

## Computation of Physicochemical Parameters, inter alia, pH, in Complex (Bio)chemical Systems<sup>1</sup>

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Received February 11, 1985

Generic equations and algorithms are derived to compute, in complex (bio)chemical systems at equilibrium, the following physicochemical parameters: pH (or the concentration of any chemical species), partitions between acid and base forms, global charge, molar mean charges, ionic strength, and molar mean contributions to ionic strength. The model only requires the knowledge of existing thermodynamic constants and of the composition of the system in chemical species as the sum of the different forms other than the species under examination. It takes ionic strength aspects into consideration. Several innovations simplify the computation process: use of polyacidity constants, generalized expression of molar parameters, computation of global parameters from molar mean contributions, simplified corrections for activity, and easy iterative process for pH determination. The model always elicits a unique equilibrium state, namely, it always yields a unique pH value. Computed values always agreed with experimental measurements, thereby validating the model. Digital computer programs were prepared to use the proposed algorithms, which are also a very simple and easy way, compared to the available mathematical descriptions, to solve the problem "manually" without computer facilities. © 1985 Academic Press, Inc.

KEY WORDS: pH determination; computer methods; organic acids; polyacids.

One of the most important parameters in chemistry and biotechnology is pH. Curiously enough, although numerous reliable electrodes are available to measure pH, its prediction in complex systems generally requires complex mathematical descriptions (1, 2). When the number of acid-base species is large (more than three), the system of equations becomes apparently very difficult to handle and, with limited computer facilities, only approximate solutions can be obtained (see (3), p. 145).

This statement also applies to many other physicochemical parameters and becomes crucial when the latter cannot be directly measured as is most generally the case with

the partition of a species among its different forms.

This paper describes rational algorithms to compute, for any (bio)chemical system at equilibrium, state parameters such as pH (or the concentration of other chemical species), global charge, or ionic strength, and molar parameters, namely, the partition of a chemical species among its different forms and others which will be defined below.

### SYSTEMS, CHEMICAL SPECIES, AND FORMS

A closed system made of an aqueous solution is considered. "Chemical species,"  $s$  (or  $m$ ), are defined as individual species in solution. For example,  $\text{NaNO}_3$  is composed of two chemical species: sodium and nitrate ions,  $\text{Na}^+$  and  $\text{NO}_3^-$ . Chemical species may exist in different forms,  $H_iA$ , defined by the number of

<sup>1</sup> The authors wish to thank "Anjou Recherches," Maisons-Laffitte, France, for a PhD grant to A.P. and the "Institut pour l'Encouragement à la Recherche dans l'Industrie et l'Agriculture (IRSIA)" for a PhD grant to D.P.

protons.  $i$  (or  $j$ ). As yet, forms of chemical species are limited to their different acid–base forms. Chelates or complexes are not taken into consideration. For example, the maleate species is the sum of three forms: maleic acid, monohydrogenomaleate, and maleate.

### MONOACIDITY AND POLYACIDITY CONSTANTS

Two forms which differ by one proton are in equilibrium according to



The monoacidity constant,  $K(\ell)$ , related to the above equilibrium is

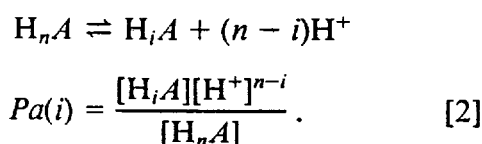
$$K(\ell) = \frac{[H_iA^{a-1}][H^+]}{[H_{i+1}A^a]} \quad [1]$$

where  $\ell = n - i$ ,  $n$  is the maximum number of protons of the given acid–base species and  $i$  can vary from 0 to  $n$ .

Whereas monoacidity constants show the partition among acid–base forms clearly, they do so only in a qualitative way and they complicate its quantitative computation.

Any form  $H_iA^a$  is univocally identified by the number of protons. Consequently in the following equations the charge  $a$  will be omitted.

The polyacidity constant,  $Pa(i)$ , involves any of the forms  $H_iA$  and the most protonated forms  $H_nA$ , and is defined as the equilibrium constant of the reaction



As will be seen below, polyacidity constants make the quantitative computation of partitions much easier.

Combining equations [1] and [2] yields

$$Pa(i) = \pi \prod_{\ell=1}^{n-i} K(\ell) \quad [3]$$

For  $i = n$ , the polyacidity constant can be easily determined from Eq. [2]:

$$Pa(n) = 1. \quad [4]$$

As an example, the polyacidity constants of the maleate forms are given in Table 1.

