V_0\cdot\frac{(n-\bar{n})\cdot C_0-\alpha}{C+\alpha} \qquad [24]$$

In particular, for titration of HL (q = n = 1) with MOH we have

$$V=V_0\cdot\frac{(1-\bar{n})\cdot C_0-\alpha}{C+\alpha} \qquad [25]$$

where

$$\bar{n}=f_1=\frac{K_1^H\cdot[H^+]}{1+K_1^H\cdot[H^+]}=\frac{[H^+]}{K_1+[H^+]},$$

$$K_1^H=1/K_1=\frac{[HL]}{[H^+][L^-]}$$

See Equations [1], [3], [10], and [11].

Titration of V_0 mL of C_0 mol/L $M_kH_{n-k}L$ with V mL of C mol/L MOH

From:

$$\alpha+[M^+]+\sum_{i=0}^{q}(i-n)\cdot[H_iL^{+i-n}]=0,$$

$$\sum_{i=0}^{q}[H_iL^{+i-n}]=\frac{C_0V_0}{V_0+V},\quad [M^+]=\frac{k\cdot C_0V_0+CV}{V_0+V}$$

and Equation [10], we have

$$V=V_0\cdot\frac{(n-k-\bar{n})\cdot C_0-\alpha}{C+\alpha} \qquad [26]$$

Titration of V_0 mL of C_0 mol/L $M_kH_{n-k}L$ with V mL of C mol/L HB

From:

$$\alpha+[M^+]+\sum_{i=0}^{q}(i-n)\cdot[H_iL^{+i-n}]-[B^-]=0,$$

$$\sum_{i=0}^{q}[H_iL^{+i-n}]=\frac{C_0V_0}{V_0+V},$$

$$[M^+]=\frac{k\cdot C_0V_0}{V_0+V},\quad [B^-]=\frac{CV}{V_0+V}$$

and Equation [10] we have

$$V=V_0\cdot\frac{(\bar{n}+k-n)\cdot C_0+\alpha}{C-\alpha} \qquad [27]$$

Titration of V_0 mL of C_0 mol/L $H_{n+k}LB_k$ with V mL of C mol/L MOH

From:

$$\alpha+[M^+]+\sum_{i=0}^{q}(i-n)\cdot[H_iL^{+i-n}]-[B^-]=0,$$

$$\sum_{i=0}^{q}[H_iL^{+i-n}]=\frac{C_0V_0}{V_0+V},$$

$$[B^-]=\frac{k\cdot C_0V_0}{V_0+V},\quad [M^+]=\frac{CV}{V_0+V}$$

and Equation [10] we have

$$V=V_0\cdot\frac{(n+k-\bar{n})\cdot C_0-\alpha}{C+\alpha} \qquad [28]$$

In particular, for k = q – n, i.e., n + k = q, from Equation [28] we get

$$V=V_0\cdot\frac{(q-\bar{n})\cdot C_0-\alpha}{C+\alpha} \qquad [29]$$

For k = n, from Equation [27] we have

$$V=V_0\cdot\frac{\bar{n}\cdot C_0+\alpha}{C-\alpha} \qquad [30]$$

For ease of computation, it is sometimes advisable to rewrite the related equation for titration curve into the form $V_0+V=\phi(\text{pH})$. For example, Equations [20], [24], and [25] can be written as follows:

$$V_0+V=V_0\cdot\frac{C_0+C}{C+\alpha} \qquad [20a]$$

$$V_0+V=V_0\cdot\frac{(n-\bar{n})\cdot C_0+C}{C+\alpha} \qquad [24a]$$

$$V_0+V=V_0\cdot\frac{(1-\bar{n})\cdot C_0+C}{C+\alpha} \qquad [25a]$$

This enables simplifying some derivation procedures, e.g., ones involved with differentiation The value 1 – $\bar{n}$ in Equation

[25a] is also called the deprotonation number (Albert and Serjeant, 1984). In general, the degree of deprotonation (Egneus, 1968; Kankare, 1973) is the factor that multiplies the initial concentration C_0 in the numerator of Equations [24], [26], and [27]. On rearrangement of these expressions we may obtain the value of $\bar{n}$ as a function of the rest of the parameters, which may be determined by evaluating the hydrogen ion concentration from electromotive force measurements. We may calculate the value of dissociation constants (Meloun et al., 1988; Asuero, 1990; Ramis Ramos and García Alvarez-Coque, 1989; Czerminski et al., 1990; Lambert and Dalga, 1990) from the pairs of data $\bar{n}$, pH for diprotic or triprotic acids by using the least squares method (Asuero, 1992b; Asuero and Bueno, 2011; Sayago et al., 2004; Sayago and Asuero, 2004; Asuero et al., 2006; Asuero and Gonzalez, 2007) or by nonlinear least squares (Qiang and Adams, 2004; Meloun et al., 1988; Lambert and Dalga, 1990).

All the relationships derived in this section can also be presented in terms of the fraction titrated Φ (Equation [9]); see Table 4, where some other D+T systems are also included, and further formation functions:

$$\bar{m} = \frac{\sum_{i=1}^{p} i \cdot [H_i\text{Ł}^{+i-m}]}{\sum_{i=0}^{p} [H_i\text{Ł}^{+i-n}]} = \frac{\sum_{i=1}^{p} i \cdot 10^{\log K_{\text{Ł}i}^{H} - i\cdot pH}}{\sum_{i=0}^{p} 10^{\log K_{\text{Ł}i}^{H} - i\cdot pH}} \quad [31]$$

$$\bar{n}_{\mathrm{N}} = \frac{[NH_4^+]}{[NH_4^+] + [NH_3]} = \frac{10^{\log K_{1N}^{H} - pH}}{10^{\log K_{1N}^{H} - pH} + 1} \quad [32]$$

are applied, where:

$$[H_iL^{+i-m}] = K_{Li}^{H} \cdot [H^+]^i [L^{-\mathrm{m}}]\ (i = 0, \ldots, r)$$

$$[NH_4^+] = K_{1N}^{H} \cdot [H^+][NH_3] (\log K_{1N}^{H} = 9.35);$$

$$K_{L0}^{H} = 1; M^+ = K^+, Na^+$$

TABLE 4

Expressions for Φ with A and B, related to some D+T acid-base systems; $M^+ = Na^+, K^+$; $B^- = Cl^-, NO_3^-$; k = 0,. . . ,n (No. 1–4, 6–11), k = 0,. . . ,q-n (No. 5); l = 0,. . . ,m, $[H^+] = 10^{-pH}$ (Michalowski, 1981).

No.	A	B	Φ =
1	HCl	MOH	$\frac{C}{C_0} \cdot \frac{C_0 - \alpha}{C + \alpha}$
2	MOH	HB	$\frac{C}{C_0} \cdot \frac{C_0 + \alpha}{C - \alpha}$
3	$M_kH_{n-k}L$	MOH	$\frac{C}{C_0} \cdot \frac{(n - k - \bar{n}) \cdot C_0 - \alpha}{C + \alpha}$
4	$M_kH_{n-k}L$	HB	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k - n) \cdot C_0 + \alpha}{C - \alpha}$
5	$H_{n+k}LB_k$	MOH	$\frac{C}{C_0} \cdot \frac{(n + k - \bar{n}) \cdot C_0 - \alpha}{C + \alpha}$
6	$(NH_4)_kH_{n-k}L$	MOH	$\frac{C}{C_0} \cdot \frac{(n - k \cdot \bar{n}_{\mathrm{N}} - \bar{n}) \cdot C_0 - \alpha}{C + \alpha}$
7	$(NH_4)_kH_{n-k}L$	HB	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k \cdot \bar{n}_{\mathrm{N}} - n) \cdot C_0 + \alpha}{C - \alpha}$
8	$M_kH_{n-k}L$	$M_lH_{m-l}\,\text{Ł}$	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k - n)C_0 + \alpha}{(m - l - \bar{m})C - \alpha}$
9	$M_kH_{n-k}L$	$(NH_4)_lH_{m-l}\,\text{Ł}$	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k - n) \cdot C_0 + \alpha}{(m - l \cdot \bar{n}_{\mathrm{N}} - \bar{m}) \cdot C - \alpha}$
10	$(NH_4)_kH_{n-k}L$	$M_lH_{m-l}\,\text{Ł}$	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k \cdot \bar{n}_{\mathrm{N}} - n) \cdot C_0 + \alpha}{(m - l - \bar{m}) \cdot C - \alpha}$
11	$(NH_4)_kH_{n-k}L$	$(NH_4)_lH_{m-l}\,\text{Ł}$	$\frac{C}{C_0} \cdot \frac{(\bar{n} + k \cdot \bar{n}_{\mathrm{N}} - n) \cdot C_0 + \alpha}{(m - l \cdot \bar{n}_{\mathrm{N}} - \bar{m}) \cdot C - \alpha}$

Inspection of Table 4 reveals some regularities. For example, the numerator in the related fraction is related to D, and the denominator to T. All the fractions can be presented in compact, generalized forms:

$$V = V_0 \cdot \frac{R_A \cdot C_0 - \alpha}{R_B \cdot C + \alpha} \leftrightarrow \Phi = \frac{C}{C_0} \cdot \frac{R_A \cdot C_0 - \alpha}{R_B \cdot C + \alpha} \quad [33]$$

where R_{A} and R_{B} are involved with A in D and B in T, respectively. Among other regularities, one can notice that $(n - k\bar{n}_{\mathrm{N}} - \bar{n})C_0 - \alpha = -((\bar{n} + k\bar{n}_{\mathrm{N}} - n)C_0 + \alpha)$, when HB is substituted for MOH as T (no. 6 and no. 7 in Table 4). This enables avoiding extensive formulation, exemplified by Zaher and Vanrolleghem (2006).

The method as devised here is more general and complete than the previous expressions (de Levie, 1996a, b, 1999c; Rosset et al., 1979, 1991; Desbarres and Bauer, 1975; Johansson and Johansson, 1979; Knudson and Nimrod, 1997; Billes and Toth, 1986; Moisio and Heikonen, 1996a; Glaiser, 1999) reported. It should be noticed that the formulation of an equation for a titration curve on the basis of charge and concentration balances for acid-base systems is more natural/convenient/straightforward than an approach based on application of proton balance (de Levie, 2001a; Maccà, 1997) instead of charge balance, practiced by votaries of stoichiometry and inferences based on (Asuero et al., In preparation) a chemical reaction notation.

In this context we may mention that in 1966 Fleck (Fleck, 1966) derived an equation for dibasic acid in which the volume of titrant can be calculated as a function of hydrogen ion concentration. Since then, the inverse approach, i.e., the expression of titration curves in the form V = V(pH), has been advocated by a number of authors (Waser, 1967; Nowogrocki et al., 1976; Still and Sara, 1977; Stairs, 1978; Ramette, 1981; Willis, 1981), in a pioneering way.

Effect of CO_2 in NaOH on the Plots of Acid-Base Titration Curves

Some authors have studied the influence of CO_2 in the acid-base titration curves (Maccà, 1986; Wozniak and Nowogrocki, 1981; Michalowski, 1988b). Let us assume a D+T system composed of V_0 mL of C_0 mol/L analyte A as D and V mL of T with NaOH (C mol/L) + CO_2 (C_1 mol/L), i.e., NaOH is partially transformed into carbonate. The titration curve can be presented by the relation

$$\Phi = \frac{C}{C_0} \cdot \frac{R_A \cdot C_0 - \alpha}{C - (2 - \bar{m}) \cdot C_1 + \alpha} \quad [34]$$

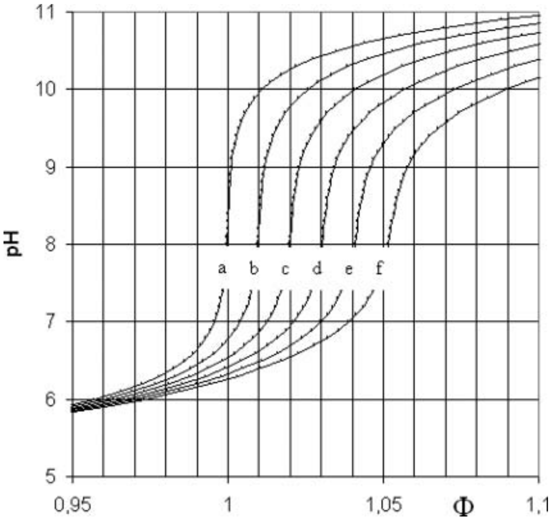


FIG. 1. The pH vs. Φ relationships plotted at $C_0 = 0.01$ mol/L HL ($\log K_1^H = 4.65$), $C = 0.1$ mol/L and C_1 [mol/L]: (a) 0; (b) 0.001; (c) 0.002; (d) 0.003; (e) 0.004; (f) 0.005.

(compare with Equation [33]), where

$$\bar{m} = \frac{2[H_2L]+[HL^-]}{[H_2L]+[HL^-]+[L^{-2}]} = \frac{2[H^+]^2+K_1[H^+]}{[H^+]^2+K_1[H^+]+K_1K_2} = \frac{2\cdot 10^{16.4-2pH}+10^{10.1-pH}}{10^{16.4-2pH}+10^{10.1-pH}+1} \qquad [35]$$

and, in particular, $R_A = 1 - \bar{n}$ for acetic acid ($A = HL$, $q = n = 1$), and $R_A = 3 - \bar{n}$ for $A = H_3PO_4$ ($q = n = 3$); $\bar{n}$ is expressed by Equation [10]. As results from Fig. 1, for $A = HL$ (acetic acid, $\log K_1^H = 4.65$), $R_A = 1 - \bar{n}$ ($q = n = 1$), the titration curves related to different C_1 values scatter distinctly at the vicinity of the main inflection point. The growth in error of the analysis is nearly proportional to C_1 value. The NaOH solution contaminated with CO_2 acts as pure NaOH up to a pH of approximately 4. For phosphoric acid, the effect of C_1 value is relatively small at the vicinity of $\Phi = 1$ (Fig. 2a) and great at the vicinity of $\Phi = 2$ (Fig. 2b). One should note that the so-named carbonate-free commercial ampoules with NaOH contain 0.5–1.5% carbonate (Martell and Motekaitis, 1992; Vesala, 1992).

Complex Acid-Base Systems

One can also refer to a more general case, where V_0 mL of a solution containing a mixture of acid-base systems: $K_{m_k}H_{n_k-m_k}L_{(k)}$ (C_{0k}, $k = 1,\ldots,p$; $m_k = 0,\ldots,n_k$) + $H_{m_k+n_k}L_{(k)}B_{m_k}$ (C_{0k}, $k = p+1,\ldots,P$; $m_k = 0,\ldots,q_k-n_k$)+ HB (C_a) + MOH (C_b) is titrated with V mL of C mol/L solution of $M_mH_{n-m}L$ (C). From the balances:

$$\alpha + [K^+] + [M^+] - [B^-] + \sum_{k=1}^{p}\sum_{i=0}^{q_k}(i-n_k)\left[H_iL_{(k)}^{+i-n_k}\right] + \sum_{i=0}^{q}(i-n)\left[H_iL^{+i-n}\right] = 0$$

$$[K^+] = \sum_{k=1}^{p} m_k\cdot C_{0k}\cdot V_0/(V_0+V)$$

$$[B^-] = \sum_{k=p+1}^{P} m_k\cdot C_{0k}\cdot V_0/(V_0+V) + C_a\cdot V_0/(V_0+V)$$

$$[M^+] = m\cdot C\cdot V/(V_0+V) + C_b\cdot V_0/(V_0+V)$$

$$\alpha + [K^+] + [M^+] - [B^-] + \sum_{k=1}^{P}\sum_{i=0}^{q_k}(i-n_k)[H_iL_{(k)}^{+i-n_k}] + \sum_{i=0}^{q}(i-n)[H_iL^{+i-n}] = 0$$

and the formation functions:

$$\bar{n}_k = \frac{\sum_{i=0}^{q_k} i\cdot[H_iL_{(k)}^{+i-n_k}]}{\sum_{j=0}^{q_k}[H_jL_{(k)}^{+i-n_j}]} \qquad [36]$$

after further transformations similar to ones specified above, we get the relation

$$V = V_0\cdot\frac{X+Y+\Delta+\alpha}{Z-\alpha} \qquad [37]$$

where α (Equation [19]), and:

$$\Delta = C_b - C_a \qquad [38]$$

$$X = \sum_{k=1}^{p}(\bar{n}_k + m_k - n_k)\cdot C_{0k};$$

$$Y = \sum_{k=p+1}^{P}(\bar{n}_k - m_k - n_k)\cdot C_{0k};$$

$$Z = (n - m - \bar{n})\cdot C \qquad [39]$$

See Equation [33]. Acid-base systems of similar complexity were considered recently in context with the isohydricity property (Michałowski et al., 2010c), where, for example, the titration of an acid by another acid was suggested and applied to practical purposes.

The formulation presented above is far more straightforward and more general than those presented elsewhere (de Levie, 1996a, b; Billes and Toth, 1986; Nowogrocki et al., 1976; Wozniak, 1977; Rojas-Hernández and Ramirez-Silva, 2002).

Composition of acid-base systems considered above can be completed by hydroxo-complexes $Me_{(k)}(OH)_i^{+u_k-i}$ formed by some metal ions, $Me_{(k)}^{+u_k}$ ($k = 1,\ldots,U$). In latter parts of this article, for simplicity of notation, we apply the simplifying assumptions that (1) no soluble complexes are formed between $Me_{(k)}^{+u_k}$ and $L_{(l)}^{-n_l}$ species or they can be omitted in considerations, and (2) no insoluble forms (precipitates), e.g., hydroxides, enter the system considered (the system is a homogeneous one).

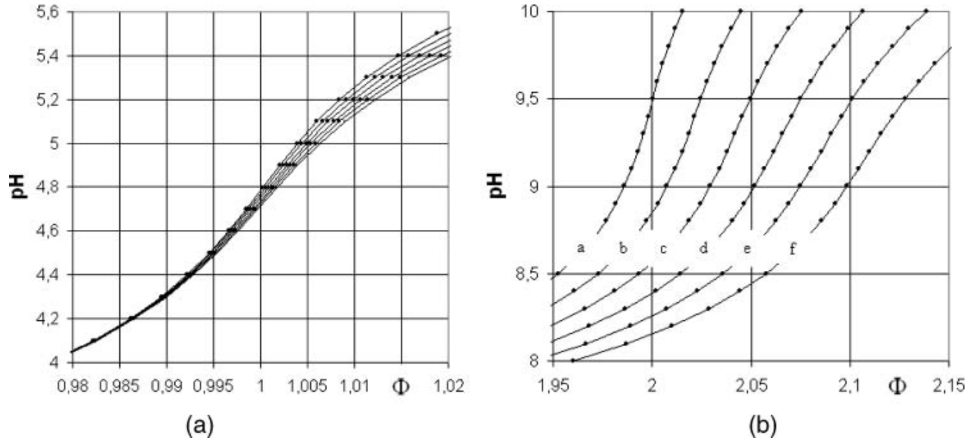


FIG. 2. The pH vs. Φ relationships plotted at $C_0 = 0.01$ mol/L H_3PO_4 ($\log K_i^H = 12.3, 19.5, 21.6$), $C = 0.1$ mol/L and C_1 [mol/L]: (a) 0; (b) 0.001; (c) 0.002; (d) 0.003; (e) 0.004; (f) 0.005.

The composition of soluble hydroxo-complexes $Me_{(k)}(OH)_i^{+u_k-i}$ can be expressed with use of the formation function

$$\bar{n}_k^{\cdot} = \frac{\sum_{i=0}^{r_k} i \cdot [Me_{(k)}(OH)_i^{+u_k-i}]}{\sum_{j=0}^{r_k} [Me_{(k)}(OH)_j^{+u_k-j}]} \qquad [40]$$

Simms Constants

The expressions for $q_k - \bar{n}_k$ (k = i, j) can be rewritten in terms of Simms constants (Simms, 1926a, b; Muralt, 1930; Klas, 1968, 1975; Johansson and Johnsson, 1979) g_{kl} or hybrid Simms constants (Fishtik and Povar, 2006; Michałowski, 1992; Michałowski and Gibas, 1994)g_{kl}^*:

$$q_k - \bar{n}_k = \sum_{i=1}^{q_k} ([H^{+1}]/g_{ki} + 1)^{-1} = \sum_{i=1}^{q_k} (h/g_{ki}^* + 1)^{-1} \qquad [41]$$

where

$$g_{ki}^* = \gamma \cdot g_{ki} \qquad [42]$$

and h is activity and γ is activity coefficient of hydrogen ions. The Simms constants are interrelated with successive dissociation constants K_i (i = 1,. . . ,q) of the acid considered

$$K_1 = [H^{+1}][H_{q-1}L^{+q-1-n}]/[H_qL^{+q-n}], \ldots,$$
$$K_q = [H^{+1}][L^{-n}]/[HL^{+1-n}]$$

(See Equation [1]). For an acid H_nL forming the species H_lL^{+l-n} (l = 0,. . . , q), we get (Michalowski, 1992; Johansson, 1979; King, 1965; Edall and Wyman, 1958; Klotz, 1953; Cohn and Edsall, 1943) a series of interrelations:

$$K_1 = \sum_{i=1}^{q} g_i$$

$$K_1 \cdot K_2 = \sum_{i=1}^{q-1} \sum_{j=i+1}^{q} g_i \cdot g_j$$

$$K_1 \cdot K_2 \cdot K_3 = \sum_{i=1}^{q-2} \sum_{j=i+1}^{q-1} \sum_{k=j+1}^{q} g_i \cdot g_j \cdot g_k$$

$$K_1 \cdot K_2 \cdot \ldots \cdot K_q = g_1 \cdot g_2 \cdot \ldots \cdot g_q \qquad [43]$$

Another approach for derivation of the formulas was applied by Kankare (1975).

The $\bar{n}_k^{\cdot}$(Equation [40]) can be expressed in terms of Simms constants too. For this purpose, we apply the equilibrium constants $K_{ik}^{\cdot}$(i = 1,. . . , r_k) related to reactions

$$Me_{(k)}(OH)_{i-1}^{+u_k-i+1} + H_2O = Me_{(k)}(OH)_i^{+u_k-i} + H^+,$$

$$K_{ik}^{\cdot} = \frac{[Me_{(k)}(OH)_i^{+u_k-i}][H^+]}{[Me_{(k)}(OH)_{i-1}^{+u_k-i+1}]} \qquad [44]$$

Then we have, by turns:

$$[Me_{(k)}(OH)_{i-1}^{+u_k-i+1}] = \prod_{l=1}^{i} K_{lk}^{\cdot} \cdot \frac{[Me_{(k)}^{+u_k}]}{[H^+]^i} \qquad [45]$$

$$\bar{n}_k^{\cdot} = \frac{\sum_{i=1}^{r_k} i \cdot [H^+]^{r_k-i} \cdot \prod_{l=1}^{i} K_{lk}^{\cdot}}{\sum_{i=0}^{r_k} [H^+]^{r_k-i} \cdot \prod_{l=0}^{i} K_{lk}^{\cdot}} \qquad [46]$$

where $K_{0k}^{\cdot} \equiv 1$. Equation [46] has salient similarities with the expression for $q_k - \bar{n}_k$ (Equation [41]) for a polyprotic acid. Then one can write:

$$\bar{n}_k^{\cdot} = \sum_{j=1}^{r_k} \left(1 + h/g_{jk}^{\cdot}\right)^{-1} \qquad [47]$$

In Table 5 are compiled references to the main chemical and biochemical articles published dealing with the Simms constants topic.

