Simultaneous Determination of All Species Concentrations in Multiequilibria for Aqueous Solutions of Dihydrogen Phosphate Considering Debye–Hückel Theory

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Supporting Information

ABSTRACT: Solutions of citric acid and Na$_2$HPO$_4$ were studied with the dynamical approach to multiequilibria systems. This widely employed buffer has a well-defined pH profile and allows for the study of the distribution of phosphate species over a wide pH range. The dynamical approach is a flexible and accurate method for the calculation of all species concentrations in multiequilibria considering ionic strength ($I$) via Debye–Hückel theory. The agreement between the computed pH profiles and experiment is excellent. The equilibrium concentrations of the non-hydrogen species are reported for over 30 buffer mixtures across the entire pH range. These new concentration data enable researchers to look up the equilibrium distribution of species at any pH. The data highlight the dramatic effects of ionic strength, and for example, the position of maximal H$_2$PO$_4^−$ concentration is shifted by almost an entire pH unit! From a more general perspective, the study allows for a discussion of the dependence of concentration quotients $Q_{xy}$ on ionic strength, $pQ_{xy} = f(I)$, and for the numerical demonstration that the thermodynamic equilibrium constants $K_{xy,act}(I) = K_{xy}$. The analysis emphasizes the need for measurements of the concentrations of several species in complex multiequilibria systems over a broad pH range to advance multiequilibria simulations.

1. INTRODUCTION

Systems of polyprotic acids/bases inherently involve complex equilibria. Given the pH of an acid–base system at equilibrium, the concentration of each ionic species present in solution can be deduced via the solution of a polynomial.1,2 Generally, the order of the polynomial grows with the number of species in the acid–base equilibrium and the mathematical solution can become rather complex. Similar computations for a buffer system involving one or more polyprotic species are more complicated, and it is even more challenging to determine the concentration of each species when the effect of the ionic strength ($I$) of the solution is considered. Tessman and Ivanov developed software to calculate the pH of a given mixture by solution of the $n$th degree, single-variable polynomial with consideration of ionic strength, and the results agreed with experiment.3 Numerical methods also have since been developed for the calculation of all equilibrium species using the Solver tool in Microsoft Excel.4,5

In previous work, we described the dynamical approach for the simultaneous solution of all species concentrations for multiequilibria systems of mixtures of acids and their conjugate bases.6,7 The dynamical approach entails the numerical solution of a set of first-order ordinary differential equations (ODEs) derived from the chemical equilibria expressions. This approach offers significant advantages including the ability to easily treat complex systems and the facile incorporation of Debye–Hückel theory.7 Importantly, the approach maintains a straightforward mathematical description of the multiequilibria system, which requires only basic knowledge of mass action kinetic theory.

The present study extends the dynamical approach to include equilibrium problems with several multiply charged species. Our previous study of the pH profile of the NaOH titration of citric acid showed that the effects of ionic strength can be very large, especially for the highly charged species.6 It therefore seemed prudent to explore mixtures that contain a larger number of highly charged species. The buffer system comprised of citric acid (H$_3$Cit) and dibasic sodium phosphate (Na$_2$HPO$_4$) was selected because it is a widely employed buffer system with a well-defined pH profile over a wide range of pH values. Moreover, it allows one to study the distribution of phosphate species in aqueous solution over a wide pH range. We compare our results to the experimental data sets by McIlvaine8 and Sigma-Aldrich9 and demonstrate that the dynamical approach is a convenient, flexible, and accurate method for the calculation of all species in complex acid/base equilibria at various acidities and ionic strengths. The calculated pH profile simulates the experimental data with resounding agreement. We also report the equilibrium concentrations of several species in complex multiequilibria systems over a broad pH range to advance multiequilibria simulations.

