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Effect of monomer composition on proton dissociation of weak polyacids

Sergio Paoletti[1]*, Roberto Gilli[2], Luciano Navarini[3] and Vittorio Crescenzi[4]

[1] *Institute of Biochemistry, University of Sassari, Viale S. Pietro 43/b, I-07100, Sassari, Italy*
[2] *POLY-biòs Research Centre, AREA di Ricerca, Padriciano 99, I-34012, Trieste, Italy*
[3] *POLY-tech s.c.a.r.l., AREA di Ricerca, Padriciano 99, I-34012, Trieste, Italy*
[4] *Department of Chemistry, University "La Sapienza", Piazzale A. Moro 5, I-00185, Roma, Italy*

The study of the proton dissociation process of weak polyacids (*eg α* carboxylic poly(monoprotic)acid) is based on the knowledge of the change in electrostatic free energy, G(el), as a function of the variation of the number of charges on the polymer chain. The original treatment proposed by Manning can be used to describe the proton dissociation process of weak poly(monoprotic)acids, in the absence of pH-induced conformational transitions. In order to describe the alpha dependence of pKa of weak co-poly(monoprotic)acids containing two different acidic groups in different amounts along the polymer chain, a simple modification of the model is proposed.

***Keywords*: proton dissociation, weak polyacids**

***Abbreviations used*: Due to the difficulty of using non-ASCI characters in the main text, we have used the following abbreviations:**

Annotation used in the text	*Usual annotation*
G(el)	G^{el}
10^−pH	10^{-pH}
pKa	pK_a
alpha	α
alphan	α_n
dG(el)/dalpha	$\partial G^{el}/\partial \alpha$
KA and KB	K_A and K_B
CA and CB	C_A and C_B
βA and βB	β_A and β_B
ΛpK	ΔpK
§max	ξ_{max}

Introduction

The proton dissociation of weak polyacids is a relevant process for study in the framework of the physico-chemical characterization of polyelectrolytes in solution. Among the solution behaviour of the polyelectrolytes, the potentiometric titration is closely related to the electrostatic interaction between a dissociating proton and ionized groups on a polymer chain.

Several ionic polysaccharides bear weakly acidic groups, namely the –COOH group. In a relevant number of instances, two different types of carboxylic functions are present in various amounts in the repeating unit of such polymers. Examples are, among others, uronic acid, the carboxymethyl and the pyruvic ketal groups. In general those groups will exhibit different intrinsic pK° values, thereby rendering the study of the potentiometric titration curve somewhat complicated. For pK° values without a great degree of separation and for comparable relative amounts of the groups, the apparent overall pKa(alpha) curve (alpha is the overall degree of ionization of the weak polyacid) may look quite peculiar. In particular 'bumps' in the curve

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*To whom correspondence should be addressed at present address. Department BBCM, University of Trieste, Via L. Giorgieri 1, I-34127, Trieste, Italy. Tel: +39 40 6763692; Fax: +39 40 6763691; E-mail: paolese@univ.trieste.it.

profile may appear, which might be incorrectly attributed to the presence of a pH-induced conformational transition. In fact this was proposed some time ago, and since then it has universally been accepted, that a 'bump' in the pKa (alpha) curve of a weak poly(mono-protic) acid (*ie* a polymer bearing only one type of weakly acidic groups) can be quite unambiguously attributed to a conformational transition induced by an increase in the polymer charge density via an increase in pH. This has been demonstrated to hold very well for synthetic polycarboxylates (*eg* polymethacrylic acid [1]), for acidic polypeptides (*eg* poly-L-glutamic acid [2]), for polyuronates (*eg* polygalacturonic acid, pectic acid [3]) and for microbial exopolysaccharides [4]. Recently, a theoretical treatment based on the counterion-condensation polyelectrolyte theory, as mainly developed by Manning [5], was able to account for the pKa(alpha) behaviour of such poly(monoprotic) acids [6], even with a successful extension to encompass the different flexibilities of the two conformations involved in the transition [7]. However, no extension of Manning's theory has so far been reported to account for the pKa(alpha) curve of a weak co-poly(monoprotic) acid, *ie* a polyacid bearing two types of acidic groups having different pK° values. It seemed to us not a mere theoretical exercise to attempt such a task, in particular with a view of providing an additional interpretation of 'bumps' in the pKa(alpha) curves, in contrast to the widespread interpretation as symptoms of a pH-induced conformational transition.