SOME PROPERTIES OF ACID-BASE TITRATION CURVES

Inflection Point(s)

The relationship V = V(pH) is a strictly monotonic (increasing or decreasing) function, i.e., its derivative, dV/dpH,

TABLE 5
Articles dealing with Simms titration constants

Content	Reference
It is possible to describe a binding isotherm in terms of an affinity statistical distribution of y independent (noninteracting) sites, which may be equally described in terms of y-step addition of ligands to the y-dentate center, and vice versa.	Kholin and Zaitsev, 2008; Lucho et al., 2007
Titration data corresponding to metal ions in methanol may analyzed by simpler methods following Simms titration constants, which are obtained as half-neutralization points determined as if the solution contained monovalent, noninteracting acids.	Gibson et al., 2003, 2006
Complex acid-base systems can be easily simplified and generalized, provided that the idea of Simms constants is applied, taking EDTA as an example.	Michalowski et al., 2005b
The pK spectrum of a hydrated aluminium oxide sol corresponds to the presence of acid-base groups of four main types on the surface of the sol particles, within the framework that a polybasic acid is equivalent to a corresponding number of monobasic acids.	Ryazanov and Dudkin, 2004
Every total titration curve of a polyprotic acid with N sites can be described as sum of noninteracting, so-called quasities. The titration curves of the individual sites are just a linear combination of the titration curve of these quasities (decoupled sites representation).	Ullmann, 2003
The Ising model not only can be used to derive systematically several known expressions for pK values of polyprotic molecules but also leads to new analytical results without interactions between acid-base groups.	Borkove and Koper, 1994
Regression equations of the type $(V_0 + V)^{-1}\,\varphi(\mathrm{h})$ based on the Simms titration constants are described, adaptable for determination of parameters (concentration, equilibrium constant, pH) in various systems, by means of the computer program MINUIT.	Michalowski and Gibas, 1994; Michalowski, 1992
The pH dependence of any property is the sum of one-site curves with the titration constants. In particular, each group of a multivalent molecule titrates as if a fraction of it had each of the dissociation constants of the molecule.	Dixon et al., 1991, 1994
The relationships between dissociation constants and Simms constants.	Dixon, 1973, 1974, 1975, 1988; Dixon et al., 1987
The macroscopic constants for association (K_{a1} and K_{a2}) of a mixture of independent macromolecular binding sites truly independent (with the number of sides equal to 1) are related to the titration constants (G_1 and G_2) regardless of whether the sites are independent.	Shibuya et al., 1986
A model is applied based on the simplification assumption that fulvic acid can be treated as if it contains a limited number of monoprotic acids.	Paxéus and Wedborg, 1985
The acidic group of humic substances may be treated as a mixture of monoprotic acids, even though more complex acids are undoubtedly present. The neglect of the polyprotic character of some of the acids of aquatic humus should not be of any consequence.	Purdue et al., 1984
The polyprotic acids of seawater (carbonic acid, phosphoric acid, and sulfuric acid) are treated as a mixture of monoprotic acids, but with different equilibrium constants, i.e., titration constants, in order for the determination of the alkalinity and total carbonate in seawater.	Johansson et al., 1983; Dickson, 1981
The problem of considering the ionization of diprotic acids as two independently ionizing monoprotic acids is solved with techniques of probability.	Reinhardt, 1983
A computer program designed to analyze titration data for an unknown solution functions autonomously and yields pK values and concentrations, as well as their limits of error, reporting improvements in the earlier method (Gordon, 1979) of the same author.	Gordon, 1982
The four microscopic ionization constants for glutathione with the corresponding constants for cysteine, 2-mercaptoethylamine, and cis-2-mercaptocyclobuthylamine have been determined by using the potentiometric difference titration method.	Lewis et al., 1980
Chemical parameters are determined by curve fitting from titration data for an unknown solution, the method depending on an additive form of the titration function based on Simms, also considered the limits of resolution.	Gordon, 1979

(Continued on next page)

TABLE 5
Articles dealing with Simms titration constants *(Continued)*

Content	Reference
The conditions to be fulfilled by regarding complexes of the type A_nB as no complexes of the type AB are discussed in detail, in order to give correct results.	Johannson, 1978, 1979
It is simpler to treat a diprotic acid with dissociation constants K_1 and K_2 as a mixture of two monoprotic acids with dissociation constants G_1 and G_2.	Johansson and Johansson, 1978; Pehrsson et al., 1976
If pG_2 and pG_1 (Simms titration constants) are called pK* ± log p, then pK_2 and pK_1 (molecular dissociation constants) are given by pK* ± log (p+1/p).	Dixon, 1979
In the simple case where the sites have fixed (although different) affinities, the moles of bound ligand per mole of total protein may be expressed as additives in terms of Simms constants, the site approach providing direct information about the miscroscopic aspects of binding.	Kloz and Hunston, 1975, 1979
The ionization behavior of groups at the active site of papain was determined from the pH dependence of the difference in proton content of papin and the methylthiol derivative of the thiol group at the active site of papain.	Lewis et al., 1976
The titration curve of a polyfunctional acid is identical with that of an equimolecular mixture of monofunctional acids if and only if the protonation polynomial has real zeros. A method for determining the functionality of an acid is outlined.	Kankare, 1975
An accurate and relatively simple mathematical method for the determination of the stability constants of complexes by means of the average ligand number by using the Simms concept of the dissociation of polyvalent acids is given.	Klas, 1975
Values of pK_1 and pK_2 for fulvic acid are determined using the Simms method for polyelectrolytes at 25°C and $\mu = 0.1$.	Gamble, 1970
A theoretical analysis of the stepwise equilibrium model for macromolecule-ligand interactions is presented, examining its mathematical equivalence with the model of Scatchard and obtaining accurate estimates of the equilibrium constants by using a computer algorithm.	Fletcher et al., 1970
It is possible to obtain a relatively simple and general solution of the weak polyvalent acid problem if the concept of Simms is utilized.	Klas, 1968
Titration constants of arginosuccinic acid and related compounds are given.	Ratner et al., 1953
The general equations of Simms may be obtained in a purely mathematical transformation of the classical dissociation equations given by the mass law, without any assumption.	Muralt, 1930
The titration data of a complex or impure substance may be interpreted by a graphical method in which the titration curve is compared with a curve having known titration constants. Three hypothetical examples are discussed in detail.	Simms and Levene, 1927
The titration constants of 2,5-anhydro sugar acids have been determined in connection with other work dealing with the problem of the influence of ionization on optical rotation.	Levene and Bass, 1927
The relationship between the dissociation, the intrinsic, and the titration constants, respectively, of any acid, base, or ampholyte system is given.	Simms, 1926b
The electrometric titration data of any polyvalent acid, base, or ampholyte (whether symmetrical or not) may be calculated as if it were an equivalent mixture of monoprotic acids.	Simms, 1926a

is positive or negative. Note that V = V(pH) is the inverse function against pH = pH(V), where V is the independent and pH the dependent variable, in the case of experimental titration. One can define the slope (η) of the titration curve pH = pH(V)

$$\eta = \frac{dpH}{dV} = \frac{1}{dV/dpH} \qquad [48]$$

and then, by turns:

$$\frac{d^2pH}{dV^2} = -\frac{1}{(dV/dpH)^2} \cdot \frac{d^2V}{dpH^2}$$

$$\left(\frac{dV}{pH}\right)^2 \cdot \frac{d^2pH}{dV^2} + \frac{d^2V}{dpH^2} = 0 \qquad [49]$$

At the inflection (inf) point(s) on the curve pH = pH(V), we have

$$\frac{d^2pH}{dV^2} = 0 \qquad [50]$$

Then from Equations [49] and [50], at dV/dpH $\neq$ 0 we get

$$\frac{d^2V}{dpH^2} = 0 \qquad [51]$$

i.e., the equalities [50] and [51] for inflection point(s) can be considered equivalently. This property is important in the light of the fact that functions of the type V = V(pH) can be easily formulated, as well as in more complex systems.

As was stated previously (Michalowski, 1981), the property dV/dpH $\neq$ 0 applies to all acid-base titrations made in aqueous media, but not to acid-base titrations made in some binary-solvent media (Pilarski et al., 2010; Michalowski et al., 2010b) or in redox systems (Michałowski and Lesiak, 1994; Michałowski et al., 1996, 2005c). Applying the relationships:

$$y = \frac{dV}{dpH} = \frac{dV}{d[H^+]} \cdot \frac{d[H^+]}{dpH} = -\ln 10 \cdot [H^+] \cdot \frac{dV}{d[H^+]} \qquad [52]$$

$$\frac{d^2V}{dpH^2} = \frac{d}{dpH}\left(\frac{dV}{dpH}\right) = \frac{dy}{dpH} = \frac{dy}{d[H^+]} \cdot \frac{d[H^+]}{dpH}$$
$$= (\ln 10)^2 \cdot [H^+] \cdot \frac{d}{d[H^+]}\left([H^+] \cdot \frac{dV}{d[H^+]}\right) \qquad [53]$$

we get $dV/d[H^+] + [H^+] \cdot d^2V/d[H^+]^2 = 0$ or its equivalent forms:

$$[H^+] \cdot \frac{dV}{d[H^+]} + [H^+]^2 \cdot \frac{d^2V}{d[H^+]^2} = 0$$
$$\leftrightarrow [H^+] \cdot \frac{d(V_0 + V)}{d[H^+]} + [H^+]^2 \cdot \frac{d^2(V_0 + V)}{d[H^+]^2} = 0 \; [54]$$

We refer to inflection points on the curve V = V(pH), represented by Equation [24a], rewritten into the form

$$V_0 + V = \frac{P}{Q} \qquad [55]$$

where:

$$P = V_0 \cdot ((n - \bar{n}) \cdot C_0 + C), \quad Q = C + \alpha$$

Then we get:

$$\frac{d(V_0 + V)}{d[H^+]} = \frac{1}{Q} \cdot \frac{dP}{d[H^+]} - \frac{P}{Q^2} \cdot \frac{dQ}{d[H^+]} \qquad [56]$$

$$\frac{d^2(V_0 + V)}{d[H^+]^2} = \frac{2P}{Q^3} \cdot \left(\frac{dQ}{d[H^+]}\right)^2 - \frac{2}{Q^2} \cdot \frac{dQ}{d[H^+]} \cdot \frac{dP}{d[H^+]}$$
$$+ \frac{1}{Q} \cdot \frac{d^2P}{d[H^+]^2} - \frac{P}{Q^2} \cdot \frac{d^2Q}{d[H^+]^2} \qquad [57]$$

where

$$\frac{dP}{d[H^+]} = -C_0V_0 \cdot \frac{d\bar{n}}{d[H^+]}, \quad \frac{dQ}{d[H^+]} = 1 + \frac{K_W}{[H^+]^2} \qquad [58]$$

$$\frac{d^2P}{d[H^+]^2} = -C_0V_0 \cdot \frac{d^2\bar{n}}{d[H^+]^2}, \quad \frac{d^2Q}{d[H^+]^2} = -\frac{2K_W}{[H^+]^3} \qquad [59]$$

$$\frac{d\bar{n}}{d[H^+]} = \frac{1}{[H^+]} \cdot \left(\sum_{i=0}^{q} i^2 \cdot f_i - \bar{n}^2\right)$$
$$= \frac{1}{[H^+]} \cdot \sum_{i>j=0}^{q} (i - j)^2 \cdot f_i f_j \qquad [60]$$

$$\frac{d^2\bar{n}}{d[H^+]^2} = \frac{1}{[H^+]^2}$$
$$\cdot \left(\bar{n}^2 + 2 \cdot \bar{n}^3 - (3\bar{n} + 1) \cdot \sum_{i=0}^{q} i^2 \cdot f_i + \sum_{i=0}^{q} i^3 \cdot f_i\right) \qquad [61]$$

(Compare with [51].) For a strong monoprotic acid, HB (n = 1, q = 0), we get: $\bar{n} = 0$, $d\bar{n}/d[H^+] = d^2\bar{n}/d[H^+]^2 = 0$, P = $V_0 \cdot (C_0 + C)$, $dP/d[H^+] = d^2P/d[H^+]^2 = 0$, and then, by turns:

$$[H^+] \cdot \frac{d(V_0 + V)}{d[H^+]} = -\frac{P}{Q^2}([H^+] + [OH^-])$$

$$[H^+]^2 \cdot \frac{d^2(V_0+V)}{d[H^+]^2} = \frac{2P}{Q^3}([H^+]+[OH^-])^2 + \frac{2P}{Q^2} \cdot [OH^-]$$

$$([H^+] - [OH^-])^2 + C \cdot ([H^+] - [OH^-])$$
$$- 2 \cdot ([H^+] + [OH^-])^2 = 0 \qquad [62]$$

(See [47].) For a weak monoprotic acid, HL (q = n = 1) (see Equations [25] and [25a]), we get:

$$\bar{n} = f_1, d\bar{n}/d[H^+] = (f_1 - f_1^2)/[H^+],$$
$$d^2\bar{n}/d[H^+]^2 = -2f_1^2(1 - f_1),$$
$$P = V_0((1 - f_1)C_0 + C),$$
$$dP/d[H^+] = -C_0V_0 \cdot f_1(1 - f_1)/[H^+],$$
$$d^2P/d[H^+]^2 = 2C_0V_0f_1^2(1 - f_1)/[H^+]^2,$$

and then (Michałowski, 1981)

$$([H^+] - [OH^-])^2 + C \cdot ([H^+] - [OH^-]) - 2 \cdot ([H^+] + [OH^-])^2$$
$$= \frac{C_0V_0}{V_0 + V} \cdot \bar{n} \cdot (1 - \bar{n}) \cdot (C + [H^+] - [OH^-]$$
$$+ 2 \cdot ([H^+] + [OH^-]))$$
$$= \frac{C_0 \cdot (C + [H^+] - [OH^-])}{C_0 \cdot (1 - \bar{n}) + C} \cdot \bar{n} \cdot (1 - \bar{n}) \cdot (C + [H^+]$$
$$- [OH^-] + 2 \cdot ([H^+] + [OH^-])) \qquad [63]$$

At $\bar{n} = 0$, i.e., for HL = HB, the right-hand side of Equation [63] equals zero; see Equation [62]. On the basis of Equation [62] or [63] one can find $[H^+]_{inf}$. Putting it in the related function, [20] or [25], one obtains V_{inf}. This way, we get the coordinates (V_{inf}, pH_{inf}) for the inflection point.

Relationship between Equivalence and Inflection Points

The main task of titration is the estimation of the equivalence volume, V_{eq}, corresponding to the volume V = V_{eq} of T, where the fraction titrated value

$$\Phi_{eq} = \frac{C \cdot V_{eq}}{C_0 \cdot V_0} \qquad [64]$$

is the ratio of small natural numbers; e.g., $\Phi_{eq} = 1$ (= 1/1) for titration in a D+T system with A = HCl, B = NaOH, where $CV_{eq} = C_0V_0$. Putting this relation in Equation [20], we get:

$$\alpha = [H^+] - [OH^-] = C \cdot x, \text{ where } x = \frac{V_{eq} - V}{V_0 + V} \qquad [65]$$

Then from Equations [5], [62], and [65] we get (Michałowski, 1981; Michałowski and Stepak, 1985), by turns

$$\begin{aligned} ([H^+] + [OH^-])^2 &= C^2 \cdot x^2 + 4K_W \\ x^2 - x + 8K_W/C^2 &= 0 \\ x = x_{\text{inf}} &= \frac{1}{2} \cdot \left(1 - \left(1 - \frac{32K_W}{C^2}\right)^{1/2}\right) \\ &= \frac{8K_W}{C^2} + \left(\frac{8K_W}{C^2}\right)^2 + \cdots \qquad [66] \\ V = V_{\text{inf}} &= V_{eq} - x_{\text{inf}} \cdot \frac{V_0 + V_{eq}}{1 + x_{\text{inf}}} \\ &= V_{eq} - x_{\text{inf}} \cdot V_0 \cdot \frac{C_0/C + 1}{1 + x_{\text{inf}}} \qquad [67] \end{aligned}$$

where V_{inf} is the volume at the inflection point.

The number of articles published dealing with the mathematical treatment of titration curve to locate its inflexion points is scarce (Fournaise and Petitfaux, 1987; Hamann, 1970). A detailed study was carried out in the monoprotic acid case (Meites and Goldman, 1964).

Location of Inflection Points

The inflection points on the titration curves can be perceived in context with location of equivalence points, particularly ones for titration of mixtures of acid-base systems. As an example, let us take the titration of $V_0 = 10$ mL of the system with Na_2S (C_1)+ Na_2CO_3 (C_2)+ NaOH (C_3) as D, titrated with V mL of C = 0.1 mol/L HCl as T. The titration curve has the form

$$V = V_0 \cdot \frac{\bar{n}_1 \cdot C_1 + m \cdot C_2 + C_3 + \alpha}{C - \alpha} \qquad [68]$$

Setting $pK_{11} = 7.0$. $pK_{12} = 13.0$ for H_2S and $pK_{12} = 6.3$. $pK_{22} = 10.1$ for H_2CO_3, $pK_W = 14.0$, for water we get

$$\bar{n}_1 = \frac{2 \cdot 10^{20.0-2pH} + 10^{13.0-pH}}{10^{20.0-2pH} + 10^{13.0-pH} + 1}, \qquad [69a]$$

$$\bar{n}_2 = \frac{2 \cdot 10^{16.4-2pH} + 10^{10.1-pH}}{10^{16.4-2pH} + 10^{10.1-pH} + 1} \qquad [69b]$$

The plots of pH versus V and $\Delta pH/\Delta V = (pH_{j+1} - pH_j)/(V_{j+1} - V_j)$ versus $(V_j + V_{j+1})/2$ relationships are presented in Fig. 3(a1) and (b1). The simpler systems obtained on this basis are presented by the sets (a2), (b2) to (a7), (b7) in Fig. 3.

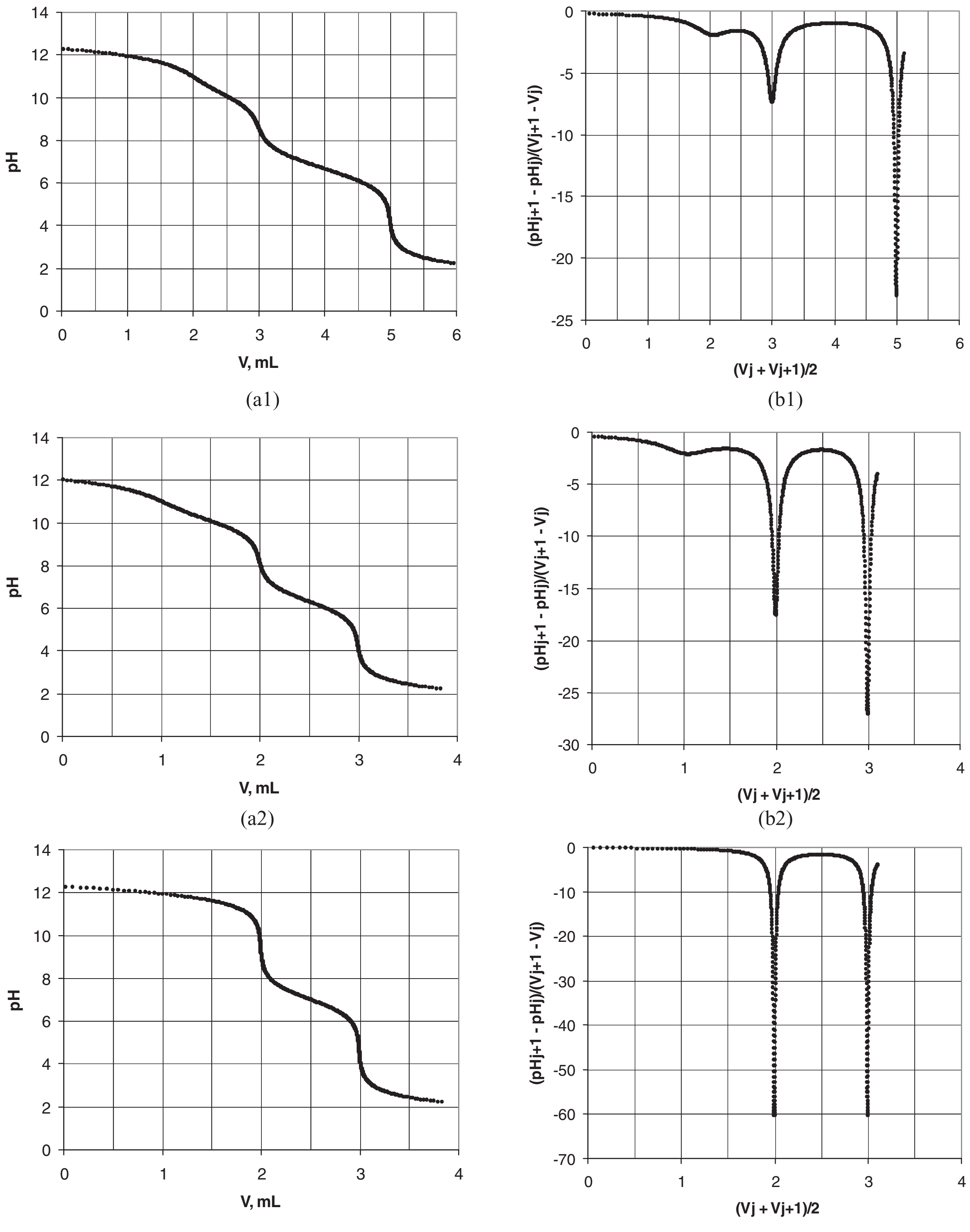
BUFFERING ACTION AND BUFFER CAPACITY

Introductory Remarks

The ability of a solution to resist attempts to change its pH is called buffer capacity (Guenther, 1975, 1991; Hulanicki and Gląb, 2005; Rilbe, 1996; Beynon and Easterby, 2002; Galster, 1991; Morel et al., 1976; Stigliani, 1996), also called the buffer index. It is usually expressed as the change in concentration of a strong base added, required for unit change ($\Delta pH = 1$) in pH of a solution.

The effectiveness of the buffering action of a solution at a given pH value is governed mainly by its buffer index (Asuero, 1996, 2007; Curtright, 2004; Dennison, 1988), defined primarily by Van Slyke (1922) and denoted by β. For the origin of the concept, which has physiological roots, see Roos and Boron (1980). Physiological buffers have great importance (Akin et al., 2008; Schmitt, 2005b; Rees et al., 1996; Fencl and Leith, 1993). Standardization of pH meter assembly and control of acidity in the region close to the physiological range, 7.3 to 8.3, are important in clinical diagnosis (Good and Izawa, 1972; Roy et al., 2009, 2010; Ferguson et al., 1980; Taha, 2005; Jungas, 2006; Blanchard, 1984).