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concentrations of the non-hydrogen species and discuss the effects of ionic strength on the equilibrium distribution. Experimentally, the concentrations of these species are seldom reported because of the inherent difficulty in their measurements. With the concentrations of these other species as a function of pH, researchers are able to quickly and easily determine the optimal pH for a desired equilibrium species distribution. From a more theoretical perspective, the computed concentrations of all species allow for a discussion of concentration quotients and their dependence on ionic strength. Moreover, the approaches described in the present paper will be useful to studies of ionic strength dependence of equilibria in general.10–13

2. PHOSPHATE RECOVERY EFFORTS AND 
H2PO4−-SELECTIVE MOLECULAR SENSORS

The citric acid/phosphate buffer systems present an excellent opportunity to study the pH dependence of phosphate concentrations in aqueous solution. Phosphates are essential nutrients for all life, and often, they are the limiting nutrient in soil for plant growth. Using mined phosphates to fertilize the soil is rapidly exhausting the supply of phosphate available.14,15 On the other hand, overuse of phosphate fertilizers and the inability to recycle them have caused eutrophication in natural waters.16,17 The citric acid/phosphate buffer system has also been explored. It is well-known that proteins selectively bind anions, including phosphates, in specific protonation states.18–21 Many of the optical sensors that have been developed are based on this protein chemistry. Some examples of well-characterized H2PO4− receptors are illustrated in Supporting Information (Figure S1), and these include H2PO4− binding amides and pyridines with a ferrocenoyl scaffold, bis-ureas,22 tetraamides together with pyridines,23 bis-indoles with pyridines,24 amides and ethers,25 and sapphirines.43 The anion recognition studies require high-accuracy concentration measurements to determine accurate complexation constants.44 Thus, knowledge of the equilibrium distribution of phosphate species becomes essential for the determination of these complexation constants in aqueous media.

3. METHODS: DYNAMICAL APPROACH TO 
EQUILIBRIUM CONCENTRATIONS

Debye–Hückel theory and its variants are the most common approach to approximate activity coefficients of ions in electrolyte solutions. To account for nonideal dynamical behavior of ionic species in solution, the concentrations of the ionic species are replaced with activities a, in the kinetic equations. The activity a, of the ith species S, with absolute charge z is calculated via eq 1. In principle, the units of [S] can be any concentration unit (molal, molar) and we used molar concentrations, which are required as initial conditions in the ODEs.

\[ a_i = f_z [S]^z \]  

\[ \log_{10}(f_z) = AE^2\left(\frac{\sqrt{I}}{1 + \sqrt{I}} - bI\right) \]  

\[ I = 0.5 \sum_i z_i^2 [S] \]

The activity coefficients, f_z, were calculated using the Davies approximation49 to Debye–Hückel theory (eq 2). The coefficient \( A = e^B/(2.3038\epsilon \sigma \epsilon_k kT) \), where e is the electron charge, \( \epsilon \) is the static dielectric constant of water, k is the Boltzmann constant, T is temperature, and \( B = (2cN_l/e \epsilon_k kT)^{1/2} \). At room temperature, A has an approximate value of 0.5108 kg^{1/2} mol^{−1/2} and B is approximately 0.3287 × 10^{8} kg^{1/2} cm^{−1} mol^{−1/2} 50. The Davies approximation includes the empirical parameter b with a static value for all ions. Davies’ original work assigns b = 0.2, and this value was shown to give improved activity coefficients for large anions at low ionic strength based on conductivity measurements.40 However, the parameter b = 0.1 also has been used in some studies for pH profiles.73 In this work, we report the results obtained using both b = 0.1 and b = 0.2. The ionic strength was calculated via eq 3. Included in eq 3 are all of the species participating in the kinetic equations and the cations contributed by the added salts. The counterion concentrations are constant and equal to the respective initial anion concentrations. The Davies equation is believed to give a possible error of 3% at I = 0.1 mol L^{−1} and 10% at I = 0.5 mol L^{−1}.51