Theoretical background

A study of the proton dissociation process of weak polyacids (*eg* a carboxylic poly(monoprotic)acid) is based on a knowledge of the change in the electrostatic free energy, G(el), as a function of the variation in the number of charges on the polymer chain.

G(el) is affected by a number of variables of the system (salt concentration, Cs, polymer concentration, Cp, and temperature, T) and is related to the experimental variable alpha, *ie* the degree of ionization. Once the pH of a solution containing the ionic polymer of known concentration, Cp (defined as the moles of ionizable groups per liter) is measured as a function of the volume of titrant of a known concentration, it is possible to define the apparent equilibrium constant, pKa, in terms of experimental parameters as follows:

$$\mathrm{pKa(alpha)} = \mathrm{pH} - \log(\mathrm{alpha}/1 - \mathrm{alpha}) \qquad (1)$$

where the degree of ionization alpha = alphan + (10^−pH/Cp) is calculated from the directly observable degree of neutralization, alphan (titrant concentration/Cp), and from the pH (for pH < 7).

The apparent dissociation constant, pKa, can alternatively be expressed as:

$$\mathrm{pKa(alpha)} = \mathrm{pK}^{\circ} + [1/(2.303\mathrm{RT})](\mathrm{dG(el)}/\mathrm{d\,alpha}) \qquad (2)$$

where G(el) is the excess electrostatic free energy of the polymer and pK° is the intrinsic pKa associated with the removal of a proton from the uncharged chain. In the original treatment proposed by Manning [5] the excess electrostatic free energy is evaluated by summing up the electrostatic interactions among all the charges on the infinitely long and rigid polymer. For univalent mobile ions and fixed charges it has been written (for §max < 1):

$$\mathrm{G(el)} = -\S\mathrm{RTIn}[1 - \exp(-\mathrm{bK})] \qquad (3)$$

where K is the Debye–Huckel parameter, b the distance between the projections of charges along the chain contour length, R the universal gas constant and T the absolute temperature.

In this treatment the linear polymer chain can be seen as an infinite line characterized by a nominal charge density parameter § defined as:

$$\S = \mathrm{e}\hat{}2/(\mathrm{Dk'Tb}) \qquad (4)$$

with e the ele ctronic charge, D the bulk dielectric constant and k′ the Boltzmann constant.

In the absence of pH-induced conformational transitions the charge density parameter, which is clearly related to the polymer conformation, remains constant. For § < 1 the dependence of pKa on the degree of ionization is given by the equation:

$$\begin{aligned}\mathrm{pKa} = {} & \mathrm{pK}^{\circ} + (\mathrm{alpha}\S\mathrm{max}/2.303)\\ & \times[2\mathrm{In}(1 - \exp(-\mathrm{bK})) + \mathrm{bK}/(\exp(\mathrm{bK}) - 1)\\ & \times[0.5(\mathrm{alpha}/2\mathrm{R} + \mathrm{alpha}) - 1)]] \end{aligned} \qquad (5)$$

where R is the ratio between salt and polymer concentration (Cs/Cp). When salt free aqueous solutions are considered R is neglected.

For the sake of brevity the complex equation for §max > 1 is not reported. For this case see [8].

This model can be satisfactorily used to describe the proton dissociation process of weak poly(monoprotic)acids, in the absence of pH-induced conformational transitions.

Extension of the model

In order to describe the alpha dependence of pKa of weak co-poly(monoprotic)acids containing two different acidic groups in differing amounts along the polymer chain, a simple modification of the model is proposed in the present work.