The buffer capacity concept refers usually to electrolytic systems, where only one proton/acceptor pair exists (Asuero, 1992a). For the integral capacity of buffers see Dai (1984). Several authors have dealt with the topic of polybasic acid buffer capacity (Van Slyke, 1922; Hesse and Olin, 1977; King and Kester, 1990; Ranaghan, n.d.; Moya-Hernández et al., 2002; Frison and Calatroni, 2005; Freiser, 1970; Bugaevski and Dunai, 1971; Bugaevski, 1969; Mukhina et al., 1970). The buffer action of heteogeneous systems (Fishtik and Povar, 2006; Pfendt, 1995; Povar, 1996, 2000; Janjic and Milosavljevic, 1978; Janjic et al., 1979) are beyond the scope of this article. A general formula for β was provided by Hesse and Olin (1977) for the system containing n-protic weak acid H_nL (q = n) together with strong acid HB and strong base MOH as the modifying components; it was an extension of the β-concept given in Butler and Cogley (1999) and Butler (1964). The β-concept refers to the "static" case, i.e., it is based on an assumption that total concentration of a buffering species remains unchanged. The diluting effects resulting from addition of an acid or base to such a system was considered in the Michałowski and Parczewski (1978), where, moreover, finite changes (ΔpH) in pH value, affected by addition of a strong acid or base, were closely related to the formulas for acid-base titration curves. The ΔpH values, called "windows" (Moisio and Heikonen, 1996b; de Levie et al., 1998), were considered later for a mixture of monoprotic acids titrated with MOH. It does not mean, however, that the related concepts of the buffer capacity, e.g., Moisio and Heikonen (1996b), were formulated and interpreted correctly. This is also important in the light of monitoring of buffering action of natural waters in automatic systems (Zaher and Vanrolleghem, 2005; Van de Steene et al., 2002; Van Vooren et al., 2001).

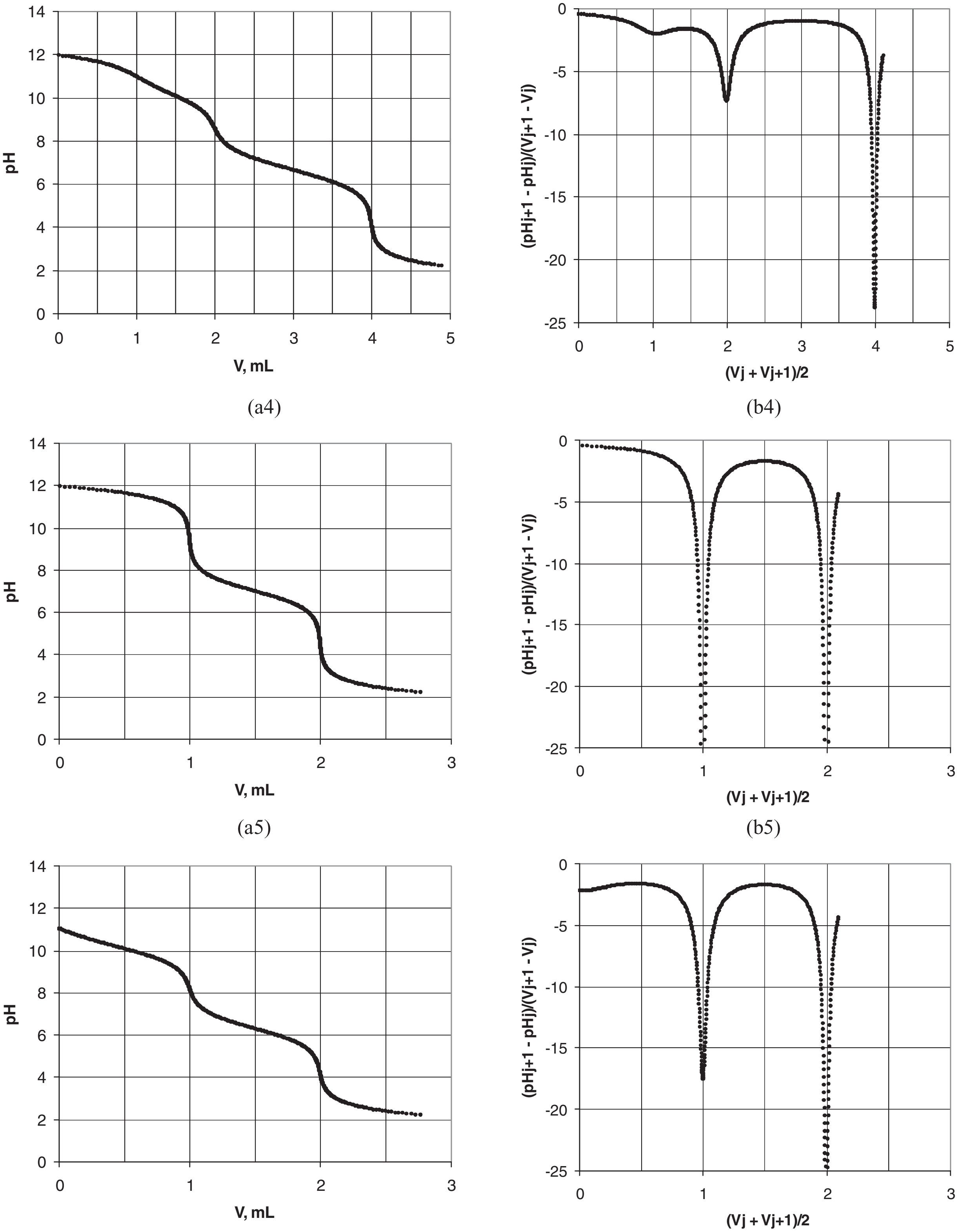


(a1) (b1)

(a2) (b2)

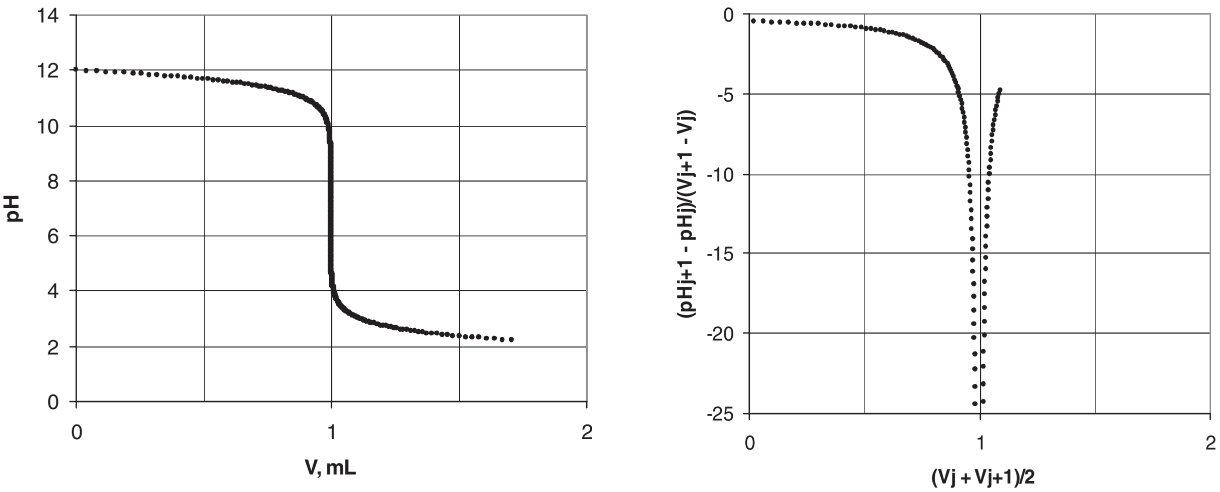
(a3) (b3)

FIG. 3. The (a) pH vs. V, (b) $\Delta pH/\Delta V$ vs. $(V_j+V_{j+1})/2$ relationships plotted, at $pH_{j+1}-pH_j = 0.02$, for the system described by Equations [68] and [69] at concentrations [mol/L]: $C_1 = C_2 = C_3 = 0.01$ (a1, b1); $C_2 = C_3 = 0.01$, $C_1 = 0$ (a2, b2); $C_1 = C_3 = 0.01$, $C_2 = 0$ (a3, b3); $C_1 = C_2 = 0.01$, $C_3 = 0$ (a4, b4); $C_1 = 0.01$, $C_2 = C_3 = 0$ (a5, b5); $C_2 = 0.01$, $C_1 = C_3 = 0$ (a6, b6); $C_3 = 0.01$, $C_1 = C_2 = 0$ (a7, b7). *(Continued)*



(a4)
(b4)
(a5)
(b5)
(a6)
(b6)

FIG. 3. (Continued)



(a7) (b7)

FIG. 3. (Continued)

From a graphical/visual viewpoint, the plot of $\beta = \beta(\mathrm{pH})$ function has some salient similarities with, for example, a derivative UV-Vis spectrum (first derivative) and with chromatograms (chromatographic "spectrum"). Factually, for well-resolved peaks related to $\beta = \beta(\mathrm{pH})$ relationship, in the medium part of the pH scale one can state linear dependence between $\beta_{\max} = \beta(\mathrm{pK}_i)$ and concentration of the buffering species, where pH $= \mathrm{pK}_i$ refers to a local maximum (maximal buffer capacity) on the pH scale. Some further similarities between acid-base titration and UV-Vis analysis exist on the basis of the linear algebra approach (Michalowski et al., 2005b; Ni, 1998).

The changes in buffer capacity can also be stated in the course of pH titration, considered as a kind of "dynamic" process. Such a case will also be considered in this article and the so-named dynamic buffer capacity (β_V), involving the dilution effect, will be introduced for this purpose.

Buffered solutions are commonly applied in classical and instrumental analyses (Table 6), e.g., in capillary electrophoresis (CE) techniques (capillary zone electrophoresis, isotachophoresis). Recently, the importance of buffer capacity was raised in the technique known as pH-static titration (Michalowski et al., 2005b, 2007; Toporek et al., Submitted). The buffer capacity is also closely related to an error in acid-base titration (Michałowski, 1989, 2001).

Basic Relationships and Notations

Let us take the following notations and basic relationships referring to the species introduced by substances $M_m H_{\mathrm{n-m}} L$ ($m = 0, \ldots, n$), $K_{m_k} H_{\mathrm{n_k - m_k}} L_{(k)}$ ($m_k = 0, \ldots, n_k$; $k = 1, \ldots, p$), and $H_{\mathrm{n_k + m_k}} L_{(k)} B_{m_k}$ ($m_k = 0, \ldots, q_k - n_k$; $j = p + 1, \ldots,$P) used in following parts of this article:

Then we have, among others:

$$\begin{aligned}\rho_k &= [H^+]\cdot\frac{d\bar{n}_k}{d[H^+]} = \sum_{i=0}^{q_k} i\cdot[H^+]\cdot\frac{df_{ik}}{d[H^+]} = \sum_{i=0}^{q_k} i\cdot\frac{df_{ik}}{d\ln[H^+]}\\ &= \frac{\sum_{i=0}^{q_k}\sum_{\mathrm{j}=0}^{q_k}(i^2 - ij)y_{ik}y_{\mathrm{jk}}}{(\sum_{\mathrm{j}=0}^{q_k} y_{\mathrm{jk}})^2} = \sum_{i=0}^{q_k}\sum_{\mathrm{j}=0}^{q_k}(i^2 - ij)\cdot f_{ik}f_{\mathrm{jk}}\\ &= \sum_{i>j=0}^{q_k}(i-j)^2\cdot f_{ik}f_{\mathrm{jk}} \qquad [70]\end{aligned}$$

TABLE 6
Buffers in instrumental analysis

Method	Reference
Liquid chromatography	Subirats et al., 2010; Box et al., 2003
LC and LC-MS	Subirats et al., 2009
Capillary electrophoresis	Fuguet et al., 2008
Chromatography and electrophoresis	Bosh and Roses, 2007; Gebahuer and Bocek, 2000
Gel electrophoresis	Liu et al., 1999
UV-visible and ultraviolet spectrophotometry	Tam, 1999; Albert and Serjeant, 1984; Perrin, 1963; Davies, 1959
Nuclear magnetic resonance spectroscopy (NMR)	Freund and Kalbitzar, 1995
Ion selective electrodes	Thomas, 1990; Dorazio, 1987; Trojanowicz, 1979
Polarography	Jordan, 1980; Elving et al., 1956
Electrophoresis	Miller and Golder, 1950

The latter equality in [70] results from the sequence of transformations:

$$\sum_{\mathrm{j}=0}^{q_k}\sum_{i=0}^{q_k}(j^2-ji)\cdot f_{\mathrm{jk}}f_{ik}=\sum_{i=0}^{q_k}\sum_{\mathrm{j}=0}^{q_k}(i^2-ij)\cdot f_{ik}f_{\mathrm{jk}}$$

$$=\frac{1}{2}\cdot\left(\sum_{\mathrm{j}=0}^{q_k}\sum_{i=0}^{q_k}(j^2-ji)\cdot f_{\mathrm{jk}}f_{ik}+\sum_{i=0}^{q_k}\sum_{\mathrm{j}=0}^{q_k}(i^2-ij)\cdot f_{ik}f_{\mathrm{jk}}\right)$$

$$=\frac{1}{2}\cdot\left(\sum_{\mathrm{j}=0}^{q_k}\sum_{i=0}^{q_k}(j^2-ji+i^2-ij)\cdot f_{\mathrm{jk}}f_{ik}\right)$$

$$=\frac{1}{2}\cdot\left(\sum_{\mathrm{j}=0}^{q_k}\sum_{i=0}^{q_k}(i-j)^2\cdot f_{\mathrm{jk}}f_{ik}\right)$$

$$=\sum_{i>j=0}^{q_k}(i-j)^2\cdot f_{ik}f_{\mathrm{jk}} \qquad [71]$$

valid for (finite) sums covering the same set of indices. Moreover, we have

$$\rho=\frac{d\bar{n}}{d\ln[H^+]}=\sum_{i>j=0}^{q}(i-j)^2\cdot f_i f_j \qquad [72]$$

From the relationship

$$\frac{dy}{dpH}=-\ln 10\cdot\frac{dy}{d\ln[H^+]} \qquad [73]$$

valid for any function y = y(pH), we have, among others:

$$d\alpha/dpH=-\beta_{H,OH}=-\ln 10\cdot([H^+]+[OH^-]) \qquad [74]$$

for y = α (Equation [19]), where

$$\beta_{H,OH}=\ln 10\cdot([H^+]+[OH^-]) \qquad [75]$$

$$\frac{d\bar{n}_k}{dpH}=-\ln 10\cdot\rho_k \qquad [76]$$

$$\frac{d\bar{n}}{dpH}=-\ln 10\cdot\rho \qquad [77]$$

Static Buffer Capacity (β)

For the system containing weak acid H_nL (C_0), strong acid, HB (C_a), and strong base, MOH (C_b), from charge and concentration balances it follows that

$$\Delta=-\alpha+C_0\cdot(n-\bar{n}) \qquad [78]$$

where $\bar{n}$ is defined in Equation [10], α in Equation [19], and Δ in Equation [38].

The differential buffer capacity, $|\beta|$, is expressed by the formula (Butler and Cogley, 1999; Hesse and Olin, 1977):

$$\beta=\frac{d\Delta}{dpH}=\beta_{H,OH}+\beta^* \qquad [79]$$

where:

$$\beta^*=\ln 10\cdot C_0\cdot\rho \qquad [80]$$

and ρ is expressed by Equation [72]. At $C_a = 0$ we have $\Delta = C_b$ and Equation [79] is rewritten in the form

$$\beta_b=\frac{dC_b}{dpH} \qquad [81]$$

or, at $C_b = 0$ ($\Delta = -C_a$), we have $\beta_a = -dC_a/d$pH. The component $\beta_{H,OH}$ (Equation [75]) in Equation [79], confusedly called in Moisio and Heikonen (1996b) a "water correction," refers to buffering action (β) of the solution at $C_0 = 0$, i.e., in absence of weak acid(s), in the possible presence of HB or/and MOH. A salt of MB type does not affect, in principle, the buffer capacity—provided that the ionic strength negligibly affects the pH and equilibrium constants values. Equation [79] applies also to the systems where maximal number (q) of protons attached to L^{-n} is equal to n or different from n; e.g., n = 4 and q = 6 for versenic acid (EDTA). Equation [79] has been the basis for a computer program (Tam, 1999), where the effects of ionic strength and temperature (Perrin and Dempsey, 1979) on pK_i were also involved.

The β-concept (Equation [79]) can easily be extended to the mixture of acid-base systems comprising $K_{m_k}H_{\mathrm{n_k-m_k}}L_{(k)}$ (C_{0k} mol/L, $m_k = 0, \ldots, n_k; k = 1, \ldots, p$) and $H_{\mathrm{n_k+m_k}}L_{(k)}B_{m_k}$ (C_{0k} mol/L, $m_k = 0, \ldots, q_k - n_k; k = p+1, \ldots, P$), C_a mol/L HB and C_b mol/L MOH, considered as D in the section on complex acid-base systems above. At V = 0 in Equation [37] we get

$$\alpha+\Delta+X+Y=0 \qquad [82]$$

where α in defined in Equation [19], Δ in Equation [35], and X and Y in Equation [39]. We have

$$\frac{d(X+Y)}{dpH}=\sum_{k=1}^{P}\frac{d\bar{n}_k}{dpH}\cdot C_{0k}=-\sum_{k=1}^{P}\beta_k^* \qquad [83]$$

where

$$\beta_k^*=\ln 10\cdot C_{0k}\cdot\sum_{i>j=1}^{q_k}(i-j)^2\cdot f_{ki}\cdot f_{kj} \qquad [84]$$

(See Equation [71].) From Equations [82] and [39] we get

$$\Delta=-(\alpha+X+Y) \qquad [85]$$

$$X+Y=-\sum_{k=1}^{P}(q_k-\bar{n}_k)\cdot C_{0k}+\sum_{k=1}^{p}(q_k+m_k-n_k)\cdot C_{0k}$$
$$+\sum_{k=p+1}^{P}(q_k-m_k-n_k)\cdot C_{0k} \qquad [86]$$

and then

$$\beta=\beta_{H,OH}+\sum_{k=1}^{P}\beta_k^* \qquad [87]$$

Buffer capacity of universal buffer solutions (Table 7) may be calculated by using expression [85]. A number of articles dealing with the buffer capacity of more or less complex systems (Celantano et al., 1988; Nguyen et al., 2009; Wooten, 2004, 2010; Dougherty et al., 2006; Persat et al., 2009a; Fishtik, 1998; Opanasenko et al., 1978; Urbansky and Schock, 2000; Jung and Hur, 2000; Lang and Meier, 2007; Ranaghan, n.d.; Zaher and Vanrolleghem, 2005; Moya-Hernández et al., 2002; Frison and Calatroni, 2005; King, 2002; de Levie, 1996a, 1999c; Bugaevski and Dunai, 1971; Mukhina et al., 1970; Tam, 1999; Okamoto et al., 1997; Lambert, 1990) of theoretical or applied character have been published.

The expression for β (Equation [87]) can also be written in terms of Simms constants g_{ki} involved in the relation [41] for k = 1,. . . ,P. For this purpose, one should "extract" the terms $q_k - \bar{n}_k$ in Equation [86], applying the identities:

$$\bar{n}_k + m_k - n_k = -(q_k - \bar{n}_k) + (q_k + m_k - n_k) \text{ and}$$
$$\bar{n}_k - m_k - n_k = -(q_k - \bar{n}_k) + (q_k - m_k - n_k) \quad [88]$$

obtained from expressions for X and Y (Equation [85]), and write:

$$\beta_k^* = \ln 10 \cdot [H^+] \cdot C_{0k} \cdot \sum_{i=1}^{q_k} \frac{1/g_{ki}}{([H^+]/g_{ki} + 1)^2} \quad [89]$$

is written in terms of Simms constants. For P = 1, $g_{ki} = g_i$, $C_{0k} = C_0$, $q_k = q$, Equation [89] reduces to

$$\beta^* = \ln 10 \cdot [H^+] \cdot C_0 \cdot \sum_{i=1}^{q} \frac{1/g_i}{([H^+]/g_i + 1)^2} \quad [90]$$

For the system containing a mixture $HL_{(k)}$ (C_{0k}, $k = 1, \ldots, P$) + HB(C_a)+ MOH (C_b)+ MB (C_{MB}) we get the function

$$\beta^* = \ln 10 \cdot [H^+] \cdot C_0 \cdot \sum_{k=1}^{P} \frac{1/K_{1k}}{([H^+]/K_{1k} + 1)^2} \quad [91]$$

where K_{1k} refers to the reaction $HL_{(k)} = H^+ + L^-_{(k)}$. Equation [91] (Moisio and Heikonen, 1996b) has formal similarities with Equation [90].

TABLE 7
Universal buffer solutions

Content	Reference
Universal pH scale based on switterionic buffer compounds	Wollen et al., 2007; Roy and Roy, 2006
Boric acid, citric acid, ethylenediamine, potassium dihydrogen orthophosphate, and trishidroxymethylaminomethane (TRIS), an extension of Davies's buffer (Davies, 1959) for use in ultraviolet spectrophotometry	Tam, 1999
3-nitro-2,6-dimethylpyridine, 4-cyano-2,6-dimethylpyridine, 2,6-dimethylpyridine, and 4-methoxy-2,6-dimethylpyridine	De Levie, 1996a
Pentaehylene hexamine or tetramethylene pentamine; citric acid and imidazole	Celentano et al., 1988
The mixture of alkylamine and phosphoric acid diluted with water (universal buffer system) gives the possibility of carrying out separations with basic buffers on reversed phase columns with a silica gel support.	Juergens, 1988
Preparation of universal buffer mixtures, including polynuclear species	Ramis Ramos et al., 1986
Potassium acetate, potassium dihydrogen phosphate, ethylendiammonium dichloride, and borax	Avdeef and Bucher, 1978
A Pridaux universal buffer kind is prepared by adding potassium chloride to get an ionic strength of 0.3.	Fernandez and Martin, 1977
Preparation of a Britton and Robinson universal buffer of known ionic strength	Mongay and Cerdá, 1974
Sodium carbonate, 2-amino-2-methyl propan-1:3-diol, sodium hydrogen orthophosphate, and citric acid.	Ellis, 1961
Replacement of the barbitone component of Britton and Robinson universal buffer mixture by trishydroxymethylaminomethane	Davies, 1959
Universal Britton and Robinson mixture at constant ionic strength	Frugoni, 1957
Citric acid, phosphoric, acid and boric acid (Theorell and Steinhagen buffer)	Ostling and Virtama, 1946; Küster, 1982
Solid mixture using free diethyldithiobarbituric acid instead of the sodium salt employed by Britton and Robinson	Johnson and Lindsey, 1939
Citric acid, potassium dihydrogen phosphate, boric acid, and veronal	Britton and Robinson, 1931a, b
Phenylacetic acid, phosphoric acid, and boric acid	Prideaux, 1917, 1924
Acetic acid, phosphoric acid, and boric acid	Prideaux, 1916

Dynamic Buffer Capacity and Sharpness Index

In the acid-base titration procedure, the concept of dynamic buffer capacity β_V, involving the dilution effect in the D+T system, has been introduced (Michalowski, 1981). Denoting by c the current concentration of titrant T at any point of the titration curve

$$c = \frac{CV}{V_0 + V} = \Phi \cdot \frac{C_0 C}{C + \Phi \cdot C_0} \qquad [92]$$

we get the expression for the dynamic buffer capacity $|\beta_V|$, where

$$\beta_V = \frac{dc}{dpH} = \frac{dc_V}{d\Phi} \cdot \frac{d\Phi}{dpH} = \frac{C_0 \cdot C^2}{(C + \Phi \cdot C_0)^2} \cdot \frac{1}{\eta} \qquad [93]$$

and

$$\eta = \frac{dpH}{d\Phi} \qquad [94]$$

is the sharpness index on the titration curve (Michalowski, 1981; Butler, 1964; Gonzalez et al., 1990; Smith, 1952; Svehla, 1978). For comparative assessment purposes, the absolute values for β_V (Equation [93]) and η (Equation [94]), i.e., $|\beta_V|$ and $|\eta|$, are considered.