For a buffer system of a triprotic acid, H3A, and the salt of a second triprotic acid, (M+)2(H2A−), the system of equilibria and their equilibrium equations are as follows:

\[ H_2O ⇄ H^+ + OH^- \]  

\[ H_3A ⇄ H^+ + H_2A^- \]  

\[ K_1 = a[H^+]a[H_2A^-]/a[H_3A] \]  

\[ H_2A^- ⇄ H^+ + HA^- \]  

\[ K_1 = [H^+]a[HA^-]/a[H_2A^-] \]  

\[ HA^- ⇄ H^+ + A^- \]  

\[ K_3 = a[H^+]a[A^-]/a[HA^-] \]  

\[ H_2B^{−2} ⇄ H^+ + HB^{−2} \]  

\[ K_2 = a[H^+]a[HB^{−2}]/a[H_2B^{−2}] \]

\[ HB^{−2} ⇄ H^+ + B^{−3} \]  

\[ K_3 = a[H^+]a[B^{−3}]/a[HB^{−2}] \]

The equilibrium constants are given as \( K_{xy} \), where x denotes the identity of the acid and y is the dissociation number. For citric acid (H3Cit, 2-hydroxypropane-1,2,3-tricarboxylic acid) at room temperature, the pK values of the carboxyl group attached to C2 is 3.13 and the pK values for the second and third dissociations are 4.76 and 6.40.44 The pK values of phosphoric acid at room temperature are 2.16, 7.21, and 12.32.34,55 Note that the dynamical method can be employed at other temperatures with the consideration of the temperature dependence of the equilibrium constants via the van’t Hoff equation. The ionic strength dependence of the pK values of various acids has been studied, and in solutions with ionic strengths below 0.6, the changes to the above pK values are less than 0.3 for both citric acid and phosphoric acid.56

The equilibria of eqs 4–10 lead to the following kinetic differential equations according to general mass action kinetics:

\[ \frac{df(x)}{dt} = \sum_{i} \frac{f_i}{K_i} \]

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Table 1. Reported and Calculated pH Values and Ionic Strengths for a Series of Mixtures\(^a\) of the Buffer Solution

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<th>mix.</th>
<th>([H_3Ct]_0) (g/L)</th>
<th>([HPO_4^{2-}]_0) (g/L)</th>
<th>(\text{pH}_{\text{expt.}})</th>
<th>(f = 1)</th>
<th>(b = 0.1)</th>
<th>(b = 0.2)</th>
<th>(\text{lit.})</th>
<th>(\text{ionic strength})</th>
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\(^a\)Volumes of buffer solutions given in ref 8 were converted to concentrations (g/L). I reported in mol/L. \(^b\)Calculated using the method described in ref 5 (see the Supporting Information).

\[
\frac{d[H^+]}{dt} = k_{11f}[H_4A] - f_1^H k_{11b}[H^+][H_2A] + f_1 k_{12f}[H_2A]
\]

\[
\frac{d[A^-]}{dt} = f_1 k_{13f}[H_4A^+] - f_1 f_3 k_{13b}[H^+][A^-]
\]

\[
\frac{d[H_3O^+]}{dt} = f_1 f_2 k_{21b}[H^+][H_2A^-] + f_1 k_{22}[H_2A^-] - f_1 k_{31b}[H^+][A^-] + k_{11f}[H_3O^+]
\]

\[
\frac{d[H^+]}{dt} = f_1 f_2 k_{21b}[H^+][H_2B^-] + f_1 k_{22}[H_2B^-] - f_1 f_3 k_{23b}[H^+][B^-] + f_2 k_{13b}[H_2B^+] + k_{11f}[H^+]
\]

\[
\frac{d[B^-]}{dt} = f_1 f_2 k_{21b}[H^+][B^-] - f_1 f_3 k_{23b}[H^+][B^-] + f_2 k_{13b}[H_2B^+] + f_1 k_{23b}[H^+][B^-] - f_1 f_3 k_{23b}[H^+][B^-]
\]