Polyacidity constants can be utilized to express the concentration ratio of two forms of a given chemical species:

$$\frac{[H_iA]}{[H_jA]} = \frac{\frac{Pa(i)[H_nA]}{[H^+]^{n-i}}}{\frac{Pa(j)[H_nA]}{[H^+]^{n-j}}} = \frac{Pa(i)[H^+]^j}{Pa(j)[H^+]^i} \quad [5]$$

As an example, at pH 7, the ratio maleate/maleic acid can be computed from Table 1 and is found equal to  $1.22 \times 10^6$ . For a better intuitive comprehension of the equation below, it is interesting to note from Eq. [5], that the concentration of a given form  $H_jA$  is proportional to  $Pa(j)[H^+]^j$ .

### PARTITIONS AMONG DIFFERENT FORMS

The partition of any given acid–base species  $s$  among its different  $n + 1$  forms is given by a series of  $(n + 1)$   $\Phi(i)$  equations, each of which represents the fraction of one form containing  $i$  protons:

$$\Phi(i) = \frac{[H_iA]}{C(s)} \quad [6]$$

where

$$C(s) = \sum_{j=0}^n [H_jA] \quad [7]$$

is the total concentration of the  $s$  species. Combining Eqs. [6] and [7] and substituting  $[H_iA]$  and  $[H_jA]$ , respectively, by  $Pa(i)[H^+]^i$  and  $Pa(j)[H^+]^j$ , according to Eq. [5], it follows that

$$\Phi(i) = \frac{Pa(i)[H^+]^i}{\sum_{j=0}^n Pa(j)[H^+]^j} \quad [8]$$

Partition equations are generated in the same way in complexometry (4). As an example, at pH 7, the partition of the species maleate among its different acid–base forms is calculated in Table 1.

TABLE I  
MOLAR PARAMETERS OF THE MALEATE SPECIES

	$i(\text{protons})$ (-)	$z(i)$ (-)	$Pa(i)$ (M <sup>2-i</sup> )	$Pa(i)[H^+]^i$ (M <sup>2</sup> )	$(i)^a$ (-)	$z(i)Pa(i)[H^+]^i$ (M <sup>2</sup> )	$\frac{1}{2}z^2(i)Pa(i)[H^+]^2$ (M <sup>2</sup> )
Maleic acid	2	0	1	10 <sup>-14</sup>	7.35 × 10 <sup>-7</sup>	0	0
Monohydrogenomaleate	1	-1	1.42 × 10 <sup>-2</sup>	1.42 × 10 <sup>-9</sup>	0.104	-1.42 × 10 <sup>-9</sup>	7.10 × 10 <sup>-10</sup>
Maleate	0	-2	1.22 × 10 <sup>-8</sup>	1.22 × 10 <sup>-8</sup>	0.896	-2.44 × 10 <sup>-8</sup>	2.44 × 10 <sup>-8</sup>
Sum of all forms	—	—	—	1.36 × 10 <sup>-8</sup>	1.000	-2.58 × 10 <sup>-8</sup>	2.51 × 10 <sup>-8</sup>
$\zeta(s)$ (M) <sup>b</sup>	—	—	—	—	—	-1.90	—
$\alpha(s)$ (M) <sup>c</sup>	—	—	—	—	—	—	1.85

Note.  $T = 25^\circ\text{C}$ ,  $\text{pH} = 7$ ,  $K(1) = 1.42 \times 10^{-2}$  M,  $K(2) = 8.57 \times 10^{-7}$  M.

<sup>a</sup> According to Eq. [8].

<sup>b</sup> According to Eq. [10].

<sup>c</sup> According to Eq. [16].

### MOLAR MEAN CHARGES AND GLOBAL CHARGE

The molar mean charge,  $\zeta(s)$ , of a given species  $s$  can be defined as

$$\zeta(s) = \frac{\sum_{j=0}^n z(j)[H_j A]}{C(s)} = \sum_{j=0}^n z(j)\Phi(j) \quad [9]$$

where  $z(j)$  is the charge of the form containing  $j$  protons.

Combining Eqs. [8] and [9] yields

$$\zeta(s) = \frac{\sum_{j=0}^n z(j)Pa(j)[H^+]^j}{\sum_{j=0}^n Pa(j)[H^+]^j} \quad [10]$$

As an example, at pH 7, the molar mean charge of the maleate species is found equal to -1.90. Data, computation, and result are summarized in Table 1.