Referring to Equation [37], one can calculate the current concentration c [mol/L] of $M_mH_{n-m}L$ in the D+T

$$c = \frac{CV}{V_0 + V} = C \cdot \left(1 - \frac{Z - \alpha}{X + Y + Z + \Delta}\right) \qquad [95]$$

where the relations [39] are involved. Then we have:

$$(Z - \alpha)/(X + Y + Z + \Delta) = 1 - c/C,\ 1/(X + Y + Z + \Delta) = (1 - c/C)/(Z - \alpha)$$

and the dynamic buffer capacity, β_V, results from the relations:

$$\begin{aligned}\frac{dc}{dpH} &= \frac{C - c}{Z - \alpha} \cdot \left(C \cdot \frac{d\bar{n}}{dpH} + \frac{d\alpha}{dpH} + (1 - c/C) \cdot \left(\frac{d(X + Y)}{dpH} - C \cdot \frac{d\bar{n}}{dpH}\right)\right) \\ &= \frac{C-c}{Z-\alpha} \cdot \left(\frac{d\alpha}{dpH} + (1-c/C) \cdot \frac{d(X+Y)}{dpH} + c \cdot \frac{d\bar{n}}{dpH}\right) \\ &= -\frac{C-c}{Z-\alpha} \cdot \left(\beta_{H,OH} + c \cdot \beta^* + (1-c/C) \cdot \sum_{k=1}^{P} C_{0k} \cdot \beta_k^*\right)\end{aligned} \qquad [96]$$

$$\beta_V = -\frac{dc}{dpH} \qquad [97]$$

The relationship between β_V and η has been considered in Michałowski et al. (2010a). Note that c/C = V/(V_0+V), i.e., 1 – c/C = V_0/(V_0+V); the c and $C_{0k}V_0$/(V_0+V) values in Equation [97] refer to actual (i.e., defined point of titration) concentrations of the related buffering components.

Windowed Buffer Capacity (B_V)

The β_V value is the point assessment, $\beta_V = (\beta_V)_{pH}$, and cannot be used in the case of finite pH changes (ΔpH) corresponding to addition of a finite volume of titrant (β_V is a nonlinear function of pH). For more practical purposes, buffer capacity B_V defined by the formula

$$B_V = \left|\frac{\Delta c}{\Delta pH}\right| \qquad [98]$$

where

$$\begin{aligned}\frac{\Delta c}{\Delta pH} &= \frac{1}{\Delta pH} \cdot \int_{pH}^{pH+\Delta pH} \beta_V \cdot dpH \\ &= \frac{c(pH + \Delta pH) - c(pH)}{\Delta pH}\end{aligned} \qquad [99]$$

has been suggested. From extension in Taylor series we have (Michałowski et al., 2005a)

$$\begin{aligned}\frac{\Delta c}{\Delta pH} &= \beta_V + \frac{d\beta_V}{dpH} \cdot \frac{\Delta pH}{2} + \frac{d^2\beta_V}{dpH^2} \cdot \frac{(\Delta pH)^2}{6} + \cdots \\ &= \beta_V + \sum_{k=1}^{\infty} \left(\frac{d^k\beta_V}{dpH^k}\right)_{pH} \cdot \frac{(\Delta pH)^k}{(k+1)!}\end{aligned} \qquad [100]$$

where

$$\frac{d^k c}{dpH^k} = \left(\frac{d^k c}{dpH^k}\right)_{pH} = \left(\frac{d^{k-1}\beta_V}{dpH^{k-1}}\right)_{pH} \qquad [101]$$

From Equation [100] we see that β_V is the first approximation of B_V. The term "windowed" is adopted from Moisio and Heikonen (1996b), although the resolution of the problem is quite different; in this case, c(pH) = 0 and then Δc = c(pH+ΔpH).

The windowed buffer capacity B_V (Equation [98]) refers to finite pH changes, ΔpH, affected by a change Δc in concentration of the external agent in the mixture. The B_V concept is put against the buffer capacity concept (with ΔpH = ±1) suggested by Kolthoff and Rosenblum (1937) and the other one, based on the static buffer capacity (β) concept.

Comments on Buffer Capacity

Buffer capacity is not an univocally defined concept. One can distinguish the definitions considered from theoretical (descriptive) and practical viewpoints. The descriptive definitions are based on derivatives, β (Equation [79]) and β_V (Equation [64]), involving infinitesimal (infinitely small) pH changes (dpH), whereas the practical ones are involved with finite pH changes (ΔpH). At the point of junction of the two concepts, false (strange) interpretations or even misinterpretations of the buffer capacity concept are met in the literature, e.g., Baicu and Taylor (2002) and Izutsu and Yamamoto (1998). One should take into account that:

(a) Finite changes in pH (ΔpH, e.g., ΔpH = 1) are involved with addition of a finite volume of a reagent endowed with acid-base properties, e.g., base, of a finite concentration, and

(b) The buffer capacities β (Equation [39]), β_V (Equation [64]), and B_V (Equation [93]) are nonlinear functions of pH or volume V of titrant added.

This addition can be made according to titrimetric mode, and diluting effect should be taken into account. The (static) β concept can satisfactorily be approximated by acid-base titration realized according to coulometric mode, where volume changes can usually be neglected.

In Baicu and Taylor (2002), the formula $\beta' = dV/dpH$ has been presented as an (alleged) Van Slyke definition, with dV defined strangely as "the increment in the acid/base volume (in mmol/L, needed to change pH by one unit." Consequently, the statement that β (in the light of the Van Slyke definition) "is the reciprocal of the slope" (Baicu and Taylor, 2002) is not true.

The nice suggestion to name the buffer capacity unit a "slyke" (Baicu and Taylor, 2002) is missed in context of the formula $\beta^{\#} = dV/dpH$, different from the one suggested by Van Slyke, Equation [39]. Moreover, $\beta^{\#}$ depends on concentrations and volumes, and further misinterpretations are unavoidable.

For a weak monoprotic acid HL of moderate strength, there are two inflection points (at $d^2V/pH^2 = 0$):

1. At $V \cong V_{eq}/2$, where buffer capacity of the HL/L$^-$ system attains maximal value, and
2. At $V \cong V_{eq}$, i.e., at the point corresponding to minimal buffer capacity.

Informally (from the mathematical viewpoint only), the third inflection point occurs at V = 0.

The buffer capacity is numerically expressed to be equal to the minimum concentration of strong acid or strong base that causes the variation of buffer pH by one unit, $\Delta pH = \pm 1$. We calculate the volume (a) V_a mL of C_a mol/L HB or (b) V_b mL of C_b mol/L MOH needed to change pH value of V_0 mL of the solution containing a weak acid HL (C_1 mol/L) and its salt ML (C_2 mol/l), $C_1 + C_2 = C_0$.

Assuming additivity in volumes and neglecting the effect of ionic strength value on dissociation constant for HL, in the case (a), at initial (i) and final (f) states we have:

$$K_1^H = \frac{[HL]_i}{[H^+]_i \cdot [L^-]_i} = \frac{[HL]_f}{[H^+]_f \cdot [L^-]_f}$$

$$[M^+]_i + [H^+]_i - [OH^-]_i - [L^-]_i = 0$$

$$\text{and } [M^+]_f - [B^-]_f + [H^+]_f - [OH^-]_f - [L^-]_f = 0 \quad [102]$$

$$[HL]_i + [L^-]_i = C_0, [HL]_f + [L^-]_f = \frac{C_0V_0}{V_0+V},$$

$$[M^+]_i = C_2, [M^+]_f = \frac{C_2V_0}{V_0+V}[B^-]_f = \frac{C_aV}{V_0+V}$$

Neglecting $[H^+] - [OH^-]$ in Equation [102], after transformations we have

$$\frac{[H^+]_f}{[H^+]_i} = 10^{pH_i - pH_f} = \frac{C_2}{C_1} \cdot \frac{C_1V_0 + C_aV}{C_2V_0 - C_aV} \quad [103]$$

If V mL of KOH (C_b mol/l) is added into the initial buffer solution, we get

$$\frac{[H^+]_i}{[H^+]_f} = 10^{pH_f - pH_i} = \frac{C_1}{C_2} \cdot \frac{C_2V_0 + C_bV}{C_1V_0 - C_bV} \quad [104]$$

We have $pH_i - pH_f = 1$ at $V = V_a$ in Equation [103] and $pH_f - pH_i = 1$ at $V = V_b$ in [104]. Then we get:

$$V_a = \frac{C_0V_0}{C_a} \cdot \frac{9r}{(r+1)(r+10)} \quad [105]$$

$$V_b = \frac{C_0V_0}{C_b} \cdot \frac{9r}{(r+1)(10r+1)} \quad [106]$$

$$([HL]_f + [L^-]_f)_a = \frac{C_0V_0}{V_0+V_a} = \frac{C_0C_a(r+1)(r+10)}{9C_0r + C_a(r+1)(r+10)} \quad [107]$$

$$([HL]_f + [L^-]_f)_b = \frac{C_0V_0}{V_0+V_b} = \frac{C_0C_b(r+1)(10r+1)}{9C_0r + C_b(r+1)(10r+1)} \quad [108]$$

The formulas [105]–[108] are valid at relatively high C_0 values, for a moderately weak acid HL (compare with Chiriac and Balea (1997)).

The buffer index concepts specified above can be considered in context with homeostatic (living organisms and natural water) systems, isoelectric focusing (IEF), ion exchangers, and alkalinity, with its analytical connotations. In particular, the alkalinity (Alk) (Dickson, 1981, 1992; Stumm and Morgan, 1996; Butler, 1982) concept is applied to natural (lake, river, and sea) waters and involves other acid-base species.

ALKALINITY

Basic Problems

The buffer capacity of waters determines their sensitivity against acidification. Buffer capacity, and then alkalinity of natural waters, is attributed mainly to carbonate (CO_3^{-2}) and bicarbonate (HCO_3^-) species, comprising the carbonate alkalinity. For most surface waters, where bicarbonate predominates, the pH ranges from 6.3 to 8.3 and then bicarbonate is the dominant carbonate species in the water ($pK_1 = 6.3$ and $pK_2 = 10.1$ for H_2CO_3). Some chemical reactions and processes controlling the carbonate species concentration in natural waters include weathering of minerals, photosynthesis and respiration, anaerobic bacteria consumption of organic matter, and CO_2 dissolution. In a minor degree, alkalinity is affected by the presence of soluble species: ions of hydrolyzable salts and fulvic + humic acids, as a general class of biogenic matter, which is ubiquitous in terrestrial and aquatic environments (Aiken et al., 1985, 1992). Some non-carbonate contributors (Zhang and

Dawe, 1996) are also of anthropogenic origin. All the species are the site of acid-base reactions (Li and Tang, 1998).

Alkalinity (Alk) should be distinguished from the acid-neutralizing capacity (ANC) (Rounds and Wilde, 2001; Fillion et al., 1999); ANC is attributed to the unfiltered (raw) sample. The alkalinity thus refers to a filtered sample, i.e. the Alk measurement is made by titration of the solution obtained after passing a raw sample through 0.45 μm (or smaller pore) membrane. Some mineral species (e.g., Fe^{+2}, HS^{-}) are affected by oxidizing action of O_2 and then aeration of the sample during filtration may cause mineral precipitation and alteration of alkalinity. For example, Fe^{+3} thus formed has more acidic properties than Fe^{+2} and a higher tendency to form solid phases (e.g., iron(III) hydroxide) in the system under ambient conditions.

Alkalinity is measured in miliequivalents of the acid consumed per one liter of the water titrated (meq/L). Alk and ANC measurements are frequently done by pH titration, and the experimental data $\{(V_j, ph_j)|\ j = 1,\ldots,N\}$ are usually handled by the Gran method recommended, for example, for titration of carbonates (Michałowski et al., In preparation); this method is particularly advisable when the inflection point location on the related titration curve is impossible. In carbonate alkalinity measurements, the inflection points correspond to the solutions of $NaHCO_3$ (pH_{inf} ca. $(pK_1+pK_2)/2 = 8.2$) and H_2CO_3 ($pH = (pK_1 - \log c)/2$); e.g., at $c = 2 \times 10^{-3}$ mol/L H_2CO_3 we have pH = 4.5, which is also the pH value pre-assumed in another option of pH titration (Millero et al., 1993, 1998). Lower pH values, usually 4.0 or 3.5, were applied in the presence of non-carbonate contributors, e.g., carboxylic acids, in the titrand. The presence of a neutral salt, e.g., NaCl, makes the shift to lower pH values (Galster, 1991). Such indeterminancy provides some discrepancies in defining the alkalinity concept. This fact was pronounced by Neal who stated that "a plethora of values and approaches are presented within the literature, often without an explanation and there is a confusion over what is often measured and what assumptions have been made" (2001). Zeebe and Wolf-Gladrox (2001) stated that at least 20 different definitions of alkalinity exist. Morel and Hering (1993) considered alkalinity as "one of the most central but perhaps not the best understood concept in aquatic chemistry." Indeed, some definitions known hitherto are clumsy in notation, ambiguous, or simply incorrect (unfounded).

In order to introduce an explicit definition of alkalinity, one should refer first to some general assumptions concerning aquatic media, considered as a kind of macroscopic systems, where some general assumptions of matter preservation are obligatory.

The new concept of alkalinity presented below refers to monophase acid-base systems, where cations and anions form relatively weak complexes. In order to "homogenize" mono- and polyprotic acids and bases, particularly carbonate species, the species formed by metal ions and humic and fulvic acids (i.e., the species with undefined physicochemical properties), the Simms constants were introduced.

The Novel Formulation of Total Alkalinity and Total Acidity

The new concept of alkalinity has been suggested by Michałowski and presented in Michałowski and Toporek (2003a, b) and Michałowski et al. (2009). To introduce this concept, let us consider the D+T system with $M_{m_k}H_{n_k-m_k}L_{(k)}$ (C_{0k}, k = 1,...,P) + $H_{n_k+m_k}L_{(k)}B_{m_k}$ (C_{0k}, k = P+1,..,R) $+Me_{(k)}(OH)_{u_k-m_k}B_{m_k}$ (C_{0k}, k = R+1,...,Q) + HB (C_a) MOH (C_b) as D (V_0 mL) titrated with V mL of C mol/L HB as T. Assuming that no (soluble and/or insoluble) complexes are formed between $Me_{(k)}^{+u_k}$ and $H_jL_{(k)}^{+j-n_k}$ species, we have the balances:

$$\begin{aligned}
&\alpha + \sum_{k=1}^{R}\sum_{j=0}^{q_k}(j-n_k)\cdot[H_jL_{(k)}^{+j-n_k}] + \sum_{k=R+1}^{Q}\sum_{j=0}^{q_k}(u_k-j)\\
&\quad\cdot[Me_{(k)}(OH)_j^{+u_k-j}] + [M^+] - [B^-] = 0, \sum_{j=0}^{q_k}[H_jL_{(k)}^{+j-n_k}]\\
&\quad= \frac{C_{0k}V_0}{V_0+V}(k=1,\ldots,R), \sum_{j=0}^{q_k}[Me_{(k)}(OH)_j^{+u_k-j}]\\
&\quad= \frac{C_{0k}V_0}{V_0+V}(k=R+1,\ldots,Q),\\
&\quad[M^+] = \frac{V_0}{V_0+V}\cdot\left(\sum_{k=1}^{P}m_k\cdot C_{0k}+C_b\right),\\
&\quad[B^-] = \frac{1}{V_0+V}\cdot\left(\sum_{k=P+1}^{Q}m_k\cdot C_{0k}V_0 + C_aV_0 + CV\right)
\end{aligned} \qquad [109]$$

After further transformations (see Appendix A) we get the relation

$$CV/V_0 - (1+V/V_0)\cdot\alpha = A - \sum_{i=1}^{\Omega}C_{0i}\cdot(1+h/g_i)^{-1} \qquad [110]$$

where:

$$\begin{aligned}
A &= \sum_{k=1}^{P}(q_k+m_k-n_k)\cdot C_{0k} + \sum_{k=P+1}^{R}(q_k-m_k-n_k)\cdot C_{0k}\\
&\quad+ \sum_{k=R+1}^{Q}(u_k-m_k)\cdot C_{0k} + \Delta
\end{aligned} \qquad [111]$$

$$\Omega = \sum_{k=1}^{Q}q_k \qquad [112]$$

The parameter A (Equation [111]) involves constant parameters referring to the composition of D (before titration with T). This parameter, when referred to Equation [110], will be termed as total alkalinity (TAL), A = TAL.

On the other hand, the number Ω is the sum of all proto- and hydroxo-complexes assumed a priori in the system considered. However, within the pH range covered by titration points $\{(V_j, ph_j)|\ j = 1,\ldots,N\}$, only a part of them participate acid-base equilibria in a measurable degree. In this case, only a limited part of the components is involved in the sum on the right-hand side of Equation [110]. Then substituting Λ for Ω (where $\Lambda \leq \Omega$) in Equation [110] and applying Equation [8], we get

$$CV/V_0 = TAL + (1+V/V_0)\cdot\alpha = A - \sum_{i=1}^{\Lambda} C_{0i}\cdot(1+10^{-\mathrm{ph}}/g_i^*)^{-1} \qquad [113]$$

At ph < 9, the component $(1 + V/V_0)\cdot\alpha$ can be omitted within the middle part of pH range; it appears to be significant at the end of titration, i.e. at relatively low ph values. In this ph range, one can assume $\alpha = [H^+] = 10^{-\mathrm{ph}}/\gamma$ and rewrite Equation [113] as the regression equation

$$CV_j/V_0 = \mathrm{TAL} + (1 + V_j/V_0)\cdot 10^{-\mathrm{ph}_j}/\gamma - \sum_{i=1}^{\Lambda} C_{0i}\cdot(1+10^{-\mathrm{ph}_j}/g_i^*)^{-1} + \varepsilon_j \qquad [114]$$

that can be considered as the basic relation for total alkalinity (A = TAL). This model involves $2 + 2\cdot\Lambda$ parameters: TAL, γ and the set of pairs: $\{(C_{0i}, g_i^*)\,|\,i = 1,\ldots,\Lambda\}$. The parameters involved in [114] are found according to curve-fitting method, applied to the sum of squares

$$SS(\Lambda) = \sum_j \varepsilon_j^2 = \sum_j (\mathrm{TAL} + (1 + V_j/V_0)\cdot 10^{-\mathrm{ph}_j}/\gamma - \sum_{i=1}^{\Lambda} C_{0i}\cdot(1+10^{-\mathrm{ph}_j}/g_i^*)^{-1} - CV_j/V_0)^2 \qquad [115]$$

and a subset of experimental points $\{(V_j, \mathrm{ph}_j)\,|\,j = 1,\ldots,N_k\}$, $N_k \leq N$. The fit is realized with use of an iterative computer program; see, e.g., Michałowski (1988a, 1990, 1992), Michałowski et al. (1987, 1988, 1989, 1994, 1995, 2008), Michałowski and Gibas (1994), Janecki et al. (1999a, b, 2000a, b), Janecki and Michałowski (1999), and Ponikvar et al. (2008). It should be noted that activity, h (not concentration, $[H^+]$), of hydrogen ions is involved in Equation [114]; it is one of the advantages of the method proposed. The approach to alkalinity based on Equation [114] is dissimilar to any other known from the literature issued hitherto.

The iteration procedure is used with a smaller number of $C_{0i}\cdot(1+10^{-\mathrm{ph}}/g_i^*)^{-1}$ terms in Equation [114]. For example, we start with Λ = 2, referring to carbonate species (q = n = 2) only, and six parameters: TAL, γ, C_{01}, C_{02}, g_1^*, g_2^* are determined. To improve the fitting, the next terms (Λ = 3, 4, ...) are added subsequently. Note that the sum in Equation [114] consists of positive components, in principle. After subsequent additions, the TAL approximates its true value. Subsequent additions of the terms having similar mathematical form are very advantageous from the viewpoint of the iteration procedure.

For q = n = 2, as in the case of the system with carbonic acid ($H_2L = H_2CO_3$), from [35] we have

$$2 - m = \frac{[HL^-] + 2[L^{-2}]}{[H_2L] + [HL^-] + [L^{-2}]} = (1 + [H^+]/g_1)^{-1} + (1 + [H^+]/g_2)^{-1} \qquad [116]$$

and $g_1 + g_2 = K_1$, $g_1\cdot g_2 = K_1\cdot K_2$. Referring to D ($V_0$ mL) with $NaHCO_3$ (C_1)+ Na_2CO_3 (C_2) titrated with V mL of C mol/L HCl as T, we get the relation

$$V_0 + V = V_0\cdot\frac{(m-1)\cdot C_1 + m\cdot C_2 + C}{C - \alpha} \qquad [117]$$

that can be rearranged into the form

$$CV/V_0 - (1 + V/V_0)\cdot\alpha = (m-1)\cdot C_1 + m\cdot C_2 \qquad [118]$$

After further rearrangements we have, by turns,

$$CV/V_0 - (1 + V/V_0)\cdot\alpha = CA - (2-m)\cdot(C_1 + C_2) \qquad [119a]$$

$$CV/V_0 = CA + (1 + V/V_0)\cdot\alpha - (C_1 + C_2)\cdot((1 + 10^{-pH}/g_1)^{-1} + (1 + 10^{-pH}/g_2)^{-1}) \qquad [119b]$$

$$CV/V_0 = CA + (1 + V/V_0)\cdot\alpha - ((C_1 + C_2)\cdot(1 + 10^{-pH}/g_1^*)^{-1} + (C_1 + C_2)\cdot(1 + 10^{-pH}/g_2^*)^{-1}) \qquad [119c]$$

where

$$CA = C_1 + 2C_2 \qquad [120]$$

Comparing Equations [119c] and [113] we see that $C_{01} = C_{02} = C_1 + C_2$ (total carbonate concentration) at Λ = 2. The A value referred to carbonates is termed as carbonate alkalinity (CA), A = CA. It can also be extended on a system with an excessive amount of NaOH, $\Delta = C_b$, i.e. one equivalent to Na_2CO_3 + NaOH system.