The method calls for the assignment of the forward reaction rate constants \(k_j\), the backward reaction rate constants \(k_b\), and the initial concentrations. One significant advantage of the dynamical approach is that the species concentrations are all described as functions of time, which theoretically allows for the
4. RESULTS AND DISCUSSION

4.1. pH Calculation with the Dynamical Method. Three sets of equilibrium concentrations were computed for each buffer mixture. One set corresponds to an ideal system, where the ionic strength of the solution is considered to have no effect on equilibrium concentrations (i.e., \( f = 1 \)). The other two sets include the effects of ionic strength using activity coefficients calculated with the Davies equation with \( b = 0.1 \) or \( b = 0.2 \). The ionic strengths of the equilibrium solutions were calculated for all three data sets, and they appear in the last three columns of Table 1.

Electrometric measurements of \( H^+ \) concentrations correspond to the activity of \( H^+ \) rather than its concentration.\(^{48}\) We calculated pH values using both concentrations and activities and refer to them as pH\(_{\text{conc}}\) and pH\(_{\text{act}}\), respectively; pH\(_{\text{conc}}\) = −log([H\(^+\)]\(_{\text{conc}}\)) and pH\(_{\text{act}}\) = −log([H\(^+\)]\(_{\text{act}}\)). Therefore, six values of pH were determined for each buffer mixture and they are shown in columns 5–10 of Table 1: pH\(_{\text{conc}}\) and pH\(_{\text{act}}\) for \( f = 1 \) and pH\(_{\text{conc}}\) and pH\(_{\text{act}}\) values calculated using the Davies approximation with \( b = 0.1 \) and \( b = 0.2 \), respectively.

The experimental data\(^{8}\) are compared to the calculated pH values in Figure 1. The ratio \( \log([\text{HPO}_4^{2-}]_0/[\text{H}_3\text{Cit}]_0) \) is used as the independent variable to achieve a compact axis that uses relative concentrations of HPO\(_4^{2-}\) and H\(_3\)Cit such that any ratio increases, the solution becomes more basic and the ionic strength increases (secondary axis in Figure 1, black curve). As the ratio increases, the solution becomes more basic and the ionic strength increases (secondary axis in Figure 1, black curve).

Figure 1 illustrates that ionic strength greatly affects pH. The pH values calculated with \( f = 1 \) (solid curves) show large deviations from the experimental pH over the entire range of mixtures with an average error of 9.1 and 11.9% for pH\(_{\text{conc}}\) and pH\(_{\text{act}}\), respectively. Note that the deviation between the computed pH\(_{\text{act}}\) values and the experimental pH corresponds to the vertical distance between the two curves at a given value of \( \log([\text{HPO}_4^{2-}]_0/[\text{H}_3\text{Cit}]_0) \). A first inspection of Figure 1 might suggest that the deviation is largest in the region \( \log([\text{HPO}_4^{2-}]_0/[\text{H}_3\text{Cit}]_0) > 1 \) (average error of 9.5%). However, the largest deviations actually occur in the region \( 0.0 < \log([\text{HPO}_4^{2-}]_0/[\text{H}_3\text{Cit}]_0) < 0.1 \) (average error of 14.7%). In fact, deviations are large even at very low ionic strengths with a 10.0% error at \( I = 0.05 \) M. Orange indicators were added to Figure 1 (left) to clearly illustrate this deviation.

The agreement between experiment and the data calculated with Debye–Hückel theory and \( b = 0.1 \) (dashed curves in Figure 1) is a magnitude better with average errors of only 2.1 and 1.1% for pH\(_{\text{conc}}\) and pH\(_{\text{act}}\), respectively. The resounding agreement between experiment and the computed pH\(_{\text{act}}\) data gets even
The graph on the right side of Figure 1 compares the experimental pH values to the pHconc (green) and pHact (blue) values computed with \( b = 0.1 \) (dashed) and \( b = 0.2 \) (dotted). Relative to the \( b = 0.1 \) values, the computed \( b = 0.2 \) data sets shift to higher pH at higher ionic strength. The pHconc values are overestimated and in slightly worse agreement than their \( b = 0.1 \) counterparts with 1.7% error with respect to experimental values. However, the pHconc values still fall below the experimental pH curve and are in better agreement than the pHconc values for all \( b \) values, especially in the region of low ionic strength. The pHconc values agree with experiment better than pHact only at very low ionic strength (\( I \approx 0 \)).