The introduction of the concept of molar mean charge permits an easy computation of the global charge,  $Z$ , for a complex system of numerous chemical species:

$$Z = \sum_s \zeta(s)C(s) \quad [11]$$

where  $s$  refers to each chemical species of the system, including  $H^+$  and  $OH^-$  species.

### DETERMINATION OF THE CONCENTRATION OF ANY GIVEN CHEMICAL SPECIES BUT $H^+$ IN A COMPLEX SYSTEM

According to the electroneutrality principle, the global charge,  $Z$ , of a complex system must be equal to zero:

$$Z = \sum_s \zeta(s)C(s) = 0. \quad [12]$$

Equation [12] enables the calculations of the concentration,  $C(m)$ , of all chemical species  $m$  but hydrogen ion,  $H^+$ , which cannot be di-

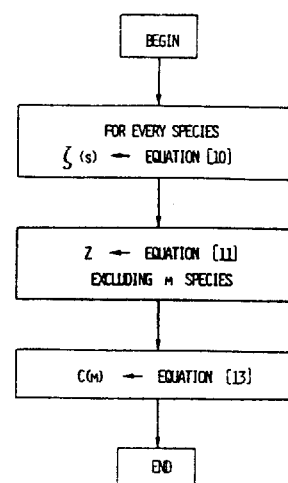


FIG. 1. Computation of  $m$  species concentration excluding ionic strength effects.

TABLE 2  
COMPUTATION OF GLOBAL PARAMETERS FOR 0.5 M MALEATE SOLUTION AT pH 7

$s$	$C(s)$ (M)	$\zeta(s)^a$ (-)	$\alpha(s)^b$ (-)	$\zeta(s)C(s)$ (M)	$\alpha(s)C(s)$ (M)
Maleate (species)	0.5	-1.90	1.85	-0.95	0.92
Na <sup>+</sup>	0 (0.95) <sup>e</sup>	+1	$\frac{1}{2}$	0 (0.95) <sup>e</sup>	0 (0.48) <sup>e</sup>
OH <sup>-</sup>	10 <sup>-7</sup>	-1	$\frac{1}{2}$	-10 <sup>-7</sup>	5 × 10 <sup>-8</sup>
H <sup>+</sup>	10 <sup>-7</sup>	+1	$\frac{1}{2}$	10 <sup>-7</sup>	5 × 10 <sup>-8</sup>
Z (M) <sup>c</sup>	—	—	—	-0.95 (0) <sup>e</sup>	—
I (M) <sup>d</sup>	—	—	—	—	(1.40) <sup>e</sup>

Note.  $T = 25^\circ\text{C}$ .

<sup>a</sup> According to Eq. [10].

<sup>b</sup> According to Eq. [16].

<sup>c</sup> According to Eq. [11].

<sup>d</sup> According to Eq. [17].

<sup>e</sup> Calculation including correct sodium ion concentration.

rectly calculated because it enters in the  $\zeta(s)$  functions:

$$C(m) = \frac{-1}{\zeta(m)} \sum_{s \neq m} \zeta(s)C(s). \quad [13]$$

In practice, the concentration of any chemical species  $m$  of a given complex system can be computed by the algorithm presented in Fig. 1.

As an example, one can compute the Na<sup>+</sup> ion concentration in a 0.5 M maleate solution at pH 7. The species to be considered are maleate (in its different forms), Na<sup>+</sup>, H<sup>+</sup>, and OH<sup>-</sup>. Table 2 summarizes the computation of the global charge,  $Z$ , which is found equal to -0.95 M. The sodium ion concentration which ensures the electroneutrality must be equal to 0.95 M.

#### DETERMINATION OF pH

The simple algorithm defined above applies to all chemical species but hydrogen ion, H<sup>+</sup>, the knowledge of which is required to calculate the molar mean charge according to Eq. [10]. Computation of the concentration in hydrogen ions, H<sup>+</sup>, will therefore require an iterative loop. At the correct pH value, the electroneutrality is respected and the global charge,  $Z$ , is

zero. If the chosen pH value is too low, the global charge becomes positive. Conversely, if the chosen pH value is too high, the global charge becomes negative. The algorithm to compute the pH of a solution is presented in Fig. 2.