Considering a mixture of two different weak non-polymeric monoprotic acids HA (dissociation constant: KA) and HB (dissociation constant: KB) in solution at two different concentrations CA and CB and assuming βA and βB to be the degree of ionization of the individual acidic groups, the total degree of ionization, alpha, can be written as:

$$\mathrm{alpha} = \mathrm{XA}(\beta\mathrm{A} - \beta\mathrm{B}) + \beta\mathrm{B} \qquad (6)$$

where XA is the molar fraction defined as CA/(CA + CB)] Being:

$$\text{pKA} - \text{pKB} = \log[(1 - \beta\text{A})\beta\text{B}/\beta\text{A}(1 - \beta\text{B})] \qquad (7)$$

from equations (6) and (7) it is possible to calculate βA (alpha) and βB(alpha), see Appendix. The pH of the system varies with alpha according to (8):

$$\begin{aligned}\text{pH(alpha)} &= \text{pKA} + \log[\beta\text{A(alpha)}/1 - \beta\text{A(alpha)}] \\ &= \text{pKB} + \log(\beta\text{B(alpha)}/1 - \beta\text{B(alpha)}) \qquad (8)\end{aligned}$$

and then

$$\text{pK}^{\circ}\text{a(alpha)} = \text{pH(alpha)} + \log(1 - \text{alpha})/\text{alpha} \qquad (9)$$

where pK°a, the total apparent dissociation constant, is a function of pKA, pKB and XA.

Let us consider a weak co-poly(monoprotic) acid containing, in differing amounts, (XA) two acidic groups characterized by the dissociation constants KA and KB respectively (polymer concentration Cp = CA + CB). In this case, pK°a(alpha), defined in equation (9), can be considered the intrinsic pKa associated with the removal of a proton from a mixture of different monomeric acids, at given alpha, in the absence of polyelectrolytic effects. Under such an hypothesis in equation (5) pK° can be substituted by pK°a(alpha) so:

$$\text{pKa(alpha)} = \text{pK}^{\circ}\text{a(alpha)} + [1/(2.303RT)](\text{dG(el)}/\text{dalpha}) \qquad (10)$$

For the above defined weak co-poly(monoprotic) acid equation (10) can be used to simulate the pKa curves, provided that KA, KB and XA are known, and in the absence of a pH-induced conformational transition. For XA equal to 0 or to 1 equation (10) reduces to equation (5) and is valid for weak poly(monoprotic)acid.

Calculations and discussion

In Figure 1 the alpha dependence of the apparent dissociation constant, pKa, is reported at three different values of $\wedge$pKo defined as pKA − pKB (§max < 1). As clearly shown in Figure 1, an inflection point in the pKa curves can be appreciated when the difference between the dissociation constants of the acidic residues exceeds 1. Upon increasing the $\wedge$pKo value, the pKa curves assume an increased sigmoidal profile.

At a constant $\wedge$pKo value, Figure 2 shows the alpha dependence of the pKa curves for three different polymer compositions (§max < 1). The pKa curve at a high molar fraction of the stronger acidic residue (XA = 0.75) shows an inflection point at 0.7 < alpha < 0.8. By decreasing the molar fraction XA the inflection point shifts to lower alpha values, and the pKa curves show a ‘bump’ which resembles what is generally observed for weak poly(monoprotic)acid undergoing a pH-induced conformational transition.