The pHconc values agree with experiment better than pHact only at very low ionic strength (\( I \approx 0 \)).

4.2. Calculation of All Species Concentrations at Equilibrium for the Series of Mixtures of Buffer Solution

Table 2 shows the concentrations (in g/L) of \( \text{H}_2\text{Cit}^- \), \( \text{H}_3\text{Cit}^- \), \( \text{HCl}\text{Cit}^- \), and \( \text{Cit}^3^- \) at equilibrium for each mixture. The computations require the specification of concentrations in units of mol/L, and the results are given in mmol/L in Table S2a and b. Again, these values are reported for both the \( f = 1 \) data set and the data sets with activity considerations.

Figure 2 shows the non-\( H^+ \) species concentrations as functions of pHact. The \( \text{H}_2\text{Cit}^-\text{m}^3 \) and \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) species are plotted on the top and bottom, respectively. The plots in Figure 2 show that the concentration maxima occur at significantly different pH values for the \( f = 1 \) (solid) and Davies (dashed) data sets. Since the \( b = 0 \) and \( b = 0.2 \) data sets give exactly the same curves, only the \( b = 0.1 \) data set is shown in Figure 2.

The \( \text{H}_2\text{Cit}^- \) concentration starts at about 16 g/L for the most acidic solution studied and decreases as the fraction of \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) increases. As the solution becomes more basic, one observes maxima for the concentrations of the conjugate bases: \( \text{H}_2\text{Cit}^- \) at pH \( \approx 4.0 \) (\( f = 1 \)) or 3.4 (Davies), \( \text{HCl}\text{Cit}^- \) at pH \( \approx 5.6 \) (\( f = 1 \)) or 4.8 (Davies), and \( \text{Cit}^3^- \) at pH \( \approx 7.0 \) (\( f = 1 \)) or 6.2 (Davies).

High concentrations of \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) occur at high pH. Even at the most basic pH values studied, only a small fraction of \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) is deprotonated. Thus, the \( \text{PO}_4^{\text{m}^-\text{m}^-} \) curve essentially lies on the pHact axis and \( \text{PO}_4^{\text{m}^-\text{m}^-} \) never reaches \( 0.01 \) g/L. As the fraction of citric acid increases, the pH decreases and \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) is protonated. The concentration of \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) is highest at pH \( \approx 6.4 \) (\( f = 1 \)) or 5.6 (Davies). Further protonation of \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) occurs only to a small extent, and \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) remains the dominant \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) species in solution. The concentration of neutral \( \text{H}_2\text{PO}_4^-\text{m}^-\text{m}^- \) only goes through a shallow maximum at pH \( \approx 2.9 \) (\( f = 1 \)) or 2.7 (Davies).
The appropriate pH to maximize $[\text{HPO}_4^{2-}]$ and diminish interference from its conjugate base is 5.4, as given by the Davies curve. Conversely, to directly compare the ability of a receptor to selectively bind $[\text{HPO}_4^{2-}]$ over $[\text{HPO}_4^{3-}]$, one should select a pH where both of these species exist in similar quantities. An appropriate pH for such a measurement would not be 7.5, as suggested by the $f=1$ curve, but 6.8, as suggested by the Davies curve.