As an example, the pH value of a mixture of 0.1 M maleic acid and 0.1 M sodium ion was computed. Data, computation, and results

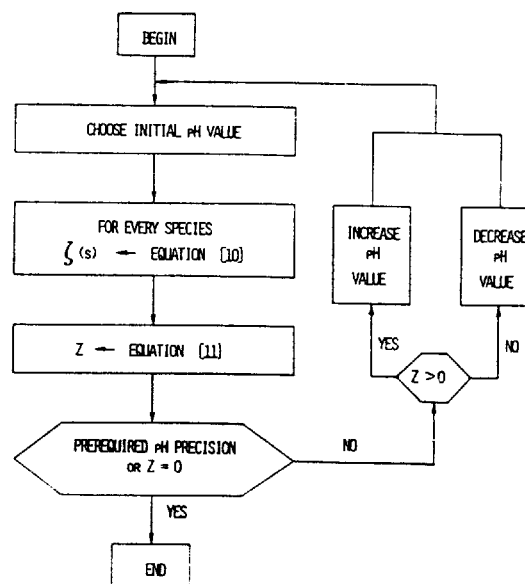


FIG. 2. Computation of pH value excluding ionic strength effects.

TABLE 3

COMPUTATION OF THE pH VALUE OF A MIXTURE OF  
0.1 M SPECIES MALEATE AND 0.1 M SODIUM ION

$r^a$	Z (M)	Sign (of Z)	Sign $\Delta$ pH	pH (-)
0	—	—	—	7
1	$-9.0 \cdot 10^{-2}$	-1	-3.5	3.5
2	$2.2 \cdot 10^{-3}$	+1	+1.75	5.25
3	$-1.3 \cdot 10^{-2}$	-1	-0.875	4.38
4	$-1.7 \cdot 10^{-3}$	-1	-0.437	3.94
5	$1.8 \cdot 10^{-4}$	+1	+0.218	4.16
6	$-6.6 \cdot 10^{-4}$	-1	-0.109	4.05
7	$-2.3 \cdot 10^{-4}$	-1	-0.055	3.99
8	$-2.3 \cdot 10^{-5}$	-1	-0.027	3.97
9	$8.0 \cdot 10^{-5}$	+1	+0.014	3.98
10	$2.9 \cdot 10^{-5}$	+1	+0.007	$3.99 \pm 0.01$

Note. Algorithm: see text,  $T = 25^\circ\text{C}$ .<sup>a</sup> Iteration index.

are summarized in Table 3. The species to be considered are maleate (in its different forms),  $\text{Na}^+$ ,  $\text{H}^+$ , and  $\text{OH}^-$ . A first pH value of 7 is chosen. At this pH, the molar mean charges can be calculated according to Eq. [10] (see Table 2). A global charge of  $-90 \text{ mM}$  is found; the pH value must thus be decreased. New pH values,  $\text{pH}_2$ , can be computed with an iterative equation such as

$$\text{pH}_2 = \text{pH}_1 + \text{Sign } \Delta\text{pH} \quad [14]$$

where  $\text{pH}_1$  is the previous value,  $\Delta\text{pH}$  is initially made equal to 3.5 and divided by 2 at each iteration, and Sign equals +1 when Z is positive, Sign equals -1 when Z is negative, and Sign equals zero when Z is nought. Z is the global charge computed with the previous pH value,  $\text{pH}_1$ . After 10 cycles (see Table 3), a pH value of 3.99 ( $\pm 0.01$ ) is found with an absolute global charge lower than 0.1 mM.

#### MOLAR MEAN CONTRIBUTIONS TO IONIC STRENGTH AND IONIC STRENGTH

The molar mean contribution to ionic strength,  $u(s)$ , of a given species  $s$  is defined as

$$u(s) = \frac{\frac{1}{2} \sum_{j=0}^n z(j)^2 [\text{H}_j\text{A}]}{C(s)} = \frac{1}{2} \sum_{j=0}^n z(j)^2 \Phi(j). \quad [15]$$

Combining Eqs. [8] and [15], one finds

$$u(s) = \frac{\frac{1}{2} \sum_{j=0}^n z(j)^2 Pa(j) [\text{H}^+]^j}{\sum_{j=0}^n Pa(j) [\text{H}^+]^j}. \quad [16]$$

As an example, the molar mean contribution of maleate to ionic strength at pH 7 was computed. Data, computation, and results are summarized in Table 1. The molar mean contribution of the maleate species to ionic strength is found equal to 1.85.