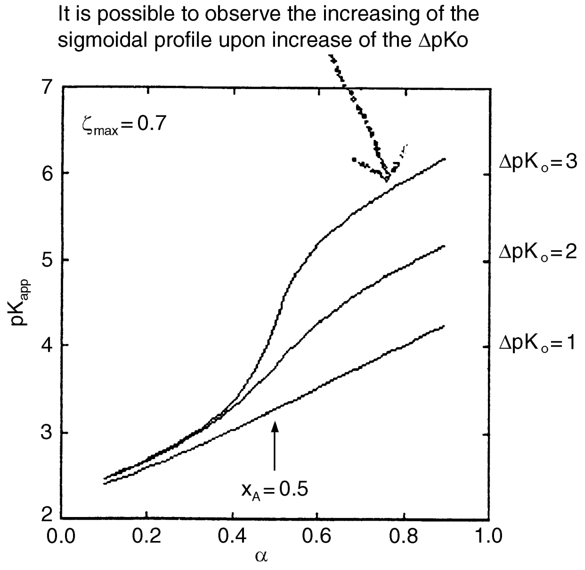
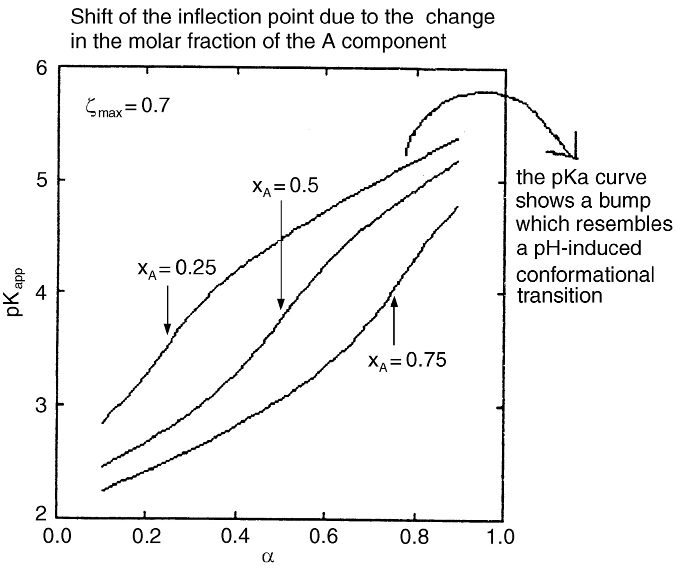

It is possible to observe the increasing of the sigmoidal profile upon increase of the ΔpKo

Figure 1. *a* dependence of apparent dissociation constant at three different values of ΔpK_a. ($C_s = 0\,M$, $C_p = 1 \times 10^{-3}\,eq\,l^{-1}$, $pK_A = 2$, $pK_B = 3$, 4 and 5 respectively.)


Shift of the inflection point due to the change in the molar fraction of the A component

the pKa curve shows a bump which resembles a pH-induced conformational transition

Figure 2. *a* dependence of apparent dissociation constant at three different molar fraction. x_A. ($C_s = 0\,M$, $C_p = 1 \times 10^{-3}\,eq\,l^{-1}$, $pK_A = 2$, $pK_B = 4$.)

The effect of the polymer composition when §max > 1, is shown in Figure 3.

Comparison with experimental data

In order to test the present extension of the original Manning approach, experimental data obtained on the microbial acidic exopolysaccharide succinoglycan, used as a model compound, have been fitted. The experimental data refer to

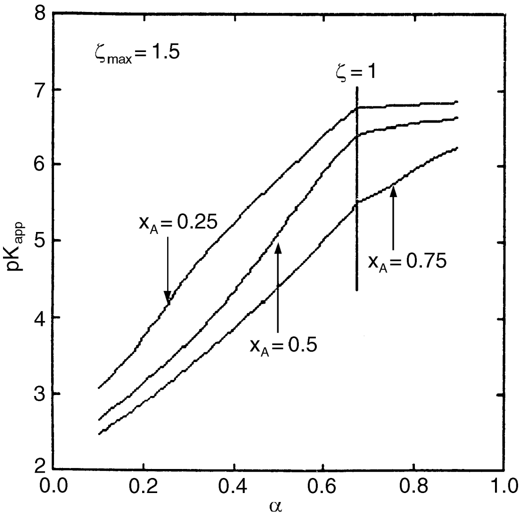


Figure 3. *α* dependence of apparent dissociation constant at three different molar fraction. x_A. ($C_s = 0\,M$, $C_p = 1 \times 10^{-3}\,eq\,l^{-1}$, $pK_A = 2$, $pK_B = 4$.)

potentiometric titrations with a standard NaOH of a purified commercial sample of succinoglycan (Shellflo-S by Shell Co.) in aqueous solution (both in water and in 0.1 M NaCl) carried out at 25 °C at a fixed polymer concentration of 2.0*10^ −3 eq l^{-1}.

Succinoglycan appears to be an appropriate model compound since it contains two different acidic groups because of the presence in its repeating unit of succinate and pyruvate substituents. Moreover, for this ionic polysaccharide, no evidence for a pH-induced conformational transition is to our knowledge, reported in the literature.