The total acitidy (TAC) concept can also be formulated. Considering relatively acidic D+T system with $M_{m_k}H_{n_k-m_k}L_{(k)}(C_{0k}, k = 1,\ldots,P) + H_{n_k+m_k}L_{(k)}B_{m_k}(C_{0k}, k = P+1,\ldots,R) + Me_{(k)}(OH)_{U_k-m_k}B_{m_k}(C_{0k}, k = R+1,\ldots,Q)$ + HB (C_a) + MOH (C_b) as D (V_0 mL) titrated with V mL of C mol/L MOH as T, and putting −C for C in Equation [113], we get the relation with TAC = A (Equation [111] involved

$$CV/V_0 = \sum_{i=1}^{\Lambda} C_{0i}\cdot(1 + 10^{-ph}/g_i^*)^{-1} - \mathrm{TAC} - (1 + V/V_0)\cdot 10^{-ph}/\gamma \qquad [121]$$

valid under assumptions similar to ones applied for the TAL formulation. In other words, A = TAC, when referred to Equation [121].

The formulation with Simms constants involved was formerly applied by Dickson (1981) and Pehrsson et al. (1976). However, the novel approach to the problem in question is quite

TABLE 8
Titrimetric determination of acid-base mixtures in the past 12 years

Content	Reference
Ammonium, nitrite, acetic acid, bicarbonate, and phosphate are measured in water and sludge samples in ANR or ASD reactors from the resulting raw titrimetric data processed with an Excel-based program using the Solver function.	Van Hulle et al., 2009
Determination of H^+, NH_3OH^+, and NH_4^+ in Rashing synthesis mixture of industrial importance by a method based on moving window strategy, which simultaneously chooses the optimal pH region and latent variables by partial least squares regression (PLS) of potentiometric titration data.	Fang et al., 2009
Analysis of mixtures of ascorbic acid, citric acid, and tartaric acis by potentiometric titration with partial least squares calibration (PLS).	Akhond et al., 2006
Low concentrations of citric acid in a mixture of other weak acid/base by a four-point titration procedure (volatile acids not present) of a five-point procedure for anaerobic environments where volatile fatty acids may be encountered.	Lahav et al., 2005
An artificial neural network (ANN) applied as a multivariate calibration tool via potentiometric acid-base titration. Two hydroxycinnamic acids and two hydroxilated benzoic acids were titrated using tetrabutylammoniumhydroxide in 2-propanol.	Aktas and Yasar, 2004
The method uses individual potentiometric titration data for tartaric process production from maleic acid (with epoxysuccinic acid as intermediate). It is necessary to quantify the concentration of all three acids in order to determine the progress of the reaction.	Castro Montoya et al., 2003
Simultaneous determination of four weak organic acids (antranilic, nicotinic, picolinic, and sulfanilic acids) with the aid of a three-layered feed-forward artificial neural network (ANNA) trained by lack propagation learning to model the complex nonlinear relationship.	Shamsipur et al., 2002
Mixtures of organic acids with similar pK (mixtures of o-m and p-chlorobenzoic acids) were determined simultaneously from differences in titration spectra by using principal component regression (PCR).	Zhu, 1999
The linear titration equation of mixtures of acids (two five-component systems) was derived and the potentiometric data obtained were processed by multivariate calibration approaches such as class least squares (CLS), principal component regression (PCR), and partial least squares (PLS).	Ni, 1998

different from ones specified previously. Moreover, such an approach should not depend, in principle, on the pH range covered by experimental points in the range of lower pH values. It is not the case in the alkalinity measurements practiced hitherto. Applicability of the Simms constants concept seems to be obvious in modeling some complex systems, such as humic and fulvic acids, where the composition, number of active (–COOH, –OH, NH_2) groups in particular molecules, and their equilibrium constants are undefined a priori. In this case, an extension of the related model is involved with addition of one or more uniform terms of $C_{0j}\cdot(1 + 10^{-ph}/g_j^*)^{-1}$ type. Each component of this type provides two new parameters: C_{0j} and g_j^*.

It should also be noticed that there are no differences between protons generated or consumed in dissociation and hydrolysis, complexation, precipitation, or redox reactions, exemplified by the reaction notations: $Fe^{+3} + H_2O = FeOH^{+2} + H^+$, $Fe^{+3} + 3H_2O = \mathbf{Fe(OH)}_3 + 3H^+$ (hydrolysis); $Ag^+ + 2HCN = Ag(CN)_2^{-1} + 2H^+$ (Ag^+ acts there as a strong acid (Michałowski et al., 2005c, 2007)). On the other hand, MnO_4^- acts as the multifunctional base in redox reactions (Michałowski et al., 2005c, 2009; Michałowski and Toporek, 2003b). For these reasons, the reservation put on the step of alkalinity formulation, where the complexes other than proto- and hydroxo-complexes were excluded or neglected, can be highly weakened.

Another option applicable in the case of the systems where protons are involved in side (complexation and/or redox) reactions, seems to be an application of the term $(1+10^{a(pg_H^*-ph)})^{-1}$, with additional parameter a, as one in the empirical Hill equation (reviewed by Goutelle et al. (2008)); see also Onufriev et al. (2001) and Weiss (1997).

FINAL COMMENTS

pH and acid-base equilibria are important topics, and some aspects of them have been treated in this journal (Asuero, 2007; Michałowski et al., 2005a; Michałowski, 2010; Casado-Riobó, 2005, 2008; de Levie, 1997b; Kubista et al., 1999; Norman and Maeder, 2006; Esteban et al., 2006). Titrimetry has been applied since the late eighteenth century (Beck, 1994; Johansson, 1988) and is one of the oldest known methods of chemical analysis that seeks to determine chemical composition (Beck, 1997; Felber et al., 2003; King, 1997) on the basis of reaction chemistry. Titrimetry may be applied to the analysis of mixtures; see Table 8. On the other hand, buffers play a vital role in solution chemistry, and also have technical and industrial applications of great worth (Chuy and Bell, 2009; Akin et al., 2008; Zaher and Vanrolleghem, 2006; Dougherty et al., 2006; Jung and Hur, 2000; Van de Steene et al., 2002; Van Vooren et al., 2001; Dartiguenave et al., 2000; Porter et al., 1995; Van der Houwen et al., 1994; Moisio and Heikenon, 1989, 1994). For the preparation of buffers see Perrin and Dempsey (1979), Albert and Serjeant (1984), Elving et al. (1956), Ramis Ramos et al. (1986), Fernandez and Martin (1977), Mongay and Cerda (1974, 1984), Beck (1994), Johansson (1988), Aktas and Yasar (2004), Castro-Montoya et al. (2003), Shamsipur et al. (2002); Zhu (1999), Porter et al. (1995), Van der Houwen et al. (1994), Moisio and Heikenon (1989, 1994), Thomson and Kessick (1981), Mauk and Scott (1981), Gomori (1955), Stoll and Blanchard (1990), and Ellis and Morrison (1982). The diprotic acid case has received considerable attention (Asuero, 1993, 2007; Ricci, 1952; Rilbe, 1993, 1994; Stoyanov and Righetti, 1997, 1998; Asuero et al., 1986c). Several spreadsheets or software programs have been devised (Oliveira et al., 2007; Ranaghan, n.d.; Eurotitrations, n.d.; Ramette, 1989, 1994, 1998; Ramette and Holmes, 1992; VAXA, n.d.; BATE, n.d.; Gutz, n.d.) to calculate pH and buffer capacity and simulate titrations even of arbitrary mixtures (Gutz, n.d.).

The contents of this review article can be outlined as follows:

1. It was shown that acid-base systems of different degrees of complexity can be presented in uniform manner. The key for such an uniformity is the application of the formation function, $\bar{n}$.
2. The effects involved with the presence of ubiquitous CO_2, particularly in the strong base solutions, were considered quantitatively.
3. The principle of a formulation with Simms constants involved was introduced and its usefulness in formulation of buffer capacity and alkalinity concepts was proven. Application of Simms constants provides a kind of "homogeneity" in complex systems (e.g., fluids in living organisms, natural waters) of undefined a priori composition.
4. The dynamic buffer capacity was presented in generalized form. The interrelation between different buffer capacity concepts was formulated.
5. A generalized approach involved with particular problems, such as inflection points on titration curves, has been suggested.
6. The new concepts of total alkalinity (TAL) and total acidity (TAC) were introduced. The TAL and TAC are based on the curve fitting applied to a nonlinear regression equation with Simms constants involved. The TAL or TAC and other parameters of the system: the Simms constants, activity coefficient of hydrogen ions are determined from the single titration curve. It should necessarily be noted that TAL and TAC involve analytical concentrations of the components endowed with acid-base properties in the sample tested, not concentrations of particular species. For example, TAL = CA = $C_1 + 2C_2$ (Equation [120]), not $[HCO_3^-] + 2[CO_3^{-2}]$ is applied for definition of carbonate alkalinity (CA). The values for TAL, CA or TAC illustrate the properties of the system tested, not analytical procedure applied for this purpose. So, e.g. the result of determination of TAL does not depend implicitly on the pH range covered in the titration made for this purpose. It is the stringent property testifying on account of the method proposed. None preliminary information on the composition of the sample tested is required, although such an information may appear to be helpful on the stage of assumption of starting values for the parameters. It is particularly advised to apply $pg_i^* = -\log(g_i^*)$, not (g_i^*) as the parameters of the system. It results from the fact that $g_i^* = 10^{-pg_i^*} > 0$ and, the parameters assume only positive values during the iteration procedure. And last but not least – the model is not referred to defined, particular species in the systems considered and any artificial "demarcation pH point", separating acidic and basic species, is not needed.

A huge number of articles found currently in the Internet under the combination of search terms *buffer capacity* and *acid-base* testifies to the necessity to formulate this term correctly. This requirement is not fulfilled in, for example, Tam (1999), where mere errors were made.

In this context, the concept of buffer capacity B_V, originating from Michałowski and Parczewski (1978), related to a simple system with a polyprotic acid, H_nL, involved and extended in the present article, seems to be the best choice for several reasons, namely:

(a) The buffer capacity is usually evaluated from results of classical pH-metric titrations where dilution effect is involved; the finite change in pH, ΔpH, is involved with a finite volume of a titrant added;
(b) The buffer capacities are related to mixtures of acid-base systems of different degrees of complexity, exemplified by fluids in living organisms and natural waters;
(c) The formula for B_V (Equation [98]) is in defined relation (Equation [100]) to β_V (Equation [97]); moreover, β_V and β (Equation [39]) are interrelated; see Equations [96] and [97].
(d) The kind and concentration of reagent in the titrant used is taken into account.

The work presented here seems to be the most extensive approach to acid-base dynamic systems, realized in titrimetric methods of analysis. Articles issued mainly within the past two decades are cited.

LIST OF SYMBOLS USED

α	$[H^+] - [OH^-]$
D	titrand
g_i, g_{ki}	Simms constants
K_i	dissociation constant (Eq. [1])

K_i^H	formation constant (Eq. [2])
M^+	non-hydrolyzable metal ion
$Me_{(k)}^{+u_k}$	hydrolyzable metal ion of k-th kind
T	titrant
V	volume [mL] of T added into D
V_0	volume [mL] of D

REFERENCES

Aiken, G. R.; McKnight, D. M.; Wershaw, R. L.; McCarthy, P. An Introduction to Humic Substances in Soil, Sediment and Water. In *Humic Substances in Soil, Sediment and Water: Geochemistry, Isolation and Characterization*; Aiken, G. R.; McKnight, D. M.; Wershaw, R. L., Ed.; Wiley Interscience: New York, 1985.

Aiken, G. R.; McKnight, D. M.; Thorn, K. A.; Thurman, E. M. Isolation of Hydrophylic Acids from Water Using Macroporous Resins. *Org. Geochem.* **1992**, *18* (4), 567–573.

Akhond, M.; Tashkhourian, J.; Hemmateenejad, B. Simultaneous Determination of Ascorbic, Citric, and Tartaric Acids by Potentiometric Titration with PLS Calibration. *J. Anal. Chem.* **2006**, *61* (8), 804–808.

Akin, H.; Brandam, C.; Meyer, X. M.; Strehaiano, P. A Model for pH Determination of a Grape Must by *Saccharomyces cerevisiae*. *Chem. Eng. Process.* **2008**, *47* (11), 1986–1993.

Aktas, A. H.; Yasar, S. Potentiometric Titration of Some Hydroxylated Benzoic Acids and Cinnamic Acids by Artificial Neural Network Calibration. *Acta Chim. Slovenica* **2004**, *51*, 273–282.

Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*, 3th ed.; Chapman and Hall: London, 1984; pp 136–175.

Asuero, A. G. A Bilogarithmic Method for the Evaluation of Acidity Constants of Amphoteric Substances from Solubility Measurements. *Int. J. Pharm.* **1989**, *52* (2), 129–137.

Asuero, A. G. Observations on the Computation of Acidity Constants of Two-Step Overlapping Equilibria from the Half Values of the Formation Function. *Anal. Lett.* **1990**, *23* (4), 747–753.

Asuero, A. G. Buffer Index in the Titration of a Monoprotic Acid with a Strong Base. *Int. J. Pharm.* **1992a**, *87* (1–3), 11–19.

Asuero, A. G. A Bilogarithmic Method for the Potentiometric Evaluation of Stability Constants of Two-Step Overlapping Equilibria. *Anal. Lett.* **1992b**, *25* (6), 1143–1155.

Asuero, A. G. Inflexion Points of the Formation Curve for Two-Step Overlapping Equilibria. *Microchem. J.* **1993**, *47* (3), 386–398.

Asuero, A. G. On the Buffer Index of a Single Weak Monoprotic Acid System. *Int. J. Pharm.* **1996**, *134* (1–2), 1–13.

Asuero, A. G. Buffer Capacity of a Polyprotic Acid: First Derivative of the Buffer Capacity and pK_a Values of Single and Overlapping Equilibria. *Crit. Rev. Anal. Chem.* **2007**, *37* (4), 269–301.

Asuero, A. G., Bueno, J. M. Fitting Straight Lines with Replicated Observations by Linear Regression. Part IV. Transforming Data. *Crit. Rev. Anal. Chem.* **2011**, *41* (1), 36–69.

Asuero, A. G.; Gonzalez, A. Fitting Straight Lines with Replicated Observations by Linear Regression. Part III. Weighting Data. *Crit. Rev. Anal. Chem.* **2007**, *37* (3), 143–172.

Asuero, A. G.; Jiménez-Trillo, J. L.; Navas, M. J. Mathematical Treatment of Absorbance versus pH Graphs of Polybasic Acids. *Talanta* **1986a**, *33* (11), 929–934.

Asuero, A. G.; Navas, M. J.; Jimenez-Trillo, J. C. Spectrophotometric Methods for the Evaluation of Acidity Constants. I. Numerical Methods for Single Equilibria. *Talanta* **1986b**, *33* (2), 195–198.

Asuero, A. G.; Jimenez-Trillo, J. L.; Navas, M. J. Spectrophotometric Methods for the Evaluation of Acidity Constants.II. Numerical Methods for Two-Step Overlapping Equilibria. *Talanta* **1986c**, *33* (6), 531–535.

Asuero, A. G.; Sayago, A.; Gonzalez, A. The Correlation Coefficients: An Overview. *Crit. Rev. Anal. Chem.* **2006**, *36* (1), 41–59.

Asuero, A. G.; Michalowski, T. Why Not Stoichiometry Versus Stoichiometry – Why Not. In preparation.

Avdeef, A. Solubility of Sparingly-Soluble Ionization Drugs. *Adv. Drug Deliv. Rev.*, **2007**, *59* (7), 568–590.

Avdeef, A.; Bucher, J. B. Accurate Measurements of the Concentration of Hydrogen Ions with a Glass Electrode: Calibrations Using the Prideaux and Other Universal Buffer Solutions and a Computer-Controlled Automatic Titrator. *Anal. Chem.* **1978**, *50* (14), 2137–2142.

Avdeef, A.; Testa, B. Physicochemical Profiling in Drug Research: A Brief Survey-of-the-Art of Experimental Techniques. *Cell. Mol. Life Sci.* **2002**, *59* (10), 1681–1689.

Baicu, S. C.; Taylor, M. J. Acid-Base Buffering in Organ Preservation Solution as a Function of Temperature: New Parameters for Comparing Buffer Capacity and Efficiency. *Cryobiology* **2002**, *45* (1), 33–48.

BATE pH calculator, Base Acid Titration and Equilibria. http://www.chembuddy.com/?left=BATE&right=pH-calculator

Beck II, C. M. Classical Analysis. A Look at the Past, Present and Future. *Anal. Chem.* **1994**, *66* (4), 225A–230A, 233A–239A.

Beck II, C. M. Towards a Revival of Classical Analysis. *Metrologia* **1997**, *34* (1), 19–30.

Beck, M. T. *Chemistry of Complex Equilibria*; Van Nostrand Reinhold: London, 1970.

Beynon, R. J.; Easterby, J. S. *Buffer Solutions, The Basis*; Taylor and Francis: New York, 2002.

Bi, S. A Simple Model for Predicting the pH Values of Acidic Natural Waters. *Anal. Chim. Acta* **1995**, *314* (1–2), 111–119.

Bijective Function. http://en.wikipedia.org/wiki/Bijective_function

Billes, F.; Toth, A. A Generalized Theory of Quantitative Analysis of Multicomponent Ampholyte (Acid, Base) Systems by Potentiometric Titration. *Acta Chim. Hun.* **1986**, *123* (1–2), 3–13.

Billo, E. J. *Excel for Chemists, A Comprehensive Guide*, 2nd ed.; Wiley: New York, 2001

Birk, T. Matrix Formulation of Complex Equilibria and Acid-Base Equilibria by Use of Extent of Reaction. *Chem. Educ.* **2009**, *14* (3), 91–95.

Birnbaum, E. R.; Walker, E. A. A Mathematical Analysis of the Bjerrum Function for the Stepwise Equilibrium Model. *J. Math. Chem.* **1987**, *1* (2), 235–247.

Blanchard, J. S. Buffer for Enzymes. *Methods Enzymol.* **1984**, *104*, 404–414

Borkovec, M.; Koper, G. J. M. Ising Models of Polyprotic Acids and Bases. *J. Phys. Chem.* **1994**, *98* (23), 6038–6045.

Boudeville, P.; Burgot, J.-L. A New pH-metric Methodology for the Determination of Thermodynamics Inclusion Constants of Guest/Cyclodextrin Complexes. *J. Pharm. Sci.* **1995**, *84* (9), 1083–1089.

Bosch, E.; Roses, M. Chromatography Buffers for Chromatography and Electrophoresis. In *Encyclopedia of Separation Science*; Elsevier: Amsterdam, 2007; Level III: Practical Applications, 1–12

Box, K.; Bevan, C.; Comer, J.; Hill, A.; Allen, R.; Reynolds, D. High-throughput Measurement of pK*a* Values in a Mixed-Buffer Linear pH Gradient System. *Anal. Chem.* **2003**, *75* (4), 883–892.

Britton, H. T. S.; Robinson, R. A. Universal Buffer Solutions and the Dissociation Constant of Veronal. *J. Chem. Soc.* **1931a**, 1456–1462.

Britton, H. T. S.; Robinson, R. A. The Use of the Antimony-Antimonious Oxide Electrode in the Determination of the Concentration of Hydrogen Ions in Potentiometric Titrations. The Prideaux-Ward Universal Buffer Mixture. *J. Chem. Soc.* **1931b**, 458–473.

Brooks, S. P. J.; Storey, K. B. Bound and Determined: A Computer Program for Making Buffers of Defined Ion Concentrations. *Anal. Biochem.* **1992**, *201* (1), 119–126.

Brown, R. J. C.; Milton, M. J. T. Observation of a Combined Dilution and Salting Effect in Buffers under Conditions of High Dilution and High Ionic Strength. *Accreditation Quality Assurance* **2003**, *8* (11), 505–510.

Bugaevski, A. A. Analogues of Buffer Capacity in Proton Equilibria. *Russ. J. Phys. Chem. USSR* **1969**, *43* (7), 1042.

Bugaevski, A. A.; Dunai, B. A. Calculation of Equilibrium Composition and Buffer Properties of Solutions with Use of Computers. *Zh. Anal. Khim.* **1971**, *26* (2), 205.

Butler, J. N. *Ionic Equilibrium: A Mathematical Approach*; Addison-Wesley: Reading, Mass., 1964.

Butler, J. N. *Carbon Dioxide Equilibria and Their Applications*; Addison-Wesley: Reading, Mass., 1982; pp 44–72.

Butler, J. N.; Cogley, D. R. *Ionic Equilibrium. Solubility and pH Calculations*; Wiley: New York, 1999.

Campbell, B. H.; Meites, L. Acid-Base Titration Curves for Acids with Very Small Ratios of Successive Dissociation Constants. *Talanta* **1974**, *21* (2), 117–122.

Casado-Riobó, A. A More Rational Treatment of the Acid-Base Equilibria Applying the Proton Condition. How the Protons in Equilibria Are Additive: Dissolution of Acids. *Crit. Rev. Anal. Chem.* **2005**, *35* (4), 289–299.

Casado-Riobó, A. A More Rational Treatment of the Acid-Base Equilibria Applying the Proton Condition, or the Hydroxyl Condition in Equilibria. How the Hydroxyl Ions Are Additive in Equilibrium: Dissolutiton of Bases, Salt and Mixtures. *Crit. Rev. Anal. Chem.* **2008**, *38* (3), 147–160.

Castro-Montoya, A. J.; Herrera-Soland, M.; Quintana-Hernández, P. A.; Serna-González, M. Potentiometric Analysis of a Reaction System of Organic Acids. *Rev. Soc. Quím. Méx* **2003**, *47* (3), 211–215.

Celentano, F. C.; Tonani, C.; Fazio, M.; Gianazza,E.; Righetti, P. G. pH Gradients Generated by Polyprotic Buffers. I. Theory and Computer Simulation. *J. Biochem. Biophys. Methods* **1988**, *16* (2–3), 109–128.

Chiodi, F. Modèle mathématique pour l'etude des équilibres physicochimiques de permanentes. *Int. J. Cosmet. Sci.* **1989**, *11* (6), 283–292.

Chiriac, V.; Balea, G. Buffer Index and Buffer Capacity for a Simple Buffer Solution. *J. Chem. Educ.* **1997**, *74* (8), 937–938.

Chuy, S; and Bell, L. N. Kinetics of an Acid-Base Catalyzed Reaction (Aspartame Degradation) as Affected by Polyol-Induced Changes in Buffer pH and pK$_a$ Values. *Food Chem.* **2009**, *74* (1), C56–C61.

Cohn, E. J.; Edsall, J. T. *Proteins, Amino Acids and Peptides*; Reinhold: New York, 1943; ch. 20, pp 451–453.