The introduction of the concept of molar mean contributions to ionic strength permits an easy computation of the ionic strength,  $I$ :

$$I = \sum_s u(s) C(s). \quad [17]$$

As an example, the ionic strength of a mixture of 0.5 M maleate species and 0.95 M sodium ions (at pH 7) can be computed and is found equal to 1.40 M. Data, computation, and result are summarized in Table 2.

#### MODELING TAKING IONIC STRENGTH EFFECTS INTO CONSIDERATION

The correct thermodynamic expression of a polyacidity constant is

$$Pa(i) = \frac{a(\text{H}_i\text{A}) a(\text{H}^+)^{n-i}}{a(\text{H}_n\text{A})} \quad [18]$$

where the  $a(\quad)$  are the activities. The relation between activities and concentrations is given by

$$a(\text{H}_i\text{A}) = f(\text{H}_i\text{A}) [\text{H}_i\text{A}] \quad [19]$$

where  $f$  stands for the activity coefficient of the form containing  $i$  protons. Activity coefficients are functions of the ionic strength (see (3), Table 3.3., p. 135).

Combining Eqs. [18] and [19] yields

$$Pa(i) \frac{f(H_n A)}{f(H_i A)} = \frac{[H_i A]}{[H_n A]} a(H^+)^{n-i}. \quad [20]$$

The activity of hydrogen ions is defined by

$$pH = -\log a(H^+). \quad [21]$$

Hence, the concentration ratio of two forms of the same chemical species becomes

$$\frac{[H_j A]}{[H_i A]} = \frac{Pa(j)}{Pa(i)} \frac{f(H_j A)}{f(H_i A)} a(H^+)^j. \quad [22]$$

Comparing Eqs. [5] and [22] yields the corrections for ionic strength effects. Namely, hydrogen ion concentrations are replaced by hydrogen ion activities and polyacidity constants are divided by the activity coefficient of the given form. These corrections must be introduced in Eqs. [8], [10], and [16].

If the ionic strength is known by another way, one can simply compute species concen-

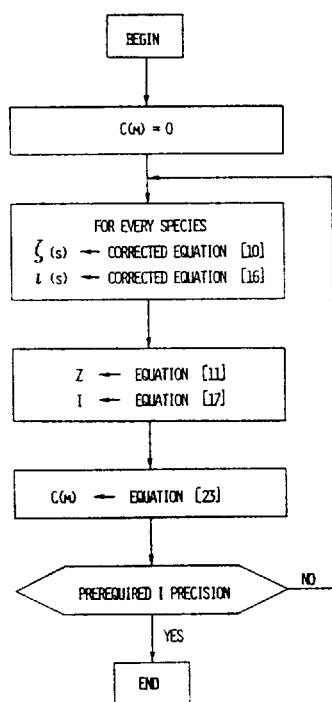


FIG. 3. Computation of  $m$  species concentration including ionic strength effects.

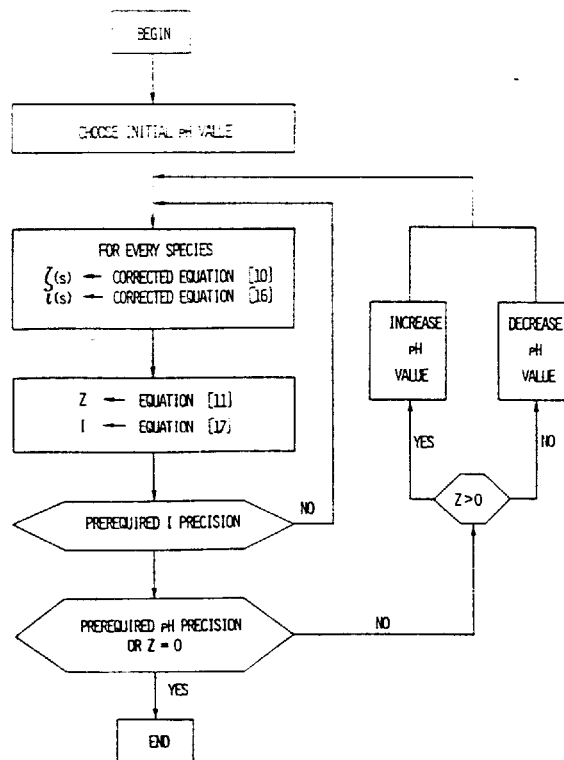


FIG. 4. Computation of pH value including ionic strength effects.