It has to be borne in mind that in order to fit the experimental data it is not necessary to resort to adjustable parameters. In fact the four structural parameters necessary for the fitting (§max, XA, pKA and pKB) can be independently obtained. For succinoglycan, the charge density parameter (§max = 0.74) [9], the determined XA, (pyruvate/succinate molar ratio of 0.4 by means of ^{1}H-NMR) and the pKA values of succinic acid (first ionization) and of pyruvic acid reported in the literature (4.2 and 2.5 respectively), have been used.

In Figure 4a and b two different sets of experimental data (in water and in 0.1 M NaCl respectively) have been fitted by following the present theoretical approach. The fitting is compared with that obtained by using the original Manning approach (in this case the pK° value is the average of the values relative to succinic and pyruvic acid). As clearly shown in Figure 4a and b, the original Manning approach fails to fit the experimental data. On the contrary, our model is a suitable mimic of the 'bump' observed, especially in water. On the basis of these results, it is clear that the 'bump' observed in the experimental pKa(alpha) curve is an indication of a partial separation of the titration of the two different classes of acidic groups along the polysaccharide chains and cannot be attributed to a pH-induced cooperative conformational transition.

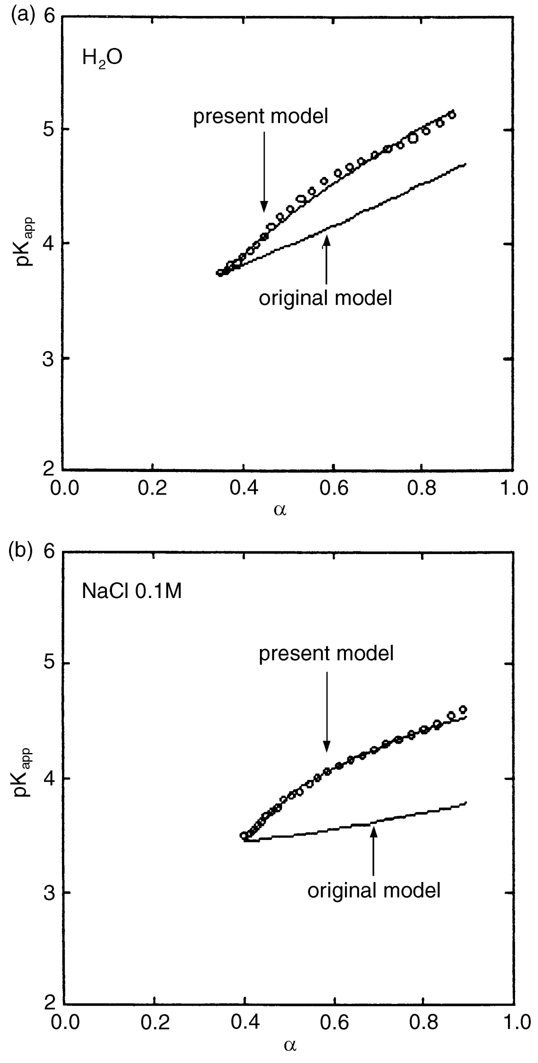


Figure 4. (a and b) Fitting of experimental data.

Conclusions

A method is proposed by which the pKa(alpha) curve of a co-poly(monoprotic) acid having two different ionizable groups of known pK° and a given molar ratio can be satisfactorily described.

The pH titration curves of many naturally occurring linear polyacids (*eg* carboxylated polysaccharides) sharing this feature with the present model, can in principle benefit by the proposed formalism. In particular, the latter may help in ascertaining whether 'bumps' in the experimental pKa(alpha) curves may stem from a pH-induced cooperative conformational transition (as often claimed) or simply from the complex interplay of different monomeric (acidic) composition and polyelectrolytic behaviour.