### 4.3. Ionic Strength Dependence of Concentration Quotients $Q_y$ and Thermodynamic Equilibrium Constants $K_y^{\text{act}}$

Generally, for the $y$th dissociation of an $m$-protic acid $H_mA$, the concentration quotient $Q_y$ is given by eq 21. In more concentrated solutions, eq 21 needs to be replaced by the corresponding expression for the thermodynamic equilibrium constants $K_y^{\text{act}}$ (eq 22) in which all concentrations $[S]$ are replaced by activities $a(S)$.

$$Q_y = \frac{[H^+][H_{m-y}A^{m-y}]}{[H_{m-y+1}A^{m-2y}]}$$  \hspace{1cm} (21)$$

$$K_y^{\text{act}} = f_y^H [H^+]a(H_{m-y}A^{m-y})/a(H_{m-y+1}A^{m-2y})$$  \hspace{1cm} (22)$$

$$K_y = \lim_{\mu \to 0} Q_y$$  \hspace{1cm} (23)$$

$$K_y = K_y^{\text{act}} \hspace{1cm} \text{for all } I$$  \hspace{1cm} (24)$$
At infinite dilution, activities and concentrations become equal and the equilibrium coefficient $K_y$ equals the concentration quotient $Q_y$ (eq 23). It is well established that the concentration quotients $Q_y$ do not equal $K_y$ even at low ionic strength. However, all of the calculations employ the numerical value of $K_y$ for all $I$. It is a direct consequence of this practice that eq 24 must hold for all $I$, that is, that the equilibrium constants $K_y$ equal the thermodynamic equilibrium constants $K_{y,act}$ not just in the limit of infinite dilution but in the entire range of ionic strength being modeled with Debye–Hückel theory.

$$Q_y = \frac{[H^+][H_3\text{-}y\text{-}A^y]}{[H_4\text{-}y\text{-}A^{y-}]}$$

(27a)

$$Q_y = \frac{[H^+][H_3\text{-}y\text{-}B^{y-}]}{[H_4\text{-}y\text{-}B^{-1y}]}$$

(27b)

$$K_{y,act} = f_y^0 [H^+](H_3\text{-}y\text{-}A^y)/a(H_4\text{-}y\text{-}A^{y-})$$

(28a)

$$K_{y,act} = f_y^0 [H^+](H_3\text{-}y\text{-}B^{y-})/a(H_4\text{-}y\text{-}B^{-1y})$$

(28b)

Previously, we plotted the concentration quotients $Q_y$ for two systems (acetate-buffered acetic acid; titration of citric acid with sodium hydroxide) using several approximations of Debye–Hückel theory and showed that $pQ_y$ is always less than $pK_y$ and that the difference between the increase increases nonlinearly as the ionic strength increases. Ganesh et al. recently reported a similar finding for a universal buffer system. We show an example of this kind of plot in Figure S2 of the Supporting Information for the first dissociation of citric acid in the buffer system.

The concentration quotients $Q_y$ were computed for all of the equilibria in the buffer system using eqs 27a and 27b and the concentrations in Table 2. Figure 3 shows the $pQ_y$ curves as functions of ionic strength for citric acid ($x = 1$, left) and phosphoric acid ($x = 2$, right). As before, red horizontal lines show the $pK_{xy}$ values at infinite dilution. The $pQ_y$ curves for all data always are less than the $pK_{xy}$ values at infinite dilution. The difference grows nonlinearly as $I$ increases, as expected, and the deviation always is larger for the $b = 0.1$ data (solid curves) than for the $b = 0.2$ data (dashed curves) for these systems. Also, for any given ionic strength, the difference between the equilibrium constants and the concentration quotients $pK_{xy} - pQ_y$ increases from the first dissociation ($y = 1$), to the second dissociation ($y = 2$), and again to the third dissociation ($y = 3$). This trend is also expected because the $z^2$ dependency of the $f$ values is more pronounced in the curves of the higher order dissociations.

We also calculated the thermodynamic equilibrium constants $K_{y,act}(I)$ using eqs 28a and 28b with the concentrations from Table 2 and the activity coefficients from the Davies equation for both $b = 0.1$ and $b = 0.2$, and the results are included in Figure 3 as blue marks. These $pK_{y,act}(I)$ values all align with the $pK_{xy}$ values at infinite dilution (red lines). This outcome of the numerical solution of the ODE systems is required by eq 24, and Figure 3 thus validates the numerical accuracy of the dynamical approach to multiequilibria system.