Connors, K. A.; Mecozzi, S. *Thermodynamics of Pharmaceutical Systems*, 2nd ed.; Wiley: New York, 2010.

Conway, B. E. *Electrochemical Data*; Elsevier: Amsterdam, 1952.

Corey, H. F. Advances in Analytical Chemistry. *Am. J. Physiol. Renal Physiol.* **2010**, *298* (2), F474.

Curtright, R.; Emry, R.; Heaton, R. M.; Markwell, J. Facilitating Student Understanding of Buffering by an Integration of Mathematics and Chemical Concepts. *Biochem. Mol. Biol. Educ.* **2004**, *32* (2), 71–77.

Cutler, D. Calculations of pH for Complex Mixtures of Acids, Bases and Ampholytes. *J. Pharm. Pharmacol.* **1986**, *38* (7), 499–501.

Czerminski, J.; Iwasiewicz, A.; Paszek, Z.; Sikorski, A. *Statistical Methods in Applied Chemistry*; Elsevier: Amsterdam, 1990.

Dai, M. Integral Capacity of Buffer. *Microchim. Acta* **1984**, *82*, 159–169.

Dartiguenave, C.; Jeandet, P.; Maujean, A. Study of the Contribution of the Major Organic Acids of Wine to the Buffering Capacity of Wine in Model Solutions. *Am. J. Enol. Viticulture* **2000**, *51* (4), 352–356.

Davies, M. T. A Universal Buffer Solution for Use in Ultra-Violet Spectrophotometry. *Analyst* **1959**, *88*, 248–251.

de Levie, R. Explicit Expressions of the General Form of the Titration Curve in Terms of Concentration. Writing a Single Closed-Form Expression for the Titration Curve for a Variety of Titrations without Using Approximation or Segmentation. *J. Chem. Educ.* **1993**, *70* (3), 209–217.

de Levie, R. General Expressions for Acid-Base Titrations of Arbitrary Mixtures. *Anal. Chem.* **1996a**, *68* (4), 585–590.

de Levie, R. Titration vs. Tradition. *Chem. Educ*. **1996b**, *1* (3), 1–18.

de Levie, R. *Principles of Quantitative Chemical Analysis*; McGraw-Hill, New York, 1997a.

de Levie, R. The pH in Graph. *Crit. Rev. Anal. Chem.* **1997b**, *27* (1), 51–76.

de Levie, R.; Moisio, T.; Heikonen, M. Computer Fitting of Entire Data Sets, as Exemplified by Acid-Base Titrations. *Kem-kemi* **1998**, *25* (2), 121–123.

de Levie, R. Redox Buffer Strength. *J. Chem. Educ.* **1999a**, *76* (4), 574–577.

de Levie, R. *Aqueous Acid-Base Equilibria and Titrations*; Oxford University Press: Oxford, 1999b.

de Levie, R. A General Simulator for Acid-Base Titrations. *J. Chem. Educ.* **1999c**, *76* (7), 987–991.

de Levie, R. The Formalism of Titration Theory. *Chem. Educ.* **2001a**, *6* (5), 272–276.

de Levie, R. Linear Graphs for Understanding Acid-Base Titrations. *Chem. Educ.* **2001b**, *6* (4), 210–216.

de Levie, R. *How to Use Excel in Analytical Chemistry: and in General Scientific Data Analysis* Cambridge: Cambridge University Press, 2001c.

de Levie, R.; Frison, G.; Calatroni, A. Solving pH Problems on a Spreadsheet. *Chem. Educ.* **2003**, *8* (5), 298–302.

de Levie, R. On Isohydric Solutions and Buffer pH. *J. Electroanal. Chem.* **2005**, *582* (1–2), 21–27.

Dennison, C. A Simple and Universal Method for Making Up Buffer Solutions. *Biomed. Educ.* **1988**, *16* (4), 210–211.

Desbarres, J.; Bauer, D. Simulation des courbes de dosage potentiometrique par emploi d'une equation universelle. Dosage par echange d'une seule particule. *Talanta* **1975**, *22* (11–12), 877–879.

Dickson, A. G. The Development of the Alkalinity Concept in Marine Chemistry. *Mar. Chem.* **1992**, *40* (1–2), 49–63.

Dickson, A. G. An Exact Definition of Total Alkalinity and a Procedure for the Estimation of Alkalinity and Total Inorganic Carbon from Titration Data. *Deep-Sea Res.* **1981**, *28A* (6), 609–623.

Dimitrov, S. D.; Kamenski, D. I. Overall Stability Constants: Estimation by Non Linear Least Squares Methods. *Comput. Chem.* **1997**, *21* (3), 167–173.

Dixon, H. B. F. Shapes of Curves of pH-Dependence of Reactions. *Biochem. J.* **1973**, *131* (1), 149–154.

Dixon, H. B. Curves of Ligand Binding. The Use of Hyperbolic Functions for Expressing Titration Curves. *Biochem. J.* **1974**, *137* (3). 443–447.

Dixon, H. B. Factorization of the Michaelis Functions. *Biochem. J.* **1975**, *151* (2), 271–274.

Dixon, H. B. F. Derivation of Molecular pK Value from pH Dependences. *Biochem. J.* **1979**, *177* (1), 249–250.

Dixon, H. B. Relations between the Dissociation Constants of Dibasic Acids. *Biochem. J.* **1988**, *253* (3), 911–913.

Dixon, H. B. Multiple Ionization in Proteins: Arsenical Analogues of Natural Phosphates. *Pure Appl. Chem.* **1994**, *66* (10–11), 2399–2402.

Dixon, H. B.; Brocklehurst, K; Tipton, K. F. pH-Activity Curves for Enzyme-Catalysed Reactions in Which the Hydron Is a Product or Reactant. *Biochem. J.* **1987**, *248* (2), 573–578.

Dixon, H. B. F.; Clarke, S. D.; Smith, G. A.; Carne, T. K. The Origin of Multiply Sigmoid Curves of pH-Dependence. *Biochem. J.* **1991**, *278* (1), 279–284.

Dorazio, P. Effects of Phosphate and HEPES MOPS Buffers on Calibration of Sodium and Potassium-Ion Selective Electrode (ISE) for Clinical Analysis. *Clin. Chem.* **1987**, *33* (6), 1005.

Dougherty, D. P.; Neta, E. D. D. C.; McFeeters, R. F.; Lubkin, S. R.; Breidt, F. Semi-mechanistic Partial Buffer Approach to Modeling pH, the Buffer Properties and the Distribution of Ionic Species in Complex Solutions. *J. Food Agric. Chem.* **2006**, *54* (16), 6021–6029.

Edsall, J. T.; Wyman, J. Polybasic Acids, Bases and Ampholytes, Including Proteins. In *Biophysical Chemistry*; Academic Press: New York, 1958; vol. 1, ch. 9, pp 477–549.

Egneus, B. The Solution Chemistry of Ethylmethylglyoxime: Part I. The Proton Complex. *Anal. Chim. Acta* **1968**, *43*, 53–62.

Ellis, D. A. A New Universal Buffer System. *Nature* **1961**, *191* (4793), 1099–1100.

Ellis, K. J.; Morrison, J. F. Buffers of Constant Ionic Stregth for Studying pH-Dependent Processes. *Methods Enzymol.* **1982**, *87*, 405–427.

Elving, P. J.; Markowitz, J. M.; Rosenthal, I. Preparation of Buffer Systems of Constant Ionic Strength. *Anal. Chem.* **1956**, *28* (7), 1179–1180.

Esteban, M.; Ariño, C.; Diaz-Cruz, J. M. Chemometrics in Electroanalytical Chemistry. *Crit. Rev. Anal. Chem.* **2006**, *36* (3), 295–313.

Eurotitrations 3.0 index. http://www.scuolaeuropeadivarese.it/software/

Fang, S.; Zhu, M.-Q.; He, C.-H. Moving Window as a Variable Selection Method in Potentiometric Titration Multivariate Calibration and Its Application to the Simultaneous Determination of Ions in Raschig Synthesis Mixtures. *J. Chemom.* **2009**, *23* (3), 117–123.

Felber, H.; Rezzonico, S.; Máriásy, M. Titrimetry at a Metrological Level. *Metrologia* **2003**, *40* (5), 249–254.

Fencl, V.; Leith, D. E. Stewart's Quantitative Acid-Base Chemistry: Applications in Biology And Medicine. *Respir. Physiol.* **1993**, *91*, 1–16.

Ferguson, W. J.; Baunschweiger, K. I.; Braunschweiger, W. R.; Smith, J. R.; McCormick, J. J.; Wasmann, C. C.; Jarvis, N. P.; Bell, D. H.; Good, N. E. Hydrogen Ion Buffers for Biological Research. *Anal. Biochem.* **1980**, *104*, 300–310.

Fernandez, C. M.; Martin, V. C. Preparation d'un tampon universel de force ionique 0,3 M. *Talanta* **1977**, *24*, 747–748.

Fillion, N.; Probst, A.; Probst, J. L. Dissolved Organic Matter Contribution to Rain Water, Throughfall and Soil Solution Chemistry. *Analusis* **1999**, *27* (5), 409–413.

Fishtik, I. Generalized approach to buffer capacity. *Z. Phys. Chem. (Neue Folge)* **1998**, *205* (2), 253–270.

Fishtik, I.; Povar, I. Buffer Capacity in Multiple Chemical Reaction Systems Involving Solid Phases. *Can. J. Chem.* **2006**, *84* (8), 1036–1044.

Fleck, G. M. *Equilibria in Solution*; Holt, Rinehart and Winston: New York, 1966.

Fletcher, J. E.; Spector, A. A.; Ashbrook, J. D. Analysis of Macromolecule-Ligand Binding by Determination of Stepwise Equilibrium Constants. *Biochemistry* **1970**, *9* (23), 4580–4587.

Fournaise, R.; Petitfaux, C. Limites à l'emploi des points d'inflexion comme points d'équivalence lors de l'exploitation des titrages acido-basiques. Intérêt de l'affinement multiparamétrique pour une analyse precise des données potentiométriques. *Analusis* **1987**, *15* (1), 33–42.

Freiser, H. Acid-Base Reaction Parameters. *J. Chem. Educ.* **1970**, *47* (12), 809–811.

Freiser, H. *Concepts & Calculations in Analytical Chemistry: A Spreadsheet Approach*; CRC Press: Boca Raton, Fla., 1992.

Freund, J.; Kalbitzer, H. R. Physiological Buffers for NMR-Spectroscopy. *J. Biomol. NMR* **1995**, *5* (3), 321–322.

Frison, G.; Calatroni, A. The Buffer Capacity of Arbitrary Salts. *Chem. Educ.* **2005**, *10* (4), 257–259.

Frison, G.; Calatroni, A. On the Existence and Uniqueness of the Equilibrium of Arbitrary Bronsted Acid-Base Mixtures. *Chem. Educ.* **2006**, *11* (3), 150–151.

Frison, G.; Calatroni, A. Some Notes on pH Computation Method and Theories; http://www.scuolaeuropeadivarese.it/software/Some_Notes.pdf

Frugoni, J. A. C. Tampone universale di Britton e Robinson a forza ionica costante. *Gazz. Chim. Ital.* **1957**, *87*, 403–407.

Fuguet, O. E.; Reta, M.; Gilbert, G.; Roses, M.; Bosch, E.; Rafols, C. Critical Evaluation of Buffering Solutions for pKa(s) Determination by Capillary Electrophoresis. *Electrophoresis* **2008**, *29* (13), 2841–2851.

Galster, H. *pH Measurement: Fundamentals, Methods, Applications, Instrumentation*; VCH: Weinheim, 1991.

Gamble, D. S. Titration Curves of Fulvic Acid: The Analytical Chemistry of a Weak Acid Polyelectrolyte. *Can. J. Chem.* **1970**, *48* (17), 2662–2669.

Gebauer, P.; Bocek, P. New Aspects of Buffering with Multivalent Weak Acids in Capillary Electrophoresis: Pros and Cons of the Phosphate Buffer. *Electrophoresis* **2000**, *21* (14), 2809–2813.

Giaffreda, E.; Tonani, C.; Righetti, P. G. pH Gradient Simulator for Gel Electrophoretic Techniques in a Windows Environment. *J. Chromatogr.* **1993**, *630* (1–2), 313–327.

Gibson, G.; Neverov, A. A.; Brown, R. S. Potentiometric Titration of Metal Ions in Methanol. *Can. J. Chem.* **2003**, *81* (6), 495–504.

Gibson, G. T. T.; Mohamed, M. F.; Neverov, A. A.; Brown, R. S. Potentiometric Titration of Metal Ions in Ethanol. *Inorg. Chem.* **2006**, *45* (19), 7891–7902.

Glaister, P. Titration Curve Analysis: Some Observations. *J. Chem. Educ.* **1997**, *74* (7), 760–761.

Glaiser, P. A Unified Titration Formula. *J. Chem. Educ.* **1999**, *76* (1), 132.

Golonanov, V. I. Application of the Bjerrum Function to the Potentiometric Titration of Aluminium by Fluoride Ions. *J. Anal. Chem.* **2006**, *61* (4), 369–374.

Gomori, G. Preparation of Buffers for Use in Enzyme Studies. *Methods Enzymol.* **1955**, *24*, 53–68.

Gonzalez, G. G.; Jimenez, A. M.; Asuero, A. G. Titration Errors in Acid-Base Titrations. *Microchem. J.* **1990**, *41* (1), 113–120.

Good, N. E.; Izawa, S. Hydrogen Ion Buffers. *Methods Enzymol.* **1972**, *24*, 53–68.

Gordon, W. E. Component Discrimination in Acid-Base Titration. *J. Phys. Chem.* **1979**, *83* (11), 1365–1377.

Gordon, W. E. Data Analysis for Acid-Base Titration of an Unknown Solution. *Anal. Chem.* **1982**, *54* (9), 1595–1601.

Goutelle, S.; Maurin, M.; Rougier, F.; Barbaut, X.; Bourguignon, L.; Ducher, M.; Maire, P. The Hill Equation: A Review of Its Capabilities in Pharmacological Modelling, *Fundam. Clin. Pharmacol.* **2008**, *22*, 633–648.

Gran, G. Determination of the Equivalence Point in Potentiometric Titrations. Part II, *Analyst*, **1952**, *77*, 661–671.

Guenther, W. B. *Chemical Equilibrium. Principles and Application for the Life Sciences*; Plenum Press: New York, 1975.

Guenther, W. B. *Unified Equilibrium Calculations*; Wiley: New York, 1991.

Guiñon, J. L. Comments on Calculation of pH Value of a Mixture of Solutions. *Chem. Eng. Sci.* **1987**, *42* (2), 392.

Gustafsson, T. K.; Skrifvars, B. O.; Sandström, K. V.; Waler, K. V. Modeling for pH Control. *Ind. Eng. Chem. Res.* **1995**, *34* (3), 820–827.

Gutz, I. G. R. CurTiPot, Acid-Base and pH Titration. http://www2.iq.usp.br/docente/gutz/Curtipot_.html

Hamann, S. D. Theory of Titration of Polybasic Acids 2. Conditions of Existence of Inflexion Near Equivalence Points. *Aust. J. Chem.* **1970**, *23* (9), 1749–1765.

Harris, D. C. *Quantitative Chemical Analysis*, 8th ed.; W.H. Freeman: New York, 2010.

Heck, A.; Kędzierska, E.; Rogers, L.; Chmurska, M. Acid-Base Titration Curves in an Integrated Computer Learning. *Chem. Educ.* **2009**, *14* (4), 164–174.

Heil, G.; Schäfer, H. Modeling and Graphic Presentation of Acid-Base Titration Curves. Presentation of an Alternative Model. *Chem. Educ.* **2002**, *7* (6), 339–346.

Hesse, R. and Olin, A. A Note on the Buffer Index of a Polyprotic Acid. *Talanta* **1977**, *24* (2), 150.

Hulanicki, A.; Głąb, S. Buffer Solutions. *Encyclopedia of Analytical Chemistry*; Wiley: New York, 2005; pp 300–304.

Irving, H.; Rossotti, J. S.; Harris, G. The Determination of Dissociation Constants of Dibasic Acids. *Analyst* **1955**, *80* (2), 83–94.

Izutsu, K.; Yamamoto, H. Applicability of 0.05mol Kg-1 Potassium Hydrogen Phthalate as Reference Value pH Standard in Water-Organic Solvent Mixture. *Talanta* **1998**, *47* (5), 1157-1163.

Janecki, D.; Michałowski, T. Evaluation of Equilibrium Constants—A New Approach. *Chem. Anal.* (Warsaw) **1999**, *44* (3B), 611–621.

Janecki, D.; Doktór, K; Michałowski, T. Determination of Stability Constants of Complexes of $M_iK_jH_kL$ Type in Concentrated Solutions of Mixed Salts. *Talanta* **1999a**, *48* (5), 1191–1197; Janecki, D.; Doktór, K; Michałowski, T. Erratum to "Determination of stability constants of complexes of $M_jK_jH_kL$ type in concentrated solutions of mixed salts": [48 (1999) 1191]. *Talanta* **1999b**, *49* (4), 945.

Janecki, D.; Styszko-Grochowiak, K.; Michałowski, T. The Catenation and Isomerisation Effects on Stability Constants of Complexes Formed by Some Diprotic Acids. *Talanta* **2000a**, *52* (3), 555–562.

Janecki, D.; Michałowski, T.; Zieliñski, M. A Simple Method of Etidronate Disodium Determination in Commercial Preparations of the Salt. *Chem. Anal.* (Warsaw) **2000b**, *45* (5), 659–666.

Janjic, T. J.; Milosavljevic, E. B. Two-Phase Buffer Systems: Theoretical Considerations. *Anal. Chem.* **1978**, *50* (4), 597–600.

Janjic, T. J.; Milosavljevic, E. B.; Srdanovic, M. K. Multicomponent Two-Phase Buffer Systems. *Anal. Chim. Acta* **1979**, *107*, 359–363.

Jano, I.; Hardcastle, J.; Jano, L. A.; Bates; K. R.; McCreary,H. E. General Equation for Determining the Dissociation Constants of Polyprotic Acids and Bases from Additive Properties. Part IV. Application to Potentiometric Titration. *Anal. Chim. Acta* **2002**, *428* (2), 309–321.

Johansson, A. Logarithmic Diagrams and Gran Curves as an Aid in Potentiometric Titrations in Complexometry. *Talanta* **1973**, *20* (1), 89–102.

Johansson, S. Numerical Evaluation of Potentiometric Acid-Base Titrations, Ph.D. Dissertation, The Royal Institute of Technology, Stockholm, 1978.

Johansson, S. Simplification of the Mathematical Evaluation of Titration Results by Regarding Complexes of the Type A_nB as N Complexes of the Type AB. *Analyst* **1979**, *104* (7), 593–600.

Johansson, A. The Development of the Titration Methods. Some Historical Annotations. *Anal. Chim. Acta* **1988**, *206*, 97–109.

Johansson, A.; Johansson, S. Automatic Titration by Stepwise Addition of Equal Volumes of Titrant. Part III. Use of Linear Equations to Calculate Equivalence Volumes in Acid-Base Titrations. *Analyst* **1978**, *103*, 305–316.

Johansson, A.; Johansson, S. Automatic Titration by Stepwise Addition of Equal Volumes of Titrant. Part IV. General-Purpose Program for Evaluating Potentiometric Acid-Base Titrations. *Analyst* **1979**, *104* (7), 601–612.

Johansson, A.; Johansson, S.; Gran, G. Automatic Titration by Stepwise Addition of Equal Volumes of Titrant. Part VIII. Determination of Alkalinity and Total Carbonate in Sea Water. *Analyst* **1983**, *108* (7), 1086–1090.

Johnson, W. C.; Lindsey, A. J. An Improved Universal Buffer. *Analytst* **1939**, *64* (7), 490–492.

Jordan, C. Ionic Strength and Buffer Capacity of Wide Range Buffers for Polarography. *Microchem. J.* **1980**, *25* (4), 492–499.

Juergens, U. Alkylamine Phosphoric Acid as a Universal Buffer System for Basic and Acidic Mobile Phases in HPLC. *J. Liq. Chromatogr.* **1988**, *11* (9–10), 1925–1940.

Jung, Y. K.; Hur, W. A New Method of On-Line Measurement of Buffer Capacity and Alkali Consumption Rate of a Fermentation Process. *J. Biosci. Bioeng.* **2000**, *90* (5), 580–582.

Jungas, R. L. Best Literature Values for the pK of Carbonic Acid under Physiological Conditions. *Anal. Biochem.* **2006**, *349* (1), 1–15.

Kankare, J. J. Determination of Dissociation Constants of Acids and Bases by Potentiostatic Titration. *Anal. Chem.* **1972**, *44* (14), 2376–2379.

Kankare, J. Determination of Composition of Mixtures of Weak Acids by Potentiostatic Titration. *Anal. Chem.* **1973**, *45* (11), 1877–1880.

Kankare, J. J. An Algebraic Approach to the Study of Titration Curves of Weak Acids and Their Mixtures. *Talanta* **1975**, *22*, 1005–1012.

Kholin, Y.; Zaitsev, V. Quantitative Physicochemical Analysis of Equilibria on Chemically Modified Silica Surfaces. *Pure Appl. Chem.* **2008**, *80* (7), 1561–1592.

King, E. J. Polyprotic Acids. In *Acid-Base Equilibria*; Pergamon Press: New York, 1965; ch. 9, pp 218–247

King, B. Review of the Potential of Titrimetry as a Primary Method. *Metrologia* **1997**, *34* (1), 77–82.

King, D. W. A General Approach for Calculating Speciation and Poising Capacity of Redox Systems with Multiple Oxidation States: Application to Redox Titrations and the Generation of pε-pH Diagrams. *J. Chem. Educ.* **2002**, *79* (9), 1135–1140.

King, D. W.; Kester, D. R. A General Approach for Calculating Polyprotic Acid Speciation and Buffer Capacity. *J. Chem. Educ.* **1990**, *67* (11), 932–933.

Klas, J. General Formula for the Calculation of the Hydrogen-Ion Concentration of Aqueous Solutions of Several Polyvalent Weak Acids. *Anal. Chim. Acta* **1968**, *41* (3), 549-550.

Klas, J. Calculation of the Stability Constants of Complexes with Respect to Simms' Conception of Dissociation of Polyvalent Acids. *Anal. Chim. Acta* **1975**, *74* (1), 220–222.

Klotz, I. M. Protein Interactions. In *The Proteins*; Neurath, H., Bailey, K, Eds.; Academic Press: New York, 1953; vol IB, ch. 8.

Klotz, I. M.; Hunston, D. L. Protein Interactions with Small Molecules. Relationships between Stoichiometric Binding Constants, Site Binding Constants, and Empirical Binding Parameters. *J. Biol. Chem.* **1975**, *250* (8), 3001–3009.

Klotz, I. M.; Hunston, D. L. Protein Affinities for Small Molecules: Conceptions and Misconceptions. *Arch. Biochem. Biophys.* **1979**, *193* (2), 314–328.