trations or pH by the preceding algorithms with corrected equations. Whenever the ionic strength is unknown, the concentration of any chemical species  $m$  but hydrogen ion is given by an iterative equation derived from Eq. [13]:

$$C(m)_2 = C(m)_1 - \frac{1}{\zeta(m)} \sum_s \zeta(s) C(s) \quad [23]$$

where  $C(m)_2$  is the new  $m$  species concentration,  $C(m)_1$  is the previous  $m$  species concentration (initially made equal to 0). The algorithm for the computation of the concentration of any chemical species  $m$  but hydrogen ion is presented in Fig. 3. In the same way, the pH computation is presented in Fig. 4. The Pascal version of these algorithms was written and is available from the authors.

#### EXPERIMENTAL VALIDATION OF THE THEORETICAL MODEL

Four solutions were prepared (Table 4). The pH's of these solutions were measured. Dav-

ies's equation (see (3), Table 3.3., p. 135) was used for the activity coefficient:

$$\text{Log } f = -KZ^2 \left( \frac{\sqrt{I}}{1 + \sqrt{I}} - 0.2I \right) \quad [24]$$

where  $K \approx 0.5$  for water at 25°C. The pre-required precisions for ionic strength and pH values are fixed to 0.01I and 0.01, respectively.

The pH and ionic strength values of these solutions were computed with the presented model. All results are given in Table 4. Agreements among experimental and computed data validate the effectiveness of computation of chemical concentration.

With the proposed computing procedure, each chemical system exhibited a unique equilibrium state, namely as concerns pH. This uniqueness is supported by Gibbs' phase rule.

## DISCUSSION

Computation of the concentration in chemical species and especially of pH in complex systems, using only classical thermodynamic constants, namely monoacidity constants (see (1), p. 145), is a long and tedious problem. This paper introduces five innovations to make computation easier. The polyacidity constants simplify the expressions of partitions among different forms, of molar mean charges and of molar mean contribu-

tions to ionic strength. Expressions of these parameters, generic to all chemical species of the system, however complex, simplify the building of the model. Global charge and ionic strength are more easily computed from molar mean charges and molar mean contributions to ionic strength. Corrections for ionic strength effect are simplified. Finally, pH is determined with a simple iteration procedure which converges very rapidly.

On these bases, one obtains an algorithm which has a modular structure and can be integrated in more complex tasks. The model is exact as no approximations are made and yields a unique and correct solution. The model is general as it may be extended to include any number of chemical species with any number of forms. Finally, the model is easy to introduce in a computer as it comprises only simple and iterative equations. The algorithms have been transformed into computer programs. It is nevertheless worth noting that they can also be very easily used for manual calculations whenever automated computing facilities are not available.

Possible uses of the proposed model are not limited to the description of the physical chemistry of complex systems. In complex systems where known chemical changes are occurring, the model may be used to predict the final physicochemical state. Conversely, the model allows prediction of the chemical

TABLE 4  
EXPERIMENTAL VALIDATION OF THE THEORETICAL MODEL

		Solution 1	Solution 2	Solution 3	Solution 4
Acetate species	(mM)	2.45	2.45	2.45	15.75
Propionate species	(mM)	2.55	2.55	2.55	18.87
Phosphate species	(mM)	2.70	2.70	2.70	15.35
Sodium ions	(mM)	432.1	439.6	440.6	31.09
Chloride ions	(mM)	428.2	430.8	430.8	0
Computed ionic strength	(mM)	432	441	443	31.1
Computed pH value		4.22	6.68	7.36	4.67
Experimental pH value		4.33	6.63	7.26	4.59

Note.  $T = 25^\circ\text{C}$ .

corrections required to obtain and maintain a desired physicochemical state. It computes mass balances which require the knowledge of partition among different acid-base forms. It can be used to simulate titration of a complex system. Programs for various applications have been written and are available from the authors.

An example of the domain of use is the control of complex anaerobic fermentation. The latter depends largely upon the physical chemistry of the ecosystem. The presented model, extended to include gas-liquid equilibrium, will permit a better comprehension

of physicochemical effects and so a possible improved control of the fermentation process.

#### ACKNOWLEDGMENT

The authors are grateful to A. Rozzi (Institute di Ricerca Sulle Acque del CNR, Bari, Italy) for helpful discussions.

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