### 4.4. Attempted Speciation of Citric Acid via $^1$H NMR Spectroscopy.

The geminal hydrogens of the two equivalent CH$_2$ groups are diastereotopic, and the AB spin system gives rise to two doublets with the same coupling constant $J_{AB}$. We measured the $^1$H NMR spectra of a dilute aqueous solution of potassium citrate (5.36 mg of K$_3$Cit in 100 mL of H$_2$O) as a function of pH by adding small aliquots of 3 M H$_2$SO$_4$. Spectra were recorded on a 600 MHz Bruker Avance III spectrometer using water suppression techniques, and a typical spectrum is shown in the Supporting Information together with a table of the chemical shifts of the four peaks at each pH (Figure S3 and Table S5). The doublets show $J = 15.3 \pm 0.4$ Hz, and the chemical

$$D = A\left(\sqrt{I} - bI \right)$$

(25)

Inserting eq 2 into eq 22 and using the abbreviation of eq 25, one arrives at eq 26 which relates the concentration quotient $Q_y$ to the thermodynamic equilibrium constant $K_{y,act}$.

$$K_{y,act} = Q_y \cdot \{10^{(2y-D)}\}$$

(26)
be determined in species in solution, and an average of the chemical shifts of all protonation states of the equation citrate solution. The determined experimentally by adding excess acid to an aqueous values are 2.53 (A) and 2.63 ppm (B), respectively (Figure 4). However, the individual shifts hydrogens are 2.84 (A) and 3.01 ppm (B), and the individual chemical shifts of the centers of the doublets are shown in Figure 4 as a function of pH.

Instead of gaining reliable speciation information from the chemical shift measurements, the best one can hope for is an additional constraint in a simultaneous fitting process of pH = f(εi) and of δHI = f(εi) with a given theoretical model for the treatment of the electrolyte solution that includes the values δ(H2Cit−) and δ(HCit3−) as variables. In any case, such attempts cannot be expected to fully succeed because eq 29 assumes that the chemical shift δHI(HCit3−) of each species is independent of pH and the changing chemical environment. However, in related studies, we and others found that pH effects on chemical shifts can be quite large (up to 0.1 ppm).70

4.5. Further Applications and Desiderata. The simulations of the pH profiles (Figure 1) show that the b = 0.1 data achieve the best match with experiment. It would be desirable to assess the quality of a specific Debye–Hückel approximation not just on the concentration of one species (pH) but on the concentration dependence of several species. This seems particularly well advised in cases where the only measured species is present in very low concentration. From our perspective, it would be highly desirable and instructive to simulate complex multiequilibria systems for which the concentrations of several species were measured simultaneously and over a broad pH range. Ideally, the measured species should include systems containing multiply charged ions in significant concentrations.

In the present study, we employed equilibrium constants at infinite dilution Ksp and the Davies equation with two discrete b values. Comparison of computed and measured pH values then suggested which b value resulted in better agreement. If one had experimental data for more species, i.e., some of the ions H3−A− and H3−B− in the present example, then one would have much tougher constraints on the precise formulation of the DH approximation. Moreover, instead of using Ksp, one would also be in a position to explore effects of Kact via iterative setting of Kact = f(I) together with the determination of the activity coefficients (eq 2) in the process of solving the ODEs. In the range 0 ≤ I ≤ 0.6, changes of the pK values up to 0.29 and 0.25 units were reported for citric acid and phosphoric acid.