Knudson, G.; Nimrod, D. Exact Equation for Calculating Titration Curves for Dibasic Salts. *J. Chem. Educ.* **1997**, *54* (8), 351.

Kolthoff, I. M.; Rosenblum, C. *Acid-Base Indicators*; Macmillan: New York, 1937; p 25.

Kościelniak, P.; Michalowski, T. An Error Mercurimetric Titration of Chloride in Presence of Sodium Nitroprusside as Indicator. *Chem. Anal.* **1986**, *31* (4), 665–668.

Kubista, M.; Nygren, J.; Elbergali, A.; Sjöback, R. Making Reference Samples Redundant. *Crit. Rev. Anal. Chem.* **1999**, *29* (1), 1–28.

Küster, F. W. *Rechentafeln für die Chemische Analytik*; Walter de Gruyter: Berlin, 1982.

Lahav, O.; Morgan, B. E. Review. Titration Methodologies for Monitoring of Anaerobic Digestion in Developing Countries—A Review. *J. Chem. Technol. Biotechnol*. **2004**, 79 (12), 1331–1341.

Lahav, O.; Shlafman, E.; Cochva, M. Determination of Low Citric Acid Concentrations in a Mixture of Weak Acid/Bases. *Water SA* **2005**, *31* (4), 497–502.

Lambert, W. J. BUFCALC: A Program for the Calculation of Buffers of Specified pH, Ionic Strength and Buffer Capacity. *J. Chem. Educ.* **1990**, *67* (2). 150–153.

Lambert, W. J.; Dalga, R. J. Potentiometric Determination of Thermodynamic and Apparent Dissociation Constants by Nonlinear Least Squares Fitting. *Drug Dev. Ind. Pharm.* **1990**, *16* (4), 719–737.

Lang, W.; Meier, N. Calculation of the pH and the Titratable Acidity in Clinically Used Infusion Solutions. *Comput. Methods Programs Biomed.* **2007**, *87* (2), 160–169.

Lenoir, T.; Manceau, A. Number of Independent Parameters in the Potentiometric Titration of Humic Substances. *Langmuir* **2010**, *26* (6), 3898–4003.

Levene, P. A.; Bass, L. W. The Effect of Ionization upon Optical Rotation. III. Relations in the 2,5-Anhydro Sugar Acids. *J. Biol. Chem.* **1927**, *74* (3), 727–737.

Lewis, S. D.; Johnson, F. A.; Shafer, J. A. Potentiometric Determination of Ionisations at the Active Site of Papain. *Biochemistry* **1976**, *15* (23), 5009–5017.

Lewis, S. D.; Misra, D. C.; Shafer, J. A. Determination of Interactive Thiol Ionizations in Bovine Serum Albumin, Glutathione, and Other Thiols by Potentiometric Difference Titration. *Biochemistry* **1980**, *19* (26), 6129–6137.

Li, J.; Tang, H. A Theoretical Calculation Model for the Acidification Capacity of Natural Waters. *Sci. Total Environ*. **1998**, *212* (2), 163–172.

Liu, Q.; Li, X.; Sommer, S. S. pK-Matched Running Buffers for Gel Electrophoresis. *Anal. Biochem.* **1999**, *270* (1), 112–122.

Lucho, A. M. S.; Panteleimonov, A. V.; Kholin, Y. V.; Gushikem, Y. Simulation of Adsorption Equilibria on Hybrid Materials: Binding of Metal Chlorides with 3-N-Propylpyridinium Silsesquioxane Chloride Ion Exchanger. *J. Colloid Interface Sci.* **2007**, *310* (1), 47–56.

Luff, R.; Haeckel, M.; Wallmann, K. Robust and Fast FORTRAN and MATLAB Libraries to Calculate pH Distribution in Marine Systems. *Comput. Geosci.* **2001**, *27* (2), 157–169.

Maccà, C. Uptake and loss of carbon dioxide in volumetric analysis. *J. Chem. Educ.* **1986**, *63* (8), 691–693.

Maccà, C. The Formulation of the Electron and Proton Balance Equations for Solving Complicated Equilibrium Problems on Redox Titrations. *Fresenius' J. Anal. Chem.* **1997**, *357* (2), 229–232.

Martell, A. E.; Motekaitis, R. J. *The Determination and Use of Stability Constants*, 2nd ed.; VCH Publishers: New York, 1992.

Maslarska, V.; Tencheva, J.; Budevsky, O. New Approach in the Treatment of Data from an Acid-Base Potentiometric Titration. *Anal. Bioanal. Chem.* **2003**, *375* (2), 217–222.

Mauk, A. G.; Scott, R. A. A Calculator Program for Determination of Phosphate Buffer Composition. *Comput. Chem.* **1981**, *5* (1), 67–69.

McMillan, G. K.; and Cameron, R. A. *Advanced pH Measurement and Control*, 3rd ed.; ISA: Research Triangle Park, N.C., 2004.

Meites, L.; Goldman, J. A. Theory of Titration Curves. Part I. The Location of Inflection Points on Acid-Base and Related Curves. *Anal. Chim. Acta* **1963**, *29*, 472–479; **1964**, *31*, 297.

Meloun, M.; Havel, J.; Högfeldt, E. *Computation of Solution Equilibria: A Guide to Methods in Potentiometry, Extraction and Spectrophotometry*; Ellis Horwood: Chichester, 1988.

Michalowski, T. Some Remarks on Acid-Base Titration Curves. *Chem. Anal.* **1981**, *26* (5), 799–813.

Michalowski, T. An Error of Liebig-Deniges Method of Determination of the Cyanide. *Chem. Anal.* **1983**, *28* (3), 313–315.

Michałowski, T. Possibilities of Application of Some New Algorithms for Standardisation Purposes. Standardisation of Sodium Hydroxide against Commercial Potassium Hydrogen Phthalate. *Analyst* **1988a**, *113* (5), 833–835.

Michalowski, T. Titration of Monoprotic Acids with Sodium Hydroxide Contaminated by Sodium Carbonate. *J. Chem. Educ.* **1988b**, *65* (2), 181–182.

Michałowski, T. Potentiometric Titrations in Acid-Base Systems; An Overview of Methods Involved. *Prace Chem.* **1989**, *32*, 15–45. (In Polish).

Michałowski, T. Some Remarks Related to Determination of Free Acids in Presence of Hydrolysable Salts. *Chem. Anal.* (Warsaw) **1990**, *35* (4–5), 375–390.

Michałowski, T. Some New Algorithms Applicable to Potentiometric Titration in Acid-Base Systems. *Talanta* **1992**, *39* (9), 1127–1137.

Michałowski, T. *Calculations in Analytical Chemistry with Elements of Computer Programming*; PK: Cracow: 2001.

Michałowski, T. The Generalized Approach to Electrolytic Systems. I. Physicochemical and Analytical Implications. *Crit. Rev. Anal. Chem.* **2010**, *40* (1), 2–16.

Michałowski, T; Gibas, E. Applicability of New Algorithms for Determination of Acids, Bases, Salts and Their Mixtures. *Talanta* **1994**, *41* (8), 1311–1317.

Michałowski, T.; Lesiak, A. Formulation of Generalized Equations for Redox Titration Curves. *Chem. Anal.* (Warsaw) **1994**, *39* (5), 623–637.

Michałowski, T.; Parczewski, A. A New Definition of Buffer Capacity. *Chem. Anal.* **1978**, *23* (6), 959–964.

Michalowski, T.; Stępak, R. Evaluation of the Equivalence Point in Potentiometric Titrations with Application to Traces of Chloride. *Anal. Chim. Acta* **1985**, *172*, 207–214.

Michałowski, T.; Toporek, M. New Concepts of Alkalinity and Acidity of Natural Waters; paper presented at Conference of PTCh and SIiTPChem., Lublin, Sept. 15–18, 2003a; section S6.

Michałowski, T.; Toporek, M. Towards Correct Definition of Alkalinity and Acidity of Natural Waters; 2nd Conference "Chemometrics—Methods and Applications," Zakopane, Oct, 16–19, 2003b; p 420–426.

Michałowski, T.; Rokosz, A.; Tomsia, A. Determination of Basic Impurities in Mixture of Hydrolysable Salts. *Analyst* **1987**, *112* (12), 1739–1741.

Michałowski, T.; Rokosz, A.; Negrusz-Szczęsna, E. Use of Padé Approximants in the Processing of pH Titration Data. Determination of the Parameters Involved in the Titration of Acetic Acid. *Analyst* **1988**, *113* (6), 969–972.

Michałowski, T.; Rokosz, A.; Kościelniak, P.; Łagan, J. M.; Mrozek, J. Calculation of Concentrations of Hydrochloric and Citric Acids Together in Mixture with Hydrolysable Salts. *Analyst* **1989**, *114* (12), 1689–1692.

Michałowski, T.; Rokosz, A.; Zachara, M. Conventional Method of Determination of Aminoacetic Acid by pH-metric Titration. *Chem. Anal.* (Warsaw) **1994**, *39* (2), 217–222.

Michałowski, T.; Rokosz, A.; Gibas, E. Standardization of Sodium Hydroxide against Tartaric Acid by pH-metric Titration in Isomolar Systems. *Acta Chem. Polon.* **1995**, *37*, 143–149.

Michałowski, T.; Wajda, N.; Janecki, D. A Unified Quantitative Approach to Electrolytic Systems. *Chem. Anal.* (Warsaw) **1996**, *41* (4), 667–685.

Michałowski, T.; Baterowicz, A.; Wójtowicz, A. Sources of Error in β-Correction Spectrophotometry. *Talanta* **2000**, *52* (2), 337–340.

Michałowski, T.; Rymanowski, M.; Pietrzyk, A.; Toporek, M. The Generalised Buffer Capacity (GBC) Concept Referred to All Types of Equilibria Joined in Electrolytic Systems. In *European Variety in Chemistry Education, Book of Abstracts*, Kraków, July 4–7, 2005; Faculty of Chemistry, Jagiellonian University: Krakow, 2005a; pp 167–169. Available at http://www.chemia.uj.edu.pl/∼eurovariety/pdf/bookofabstracts.pdf

Michalowski, T.; Toporek, M.; Rymanowski, M. Overview on the Gran and Other Linearization Methods Applied in Titrimetric Analysis. *Talanta* **2005b**, *65* (5), 1241–1253.

Michałowski, T.; Rymanowski, M.; Pietrzyk A. Nontypical Bronsted Acids and Bases. *J. Chem. Educ.* **2005c**, *82* (3), 470–472.

Michalowski, T.; Toporek, M.; Rymanowski, M. pH-Static Titration: A Quasistatic Approach. *J. Chem. Educ*. **2007**, *84* (1), 142–150.

Michałowski, T.; Kupiec, K.; Rymanowski, M. Numerical Analysis of the Gran Methods. *Anal. Chim. Acta* **2008**, *606* (2), 172–183.

Michałowski, T.; Młodzianowski, J.; Pilarski, B. Applicability of Simms Constants in Formulation of Buffer Capacity and Alkalinity; paper presented at Conference of PTCh and SIiTPChem., Łódź, Poland, Sept. 12–16, 2009; PC-07-31, 52.

Michałowski, T.; Pietrzyk, A.; Ponikvar-Svet, M.; Rymanowski, M. The Generalized Approach to Electrolytic Systems: II. The Generalized Equivalent Mass (GEM) Concept. *Crit. Rev. Anal. Chem.* **2010a**, *40* (1), 17–29.

Michalowski, T.; Pilarski, B.; Dobkowska, A.; Mlodzianowski, J. Mathematical Modeling and Physicochemical Studies on Acid-Base Equilibria in Binary-Solvent Systems. *Wiadomości Chem.* **2010b**, *54* (1–2), 124–154.

Michałowski, T.; Pilarski, B.; Asuero, A. G.; Dobkowska, A. A New Sensitive Method of Dissociation Constants Determination Based on the Isohydric Solutions Principle. *Talanta* **2010c**, *82* (5), 1965–1973.

Michałowski, T.; Pilarski, B.; Ponikar–Svet, M.; Asuero, A. G.; Kukwa, A.; Michałowski, J., New methods applicable for calibration of indicator electrodes. *Talanta*, **2011**, *83* (5), 1530–1537.

Michałowski, T.; Pilarski, B.; Asuero, A. G.; Dobkowska, A.; Młodzianowski, J. Compact Approach to Carbonate Alkalinity; In preparation.

Miller, G. L.; Golder, R. H. Buffer of pH 2 to 12 for Use in Electrophoresis. *Arch. Biochem. Biophys.* **1950**, *23*, 420–423.

Millero, F. J.; Zhang, J.-Z.; Lee, K.; Campbell, D. M. Titration Alkalinity of Seawater. *Mar. Chem.* **1993**, *44* (2–4), 153–165.

Millero, F. J.; Lee, K.; Roche, M. Distribution of Alkalinity in the Surface Waters of the Major Oceans. *Mar. Chem.* **1998**, *60* (1), 111–130.

Moisio, T.; Heikonen, M. A Titration Method for Silage Assessment. *Animal Feed Sci. Technol.* **1989**, *22* (4), 341–353.

Moisio, T.; Heikonen, M. Lactic Acid Fermentation in Silage Preserved with Formic Acid. *Animal Feed Sci. Technol.* **1994**, *47* (1), 107–124.

Moisio, T.; Heikonen, M. Expressions of the General Form of the Acid-Base Titration Curve. *Fresenius' J. Anal. Chem.* **1996a**, *356* (7), 461–462.

Moisio, T.; Heikonen, M. A Simple Method for the Titration of Multicomponent Acid-Base Mixtures. *Fresenius J. Anal. Chem.* **1996b**, *354* (3), 271–277.

Mongay, C.; Cerda, V. A Britton-Robinson Buffer of Known Ionic Stregth. *Ann. Chim.* (Rome) **1974**, *64* (5–6), 409–412.

Mongay, C.; Cerda, V. A Generalized Calculation for Preparation of Buffer Solutions of Known Ionic Strength. *Comput. Chem.* **1984**, *8* (3), 213–216.

Morales, D. A. Mathematical Modeling of Titration Curves. *J. Chemom.* **2002**, *16* (5), 247–260.

Morel, F. M. M.; Hering, J. G. *Principles and Applications of Aquatic Chemistry*; Wiley: New York, 1993; p 517.

Morel, F.; McDuff, R. E.; Morgan, J. J. Theory of Interaction Intensities, Buffer Capacities, and pH Stability in Aqueous Systems, with Application to the pH of Seawater and a Heterogeneous Model Ocean System. *Mar. Chem.* **1976**, *4* (1), 1–28.

Moya-Hernández, R.; Rueda-Jackson, J. C.; Ramírez, M. T.; Vázquez, G. A.; Havel, J.; Rojas-Hernández, A. Statistical Study of Distribution Diagrams for Two-Component Systems: Relationships of Means and Variances of the Discrete Variable Distributions with Average Ligand Number and Intrinsic Buffer Capacity. *J. Chem. Educ.* **2002**, *79* (3), 389–392.

Mukhina, T. P.; Rudnaya, L. E.; Bugaevski, A. A. Calculation of Equilibrium in Complex Systems. 4. Estimation of Buffer Properties of System. *Zh. Anal. Khim.* **1970**, *25* (4), 640.

Muralt, A. L. The Titration Constants of Multivalent Substances. *J. Am. Chem. Soc.* **1930**, *52* (9), 3518–3523.

Neal, C. Alkalinity Measurements within Natural Waters: Towards a Standardised Approach. *Sci. Total Environ.* **2001**, *265* (1), 99–113.

Nguyen, M. K.; Kao, L.; Kurtz, I. Calculation of the Equilibrium pH in a Multiple-Buffered Aqueous Solution Based on Partitioning of Proton Buffering: A New Predictive Formula. *Am. J. Physiol. Renal Physiol.* **2009**, *296* (6), F1521–F1529.

Ni, Y. Simultaneous Determination of Mixtures of Acids by Potentiometric Titration. *Anal. Chim. Acta* **1998**, *367* (1–3), 145–152.

Norman, S.; Maeder, M. Model Based Analysis for Kinetics and Equilibrium Measurements. *Crit. Rev. Anal. Chem.* **2006**, *36* (3), 199–209.

Nowogrocki, G.; Canone, J.; Wozniak, M. Exploitation générale des neutralisation de melanges de protolytes. *Bull. Soc. Chim. Fr.* **1976**, (1–2), 5–14.

Nurchi, V.; Crisponi, G. Determination of Ionization Constants of a Polyprotic Acid Mixture with Use of Least Squares Method. *Anal. Chim. Acta* **1989**, *222* (1), 359–367.

Okamoto, K. H.; Mori, K.; Ohtsuka, K.; Ohuchi, H.; and Ishii, H. Theory and Computer Programs for Calculating Solution pH, Buffer Formula, and Buffer Capacity for Multiple Component System at a Given Ionic Strength and Temperature. *Pharm. Res.* **1997**, *14* (3), 299–302.

Olin, A.; Wallen, B. A Note on the Calculation of Acid-Base Titration Curves and Their Equivalence Points. *Talanta* **1978**, *25*, (11–12), 720–721.

Oliveira, A. F.; de Souza Silva, A. F.; Tenan, M. A.; Olivo, S. L. TITGER, Una planilha electronica para simulaçao de titulaçao de mistura de compostos poliproticos. *Quim. Nova* **2007**, *30* (1), 224–228.

Onufriev, A.; Case, D. A.; Ullmann, G. M. A Novel View of pH Titration in Biomolecules. *Biochemistry* **2001**, *40*, 3414–3419.

Opanasenko, V. K.; Gerts, S. M.; Makarov, A. D. Buffer Capacity of Polyproton Substances. *Biochemistry (Moscow)* **1978**, *43* (8), 1068–1076.

Ostling, S.; Virtama, P. A Modified Preparation of the Universal Buffer Described by Teorell and Stehagen. *Acta Physiol. Scand.* **1946**, *11* (4), 289–293.

Papanastasiou, G; Kokkinidis, G. Development of Iterative Methods for the Exact Determination of Acid Dissociation Constants and Specific Reaction Rates in Various Ionic or Electrochemical Systems. A Review. *Collect. Czech. Chem. Commun.* **2003**, *68* (8), 1345–1378.

Paxéus, N.; Wedborg, M. Acid-Base Properties of Aquatic Fulvic Acid. *Anal. Chim. Acta* **1985**, *169*, 87–98.

Pehrsson, L.; Ingman, F.; Johansson, A. Acid-Base Titration by Stepwise Addition of Equal Volumes of Titrant with Special Reference to Automatic Titrations. II. Theory of Titration of Mixtures of Acids, Polyprotic Acids, Acids in Mixture with Weak Bases, and Ampholytes. *Talanta* **1976**, *23* (11–12), 781–788.

Perrin, D. D. Buffers of Low Ionic Strength for Spectrophotometric pK_a Determination. *Aust. J. Chem.* **1963**, *16* (4), 572–578.

Perrin, D. D.; Dempsey, B. *Buffers for pH and Metal Ion Control*; Chapman and Hall: London, 1979.

Persat, A.; Chambers, R. D.; Santiago, J. G. Basic Principles of Electrolyte Chemistry for Microfluidic Electrokinetics. Part I. Acid-Base Equilibria and pH Buffers. *Lab Chip* **2009a**, *9* (17), 2437–2453.

Persat, A.; Susi, M. E.; Santiago, J. G. Basic Principles of Electrolyte Chemistry for Microfluidic Electrokinetics. Part II. Coupling between Ion Mobility, Electrolysis, and Acid-Base Equilibria. *Lab Chip* **2009b**, *9* (17), 2454–2469.

Pertusatti, J.; Prado, A. G. Buffer Capacity of Humic Acid: Thermodynamic Approach. *J. Colloid Interface Sci.* **2007**, *314* (2), 484–489.

Pfendt, L. B. Two Phase Liquid and Solid-Liquid pH Buffers Based on Solubility Equilibria: Theoretical Considerations. *Analyst* **1995**, *120*, 2129–2144.

Pilarski, B.; Dobkowska, A.; Foks, H.; Michałowski, T. Modelling of Acid-Base Equilibria in Binary-Solvent Systems: A Comparative Study. *Talanta* **2010**, *80* (3), 1073–1080.

Poncelet, D. ; Pauss, A. ; Naveau, H.; Frere, J.-M.; Nyns, E.-J. Computation of Physicochemical Parameters, inter Alia pH in Complex (Bio)chemical Systems. *Anal. Biochem.* **1985**, *150* (2), 421–428.

Ponikvar, M.; Michałowski, T.; Kupiec, K.; Wybraniec, S.; Rymanowski, M. Experimental Verification of the Modified Gran Methods Applicable to Redox Systems, *Anal. Chim. Acta* **2008**, *628* (2), 181–189

Pons, M.-N.; Greffe, J.-L.; Bordet, J. Fast pH Calculations in Aqueous Solution Chemistry. *Talanta* **1983**, *30* (3), 205–208.

Porter, M. G.; Steen, R. W. J.; Kilpatrick, D. J.; Gordon, F. J.; Mayne, C. S.; Poots, R. E.; Unsworth, E. F.; Pippard, C. J. Electrometric Titration as a Method of Predicting the Chemical Composition and Corrected Dry Matter Concentration of Silage. *Animal Feed Sci. Technol.* **1995**, *56* (4), 217–220.

Povar, I. G. Buffer Properties of Heterogeneous Systems Containing Sparingly Soluble Acids and Metal Hydroxides. *Zh. Neorgan. Khim.* **1996**, *41* (7), 1220–1224.

Povar, I. G. Buffering Properties of Heterogeneous Water Salt Systems in Relation to the Components of a Low Solubility Precipitate. *Russ. J. Inorg. Chem.* **2000**, *45* (10), 1632–1636.

Prideaux, E. B. R. Use of Partly Neutralised Mixtures of Acids as Hydrion Regulators. *Proc. R. Soc. Lond.* **1916**, *92A*, 463–468.

Prideaux, E. B. R. *The Theory and Use of Indicators. An Account of the Chemical Equilibria of Acids, Alkalies and Indicators in Aqueous Solution, with Applications*; Constable & Company: London, 1917.

Prideaux, E. B. R.; Ward, A. T. Calculations on the Neutralisation of Mixtures of Acids, and a Universal Buffer Mixture. *J. Chem. Soc.* **1924**, 416–429.

Purdue, E. M.; Reuter, J. H.; Parrish, R. S. A Statistical Model of Proton Binding by Humus. *Geochim. Cosmochim. Acta* **1984**, *48* (6), 1257–1263.

Qiang, Z.; Adams, C. Potentiometric Determination of Acid Dissociation Constants (pKa) for Human and Veterinary Antibiotics. *Water Res.* **2004**, *38* (12), 2874–2890.

Ramette, R. W. *Chemical Equilibrium and Analysis*; Addison-Wesley: Reading, Mass., 1981.

Ramette, R. W. The Acid-Base Package—A Collection of Useful Programs for Proton-Transfer Systems. *J. Chem. Educ.* **1989**, *66* (10), 830.

Ramette, R. W. Titrate—A Learning Tool for Acid-Base Titrations. *J. Chem. Educ.* **1994**, *71* (3), 238–239.