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Appendix

Considering two different weak non polymeric acids
$HA \Leftrightarrow (A-) + (H+)$
$HB \Leftrightarrow (B-) + (H+)$,
their dissociation constants
1) $KA = [H+][A-]/[HA]$ and $KB = [H+][B-]/[HB]$,
their individual degree of ionization
2) $\beta A = [A-]/([HA] + [A-])$ and
$\beta B = [B-]/([HB] + [B-])$,
we can calculate the total degree of ionization:
3) $\mathrm{alpha} = ([A-] + [B-])/(CA + CB)$
where $CA = [HA] + [A-]$ and $CB = [HB] + [B-]$ and the total polymer concentration is $Cp = CA + CB$.
We can evaluate alpha as function of the total concentration Cp and the fraction of the A component (XA)
4) $XA = CA/(CA + CB)$ and $XB = (1-XA) = CB/(CA + CB)$
5) $CA = XA\ Cp$ and $CB = (1 - XA)\ Cp$
6) $[A-] = \beta A\ CA = \beta A\ XA\ Cp$
7) $[B-] = \beta B\ CB = \beta B(1 - XA)\ Cp$
8) $\mathrm{alpha} = ([A-] + [B-])/Cp = \beta A{*}XA + \beta B - \beta B{*}XA$
$= \beta A{*}XA + \beta B\ (1 - XA)$.
Knowing that
9) $pKA = pH + \log((1 - \beta A)/\beta A)$ and
$pKB = pH + \log((1 - \beta B)/\beta B)$
we can express the $\wedge pK$ value as a function of βA and βB
10) $\wedge pK = pKA–pKB = \log((1 - \beta A)\beta B/\beta A(1 - \beta B))$.
Remembering that
11) $\beta A = (\mathrm{alpha} + \beta B(XA - 1))/XA$
we can substitute (11) in (10) and express $\wedge pK$ as a function of βB and XA
12) $\wedge pK = \log([1 - (\mathrm{alpha} + \beta B(XA - 1))/XA)]\beta B/$
$[(\mathrm{alpha} + \beta B(XA - 1))/XA](1 - \beta B)$
It is now possible to solve this second degree equation in βB:
13) $10\hat{}(\wedge pK) = [XA - \mathrm{alpha} - \beta B(XA - 1)]\beta B/$
$[\mathrm{alpha} + \beta B(XA - 1)](1 - \beta A)$
if $10\hat{}(\wedge pK) = q$
14) $q\ \mathrm{alpha} + q\ \beta B\ XA–q\beta B - \mathrm{alpha}\ \beta Bq - XAq(\beta B)\hat{}2$
$+ q(\beta B)\hat{}2 - XA\ \beta B + \mathrm{alpha}\ \beta B + XA\ (\beta B)\hat{}2$
$- (\beta B)\hat{}2 = 0$
15) $(\beta B)\hat{}2(XA - XAq + q - 1) + \beta B(XAq - XA - q\mathrm{alpha}$
$+ \mathrm{alpha} - q) + q\ \mathrm{alpha} = 0$
16) $(\beta B)\hat{}2(XA - 1)(1 - q)$
$+ \beta B[(XA - \mathrm{alpha})\ (q - 1) - q] + q\mathrm{alpha} = 0$
if $q - 1 = t$
17) $\beta B = [q - (XA - \mathrm{alpha})t]\beta[((XA - \mathrm{alpha})t - q)\hat{}2 +$
$4\ \mathrm{alpha}\,q\ (XA - 1)t]\hat{}0.5/ - 2t(XA - 1)$
and finally obtain βB and βA
18) $\beta B(\mathrm{alpha}) = [q-(XA - \mathrm{alpha})t]$
$- [((XA - \mathrm{alpha})t - q)\hat{}2$
$+ 4\ \mathrm{alpha}\ q\ (XA - 1)t]\hat{}0.5/$
$- 2t(XA - 1)$
19) $\beta A\ (\mathrm{alpha}) = (\mathrm{alpha} + \beta B(XA - 1))/XA$
Remembering, from (9), that
20) $pH\ (\mathrm{alpha}) = pKA + \log(\beta A/1 - \beta A)$
$= pKB + \log(\beta B/1 - \beta B)$
we can obtain:
21) $pK^\circ(\mathrm{alpha}) = pH(\mathrm{alpha}) + \log[(1 - \mathrm{alpha})/\mathrm{alpha}]$.