Each apparent methylene proton signal δHI corresponds to the average of the chemical shifts of all protonation states of the species in solution, and a first approximation of δHI is given by the equation

$$\delta_{HI} = \sum_{i=0}^{3} c_i \times \delta_{HI}(H_i\text{Cit}^{i-3})$$

where ci are the concentration fractions of the species i and δHI(HiCiti−3) are the chemical shifts of the respective methylene-H of the individual species. If this equation holds and if the δHI(HiCiti−3) values are known, then one should be able to obtain speciation information from eq 29 (i.e., the ci values). Values for the individual chemical shifts δHI(HiCit) and δHI(Cit3−) can be determined experimentally by adding excess acid to an aqueous citrate solution. The δHI(HiCit) values for the two diastereotopic hydrogens are 2.84 (A) and 3.01 ppm (B), and the δHI(Cit3−) values are 2.53 (A) and 2.63 ppm (B), respectively (Figure 4). However, the individual shifts δ(H2Cit−) and δ(HCit3−) cannot be determined in “pure” solutions of the respective anions.

Figure 3. Comparison of the equilibrium coefficient expressions (eqs 21 and 22) for the dissociations of (a) citric acid and (b) phosphoric acid in the mixtures. Line color distinguishes between pKsp,act (green), pKact (blue), and pKsp (red). Solid, b = 0.1; dashed, b = 0.2. The pKsp,act lines are also marked with circles for improved visibility.

Figure 4. 1H NMR shifts relative to DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid) for citric acid in 90% H2O:10% D2O over the pH range 2–9.

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respectively, and these data inform about the shape of trial functions \( K_{\text{act}} = f(l) \). For the present case, Figure 2 (bottom) suggests that precise measurements of \([HCl]^{\pm}\) and pH in the range \(4 \leq pH \leq 6.5\) would allow one to test such approaches and their effects on the shape of the \([H_2PO_4^-] = f(pH)\) curves.

One further application of the dynamical approach is the indirect determination of accurate binding constants, \( K_b \), for specific ion receptors in aqueous media. The dynamical method allows for the facile inclusion of receptor terms \( R[\tau] \) and \( RIA[\tau] \) to describe the concentrations of the receptor and the receptor–ion aggregate, respectively. With these additions, a simple comparison to the experimental pH profile would allow one to estimate the \( K_b \) for the receptor. Such a simple determination of binding constants would be invaluable to studies where direct observation of the aggregating species concentrations is difficult or impossible. Even in cases where direct determination of the formation constant is possible, this approach may facilitate the study of the ionic strength dependence of \( K_b \).

5. CONCLUSION

The dynamical approach was employed to describe the complex multiequilibria buffer system of citric acid and disodium hydrogen phosphate, and the experimental pH profile was modeled with astounding accuracy. The effects of ionic strength were shown to be highly important for the calculation of the pH, and the model suggests that the non-H\(^+\) species concentrations are affected by ionic strength effects to an even greater extent. We presented a few examples of common scenarios where neglecting the ionic strength effects would drastically effect the equilibrium species distribution and, therefore, knowledge of the extent of ionic strength effects is essential. We also presented an application for the dynamical approach in the indirect determination of binding constants as functions of ionic strength, which has an immediate and practical use for researchers developing new chemical sensors.

Improvement to the dynamical approach could involve concomitant improvements to approximations of Debye–Hückel theory. The Davies approximation was tested here with the empirical parameters \( b = 0.1 \) and \( b = 0.2 \), and we have shown that the \( b = 0.1 \) data matches more closely with experiment. This can be extended to other approximations, such as the Pitzer equation, to see if increased accuracy is attained in the calculation of \([H^+]\). We note that experimental data sets in which concentration profiles for two or more species are monitored would greatly enhance the confidence in the results obtained with the dynamical approach and thereby provide an excellent system to systematically test the extensions to Debye–Hückel theory.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jced.8b00146.

A figure illustrating \( H_2PO_4^- \) specific receptors (Figure S1), tables containing the complete results computed for the data set Sigma (Tables S3 and S4), a comparison of the numerical accuracy of the dynamical approach and the equilibrium method, and results of the \( ^1H \) NMR studies of citric acid (Figure S3 and Table S5) (PDF)

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Notes

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