Ramette, R. W. Buffer Plus. *J. Chem. Educ.* **1998**, *75* (11) 504

Ramette, R. W.; Holmes, J. L. The Acid-Base Package. *J. Chem. Educ.* **1992**, *69* (12), 1010.

Ramis Ramos, G.; García Alvarez-Coque, M. C. G.; Villanueva Camañas, R. M.;. Mongay Fernández, C. On the Preparation of Simple and Universal Buffers Including Polynuclear Species. *Microchim. Acta* **1986**, *88*, 115–121.

Ramis Ramos, G.; García Alvarez-Coque, M. C. Examination of the Least Squares Method Applied to the Evaluation of Physicochemical Linearized Equations. *Anal. Chim. Acta* **1989**, *220*, 145–153.

Ranaghan, M. J. *Buffer Bench. Buffer Theory and User's Manual*; http://chembio.uconn.edu/Files/Buffer%20Bench/BB_manual.pdf

Ratner, S.; Petrac, B.; Rochovansky, O. Biosynthesis of Urea. V. Isolation and Properties of Argininosuccinic Acid. *J. Biol. Chem.* **1953**, *204* (1), 95–113.

Rees, S. E.; Andreassen, S.; Hovorka, R.; Summers, R.; Carson, E. R. Acid-Base Chemistry of the Blood—A General Model. *Comput. Methods Programs Biomed.* **1996**, *51* (1–2), 107–119.

Reinhardt, H. Ionization in Diprotic Acids. *SIAM Rev.* **1983**, *25* (1), 89–91.

Ricci, J. E. *Hydrogen Ion Concentration. New Concepts in a Systematic Treatment*; Princeton University Press: Princeton, 1952.

Righetti, P. G.; Facio, M.; Tonani, C.; Gianazza, E.; Celentano, F. C. pH Gradients Generated by Polyprotic Buffers. II. Experimental Validation. *J. Biochem. Biophys. Methods* **1988**, *16* (2–3), 129–140.

Rilbe, H. On the Use of Dimension-Less Parameter in Acid-Base Theory. II. The Molar Buffer Capacities of Bivalent Weak Acids and Bases. *Electrophoresis* **1993**, *14* (1), 202–204.

Rilbe, H. On the Use of Dimensionless Parameters in Acid-Base Theory VI. The Buffer Capacities of Equimolecular Mixtures of Monovalent Weak Protolytes as Compared to That of Bivalent Protolytes. *Electrophoresis* **1994**, *15* (5), 580–583.

Rilbe, H. *pH and Buffer Theory: A New Approach*; Wiley: New York, 1996.

Ring, T. Equilibrium or Non Equilibrium pH. *Am. J. Physiol. Renal Physiol.* **2010**, *298* (2), F 472–F473.

Roda, G.; Dallance, C.; Grazioso, G.; Liberti, V.; de Amia, M. Determination of Acid Dissociation Constants of Compounds Active at Neuronal Nicotinic Acetylcholine Receptors by Means of Electrophoretic and Potentiometric Tehniques. *Anal. Sci.* **2010**, *26* (1), 51–54.

Rojas-Hernández, A.; Ramirez-Silva, M. T. Modelo termodinámico general para curvas de valoración ácido-base de mezclas de sistemas poliácidos o polibásicos (sin polinucleación) con ácido o bases Fuertes. 2002 http://docencia.izt.uam.mx/arojas/214136_archivos/documentos/NotasARHyMTRS.pdf

Roos, A.; Boron, W. F. The Buffer Values of Weak Acids: Origin of the Concept, and First Mathematical Derivation and Application to Physicochemical Systems. The Work of M. Koppel and K. Spiro (1914). *Respir. Physiol.* **1980**, *40* (1), 1–32.

Rosset, R.; Bauer, D.; Desbarres, J. *Chimie Analytique de Solutions et Microinformatique*; Dunod: Paris, 1979.

Rosset, R.; Bauer, D.; Desbarres, J. *Chimie Analytique de Solutions et Informatique*, 2nd ed.; Masson: Paris, 1991.

Rounds, S. A.; Wilde, F. D. Alkalinity and Acid Neutralizing Capacity. In *National Field Manual for the Collection of Water-Quality Data*; F. D.; Radtke, D. B., Eds.; Techniques of Water-Resources Investigations of the United States Geological Survey, Book 9, Ch. 6.6; U.S. Dept. of the Interior, U.S. Geological Survey: Reston, VA., 2001; p. 50.

Roy, L. N.; Roy, R. N. Universal pH Scale Based on Experimental Studies of 20 Zwitterionic Buffer Compounds. *Abstracts of Papers of the American Chemical Society 231*, 2006; American Chemical Society: Washington, D. C., 2006; Meeting-Abstract 245-CHED.

Roy, R. N.; Roy, L. N.; Denton, C. E.; Dunseth, C. D.; Fuge, M. S.; Ashkenazi, S.; Durden, J. L.; Roy, C. N.; Wollen, J. T.; Hayden, S. M. Buffer Standards for the Physiological pH of the Zwitterionic Compound, HEPPSO from 5 to 55°C. *J. Solution Chem.* **2009**, *38* (11), 1417–1431.

Roy, L. N.; Roy, R. N.; Wollen, J. T.; Bwachi, A.; Stegner, J. M.; Downs, Z. M.; Mehrhoft, C. J.; Bodendorfer, B. M.; Allen, K. A.; Harmn, M. A.; Henson, I. B. 3-[4-(2-Hydroxyethyl)-1-Piperazinyl]Propanesulfonic Acid (HEPPS) and the pH of Its Buffer Solutions from (278.15 to 328.15) K. *J. Chem. Eng. Data* **2010**, *55* (3), 1327–1332.

Ryazanov, M. A.; Dudkin, B. N. The pK Spectroscopy Study of the Acid-Base Properties of Hydrated Aluminium Oxide Soils. *Colloid J.* **2004**, *66* (6), 807–810.

Sayago, A.; Asuero, A. G. Fitting Straight Lines with Replicated Observations by Linear Regression. Part II. Testing for Homogeneity of Variances. *Crit. Rev. Anal. Chem.* **2004**, *34* (3), 133–146.

Sayago, A.; Boccio, M.; Asuero, A. G. Fitting Straight Lines with Replicated Observations by Linear Regression. The Least Squares Postulates. *Crit. Rev. Anal. Chem.* **2004**, *34* (1), 39–50.

Schmitt, B. M. The Quantitation of Buffering Action I. A Formal & General Approach. *Theor. Biol. Med. Model.* **2005a**, *2* (8); doi: 10.1186/1742-4682-2-8.

Schmitt, B. M. The Quantitation of Buffering Action II. Applications of the Formal General Approach. *Theor. Biol. Med. Model.* **2005b**, *2* (9); doi: 10.1186/1742-4682-2-9.

Shamsipur, M.; Hemmateenejad, B.; Akhoud, M. Multicomponent Acid-Base Titration by Principal Component-Artificial Neural Network Calibration. *Anal. Chim. Acta* **2002**, *461* (1), 147–153.

Shibuya, N.; Goldstein, I. J.; Shafer, J. A.; Peumans, W. J.; Broekaert, W. F. Carbohydrate Binding Properties of the Stinging Nettle (Urtica doica) Rhizome Lectin. *Arch. Biochem. Biophys.* **1986**, *249* (1), 215–224.

Simms, H. S. Dissociation of Polyvalent Substances I. Relation of Constants to Titration Data. *J. Am. Chem. Soc.* **1926a**, *48* (5), 1239–1250.

Simms, H. S. Dissociation of Polyvalent Substances. II. Relation of Constants to Chemical Structure. *J. Am. Chem. Soc.* **1926b**, *48* (5), 1251–1261.

Simms, H. S.; Levene, P. A. Graphical Interpretation of Electrometric Titration Data by Use of Comparison Curves. *J. Biol. Chem.* **1927**, *70* (2), 319–325.

Skoog, D. A.; West, D. M.; Holler, F. J.; Crouch, S. R. *Fundamentals of Analytical Chemistry*, 8th ed.; Brooks/Cole: New York, 2003.

Smith, T. B. *Analytical Processes,* 2nd ed.; Edward Arnold: London, 1952.

Stairs, R. A. Unified Calculation of Titration Curves. *J. Chem. Educ.* **1978**, *55* (2), 99.

Stewart, P. A. Modern Quantitative Acid-Base Chemistry. *Can. J. Physiol. Pharmacol.* **1983**, *61* (12), 1444–1461.

Stigliani, W. M. Buffering Capacity: Its Relevance in Soil and Water Pollution. *New J. Chem.* **1996**, *20* (2), 205–210.

Still, E.; Sara, R. Calculation of Potentiometric Titration Curves. The Master Variable Concept. *J. Chem. Educ.* **1977**, *54* (6), 348–351.

Stoll, V. S.; Blanchard, J. S. Buffers: Principles and Practice. *Methods Enzymol.* **1990**, *182*, 24–38.

Stoyanov, A. V.; Righetti, P. G. Ampholyte Dissociation Theory and Properties of Ampholyte Aqueous Solution. *Electrophoresis* **1997**, *18* (11), 1944–1950.

Stoyanov, A. V.; Righetti, P. G. Can Amphoteric Substances with Very Small (Or Negative) ΔPk Difference Exist and What Properties Would Their Water Solutions Exhibit? *Electrophoresis* **1998**, *19* (2), 187–191.

Stoyanov, A. V.; Righetti, P. G. Dissociation of Polyvalent Electrolytes. *J. Chromatogr. A* **1999**, *853* (1), 35–44.

Stumm, W.; Morgan, J. J. *Aquatic Chemistry: Chemical Equilibria and Rates in Natural Waters*, 3rd ed.; Wiley: New York, 1996.

Subirats, S.; Bosch, E.; Roses, M. Buffer Considerations for LC and LC-MS. *LC GC N. Am.* **2009**, *27* (11), 1000–1004.

Subirats, X.; Roses, R.; Bosch, E. On the Effect of Organic Solvent Composition on the pH buffered HPLC Mobile Phases and the pK_a of Analytes—A Review. *Sep. Purif. Rev.* **2010**, *36* (3), 231–255.

Svehla, G. *Automatic Potentiometric Titrations*; Pergamon Press: Oxford, 1978.

Szakács, Z.; Noszal, B. Protonation Microequilibrium Treatment of Polybasic Compounds with Any Possible Symmetry. *J. Math. Chem.* **1999**, *26* (1–3), 139–155.

Szakás, Z.; Beni, S.; Varga, Z.; Orfi, L.; Keri, G.; Noszal, B. Acid-Base Profiling of Imatinib (Gleevec) and Its Fragments. *J. Med. Chem.* **2005**, *48* (1), 249–255.

Taha, M. Buffers for the Physiological pH range: Acidid Dissociation Constants of Zwitterionic Compounds in Various Hydroorganic Media. *Ann. Chim.* **2005**, *95* (1–2), 105–109.

Tam, K. Y. BUFMAKE: A Computer Program to Calculate the Composition of Buffers of Defined Buffer Capacity and Ionic Strength for Ultra-Violet Spectrophotometry. *Comput. Chem.* **1999**, *23* (5), 415–419.

Thomas, J. D. R. Mixed-Ligand Ion Buffers for Calibrating Ion Selective Electrode at Trace Levels. *Philos. Trans. R. Soc. Lond. A* **1990**, *333* (1628), 163.

Thomson, B. M.; Kessick, M. A. On the Preparation of Buffer Solutions. *J. Chem. Educ.* **1981**, *58* (9), 743–746.

Toporek, M.; Pietrzyk, A.; Rymanowski, M.; Asuero, A. G.; Michalowski, T. Principles of Computer Programming as Applied to Simulated pH-Static Titration of Cyanide According to a Modified Liebig-Deniges Method. Submitted.

Totsche, O.; Fyson, A.; Kalin, M.; Steinberg, C. E. W. Titration Curves. A Useful Instrument for Assessing the Buffer Systems of Acidic Mining Waters. *Environ. Sci. Pollut. Res.* **2006**, *13* (4), 215–224.

Trojanowicz, M. Buffer for Fluoride Electrode Calibration in the Low Concentration Range. *Talanta* **1979**, *26* (10), 985–986.

Ullmann, G. M. Relations between Protonation Constants and Titration Curves in Polyprotic Acids: A Critical View. *J. Phys. Chem. B* **2003**, *107* (5), 1263–1271.

Urbansky, E. T.; Schock, M. R. Understanding, Deriving, and Computing Buffer Capacity. *J. Chem. Educ.* **2000**, *77* (12), 1640–1644.

Ure, A. M.; Davidson, C. M., Eds. *Chemical Speciation in the Environment*, 2nd ed.; Wiley: Chichester, 2002.

Van de Steene, M.; van Vooren, L.; Ottoy, J.-P.; Vanrolleghem, P. A. Automatic Buffer Capacity Model Building for Advanced Interpretation of Titration Curves. *Environ. Sci. Technol.* **2002**, *36* (4), 715–723.

Van der Houwen, O. A. G. J.; Beijen, J. H.; Bult, A.; Underberg, W. J. M. A General Approach to the Interpretation of pH Buffer Catalyzed Degradation Profiles. *Int. J. Pharm.* **1994**, *109* (3), 191–196.

Van Hulle, S. W. H.; De Meyer, S.; Vermeiren, T. J. L.; Vergote, A.; Hogie, J.; P. Dejans, P. Practical Application and Statistical Analysis of Titrimetric Monitoring of Water and Sludge Samples. *Water SA* **2009**, *35* (3), 329–333.

Van Slyke, D. D. On the Measurement of the Buffer Values and on the Relationship of Buffer Value to the Dissociation Constant of the Buffer and the Concentration and Reaction of the Buffer Solution. *J. Biol. Chem.* **1922**, *52* (2), 525–570.

Van Vooren, L.; Van de Steene, M.; Ottoy, J.-P.; Vanrolleghem, P. A. Automatic Buffer Capacity Model Building for the Purpose of Water Quality Monitoring. *Water Sci. Technol.* **2001**, *43* (7), 105–113.

VAXA Software, ABEW – Acid base equilibrium for Windows; http://www.vaxasoftware.com/soft_eduen/abew.html

Vershinin, V. I. Calculation of the Extent of Reactions at the Equivalence Point and the Use of These Calculations in Titrimetric Analysis. *J. Anal. Chem.* **2003**, *58* (11), 1012–1017.

Vesala, A. Estimation of Carbonate Content of Base by Gran Method. *J. Chem. Educ.* **1992**, *69* (7), 577–578.

Vershinin, V. I.; Kukin, G. P. Change in the Extent of a Reaction during Titration. *J. Anal. Chem.* **2004**, *59* (2), 107–113.

Wänninen, E. Logarithmic Diagrams in Acid-Base Titrations and Estimation of Titration Errors. *Talanta* **1980**, *27* (1), 29–32.

Waser, J. Acid-Base Titration and Distribution Curves. *J. Chem. Educ.* **1967**, *44* (5), 274–276.

Weiss, J. N. The Hill Equation Revisited: Uses and Misuses, *FASEB J.* **1997**, *11* (11), 835–841

Wiczling, P.; Waszczuk-Jankowska, M.; Markuszewski, M. J.; Kaliszan, R. The Application of Gradient Reverse-Phase High Performance Liquid Chromatography to the pK_a and log K_w Determination of Polyprotic Analytes. *J. Chromatogr. A* **2008**, *1214* (1–2), 109–114.

Willis, C. J. Another Approach to Titration Curves. Which Is the Dependent Variable? *J. Chem. Educ.* **1981**, *58* (8), 659–663.

Wollen, J. T.; Dunseth, C. D.; Roy, R. N.; Roy, L. N. Universal pH Scale Based on Experimental Study of Zwitterionic Buffer Compounds BICINE and TRICINE at 25 and 37°C for I=0.16 Mol Kg^{-1}. General Poster Session III, American Chemical Society, Midwest Regional Meeting, Kansas City, Mo., November 7–10, 2007

Wooten, E. W. Science Review: Quantitative Acid-Base Physiology Using the Stewart Model. *Crit. Care* **2004**, *8* (6), 448–452.

Wooten, E. W. A New Predictive Formula for Calculation of Equilibrium pH: A Step Back in Time. *Am. J. Physiol. Renal Physiol.* **2010**, *298* (2), F471.

Wozniak, M. *Approfondissement des methods potentiometriques: proprietes acides et complexantes des acides phosphoniques et aminophosphoniques*. These, L'Université des Sciences et Techniques de Lille, 1977.

Wozniak, M.; Nowogrocki, G. An Arbitrary Correction Function for CO_2 Evolution in Acid-Base Titrations and Its Use in Multiparametric Refinement of Data. *Talanta* **1981**, *28* (8), 575–583.

Zaher, U. E.; Vanrolleghem, P. A. Automatic Initialisation of Buffer Composition Estimation for On-Line Analysis of Unknown Buffer Solutions. *Anal. Bioanal. Chem.* **2005**, *383* (4), 605–618.

Zaher, U.; Vanrolleghem, P. A. General Ion Recruiting Procedure for pH-Based Calculations. *Environ. Model. Softw.* **2006**, *21* (5), 739–743.

Zeebe, R. E.; Wolf-Gladrox, D. *CO_2 in Seawater: Equilibrium, Kinetics, Isotopes*; Elsevier: Amsterdam, 2001.

Zevatskii, Y. E.; Samailov, D. V.; Mchedlov-Petrosyan, N. O. Contemporary Methods for the Experimental Determination of Dissociation Constants f Organic Acids in Solution. *Russ. J. Gen. Chem.* **2009**, *79* (9), 1859–1889.

Zhan, X.; Li, C.; Li, Z.; Yang, X.; Zhong, S.; Yi, T. Highly Accurate Nephelometric Titrimetry. *J. Pharm. Sci.* **2004**, *93* (2), 441–448.

Zhang, Y.; Dawe, R. Effect of Organic Acids on the Determination of Carbonate Species in Solutions. *Anal. Chim. Acta* **1996**, *318* (2), 239–249.

Zhang, C.-L.; Narusawa, Y. A New Titration Method Based on Concentration-Variable Patterns. Principles and Applications to Acid-Base and Redox Titrations. *Bull. Chem. Soc. Jpn.* **1997**, *70* (3), 593–600.

Zhu, Z. Simultaneous Determination of Mixtures of Organic Acids or Bases Based on the Differences in the Titration Spectra. *Chemom. Intell. Lab. Syst.* **1999**, *45* (1), 185–190.

APPENDIX A

Adding the sides of the equalities:

$$\alpha + \sum_{k=1}^{P}\sum_{j=0}^{q_k}(j-n_k)\cdot[H_jL_{(k)}^{+j-n_k}] + \sum_{k=P+1}^{R}\sum_{j=0}^{q_k}(j-n_k)\cdot[H_jL_{(k)}^{+j-n_k}] + \sum_{k=R+1}^{Q}\sum_{j=0}^{q_k}(u_k-j)\cdot[Me_{(k)}(OH)_j^{+u_k-j}]+[M^+]-[B^-]=0$$

$$[B^-] = \frac{1}{V_0+V}\cdot\left(\sum_{k=P+1}^{R} m_k\cdot C_{0k}V_0 + \sum_{k=R+1}^{Q} m_k\cdot C_{0k}V_0 + C_aV_0 + CV\right)$$

$$\frac{1}{V_0+V}\cdot\left(\sum_{k=1}^{P} m_k\cdot C_{0k}V_0 + C_bV_0\right) = [M^+]$$

$$\sum_{k=1}^{P}\sum_{j=0}^{q_k} m_k\cdot[H_jL_{(k)}^{+j-n_k}] = \sum_{k=1}^{P} m_k\cdot\frac{C_{0k}V_0}{V_0+V}$$

$$\sum_{k=P+1}^{R} m_k\cdot\frac{C_{0k}V_0}{V_0+V} = \sum_{k=P+1}^{R}\sum_{j=0}^{q_k} m_k\cdot[H_jL_{(k)}^{+j-n_k}]$$

$$\sum_{k=R+1}^{Q}\frac{m_kC_{0k}V_0}{V_0+V} = \sum_{k=R+1}^{Q}\sum_{j=0}^{q_k} m_k[Me_{(k)}(OH)_j^{+u_k-j}]$$

obtained on the basis of Equation [109] and canceling similar terms, we get the relation

$$\alpha + \sum_{k=1}^{P}\sum_{j=0}^{q_k}(j-n_k+m_k)\cdot[H_jL_{(k)}^{+j-n_k}] + \sum_{k=P+1}^{R}\sum_{j=0}^{q_k}(j-n_k-m_k)\cdot[H_jL_{(k)}^{+j-n_k}] + \sum_{k=R+1}^{Q}\sum_{j=0}^{q_k}(u_k-j-m_k)\cdot[Me_{(k)}(OH)_j^{+u_k-j}] = \frac{C\cdot V-\Delta\cdot V_0}{V_0+V}$$

$$CV/V_0-(1+V/V_0)\cdot\alpha = \sum_{k=1}^{P}(\bar{n}_k+m_k-n_k)\cdot C_{0k} + \sum_{k=P+1}^{R}(\bar{n}_k-m_k-n_k)\cdot C_{0k} + \sum_{k=R+1}^{Q}(u_k-\bar{n}_k^{\cdot}-m_k)\cdot C_{0k}+\Delta \qquad \text{[A-1]}$$

where Equations [10], [19], [38], and [40] were used. Applying the equalities [88] in [A-1], we get

$$CV/V_0-(1+V/V_0)\cdot\alpha = A-\left(\sum_{k=1}^{P}(q_k-\bar{n}_k)\cdot C_{0k} + \sum_{k=P+1}^{R}(q_k-\bar{n}_k)\cdot C_{0k} + \sum_{k=R+1}^{Q}\bar{n}_k^{\cdot}\cdot C_{0k}\right) \qquad \text{[A-2]}$$

where A is expressed by Equation [111]. Applying Equations [36] and [40] in [A-2], we get, by turns:

$$
\begin{aligned}
CV/V_0 - (1 + V/V_0) \cdot \alpha
&= A - \left(\sum_{k=1}^{P} (q_k - \bar{n}_k) \cdot C_{0k} + \sum_{k=P+1}^{R} (q_k - \bar{n}_k) \cdot C_{0k} \right. \\
&\quad \left. + \sum_{k=R+1}^{Q} \bar{n}_k^{\cdot} \cdot C_{0k} \right) \qquad \text{[A-3]}
\end{aligned}
$$

$$
\begin{aligned}
CV/V_0 - (1 + V/V_0) \cdot \alpha
&= A - \left(\sum_{k=1}^{P} \sum_{i=1}^{q_k} C_{0i} \cdot (1 + h/g_{ki}^{*})^{-1} \right. \\
&\quad + \sum_{k=P+1}^{R} \sum_{i=1}^{q_k} C_{0i} \cdot (1 + h/g_{ki}^{*})^{-1} \\
&\quad \left. + \sum_{k=R+1}^{Q} \sum_{i=1}^{q_k} C_{0i} \cdot (1 + h/g_{ki}^{*})^{-1} \right) \qquad \text{[A-4]}
\end{aligned}
$$