



# A predictive model of organic acids separation by chromatography with strong anionic resins in sulfate form

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## ABSTRACT

Organic acids commonly have quite symmetrical chromatography profiles at low pH ( $< 1.5$ ) with strong anionic resins, but a significant tailing can be observed with succinic and citric acids. Classical adsorption models, like the Langmuir model, fail to predict this behavior, which can have a major influence on mean retention times and profile shapes, therefore on chromatography performances.

A new retention model was developed to better predict organic acid separation with strong anionic resin. This model combines a refined Langmuir adsorption model and an ion-exchange model. Organic acid adsorption is assumed to be due to hydrogen bonding with sulfate and hydrogen sulfate counter-anions on the resin. The adsorption capacity depends mostly on molecular size: up to sixteen formic acid molecules could be adsorbed per counter-anions, meanwhile only two succinic acid or one citric acid molecules could be adsorbed.

This adsorption model was then embedded in a generic and accurate modeling approach (continuous column with mass balance equations solved by the conservation element/solution element (CE/SE) method). All parameters of this column model were identified by fitting the simulation to experimental results (equilibrium curves and pulse tests). Then, the column model was validated with original experimental results from a binary mixture pulse test (formic and succinic acids). Results show that simulations are much more predictive for multi-component pulse tests, both in terms of profile shape and retention time, which cannot be captured without considering ion-exchange.

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## 1. Introduction

Chromatographic separation is a well-established technology in many domains, such as the food and feed industry [1], pharmaceutical production [2], protein and enzyme purification [3], and heavy metal separation [4]. Chromatography can separate or purify target components, even with very close properties like stereoisomers, without using a large amount of energy, chemicals, or solvent. For example, chromatography is often used to separate sugars or organic acids from hemicellulose hydrolysates or fermentation broths [5]. These applications often require high purity, high recovery rate, and low operational costs for economic reasons. Thus, chromatography is the ultimate solution when conventional separation techniques such as distillation, liquid-liquid extraction, membrane fil-

tration, or crystallization are not sufficiently selective or consume too much energy, chemicals, or solvent.

Preparative chromatography consists of pushing a mixture (generally liquid) through a column filled with a porous solid phase using a mobile phase called the eluent. Its principle is to separate different compounds according to their affinities towards both phases that affect their travel speed and retention time inside the column. The solid phase can be composed of dense or microporous resin beads. Hundreds of resin types exist on the market to separate ions or organic molecules, depending on their structures and retention mechanisms. Retention of a molecule on a resin surface often implies adsorption by Van Der Waals forces owing to its hydrophobic matrix.

Ion-exchange resins are covered with counter-anions or counter-cations, making them hydrophilic [6]. For instance, molecules such as sugars or organic acids can be separated by different adsorption mechanisms (H bond, van der Waals force, chelation) with the counter-ion fixed on the resin surface, and ionic compounds can be separated by ion-exchange or Donnan exclu-

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sion effect. For example, strong anionic resins (coated with quaternary ammonium groups) or weak anionic resins (coated with amine groups) are often used to separate organic acids by interacting with their acid group.

However, the application of chromatography at an industrial scale is severely limited by its low productivity, which impacts capital expenditures, and by how it dilutes separated compounds, which impacts both capital and operational costs because further concentration steps are required. To tackle these limiting factors, several dozen multi-column chromatography processes have been developed over the last three decades, but their development and tuning are difficult. Modeling the elution profile inside columns is a valuable tool to make predictive simulations and optimize the performance of multi-column chromatography systems. Further investigations and model development are still needed to improve prediction accuracy, evidenced by continuing research activity in this field [7–10].

For instance, our previous work found that outlet profiles of some organic acids have uncommon tailing that cannot be explained by usual Langmuir adsorption models [11]. This phenomenon was explained theoretically by considering the small fraction of organic acid dissociated into anions ( $< 1\%$  at pH below 1.5). Historically, this fraction was neglected, but it can be strongly retained on resin ion-exchange sites [11]. A new model was then proposed to better predict the behavior of organic acids with strong anionic resins. In addition, Langmuir adsorption mechanisms were described in more detail, based on Honeywell Universal Oil Products (Honeywell UOP) patent assumptions [12]. Mono-component simulation of an organic acid profile was performed using a discontinuous column model (Martin and Synge plate model [13]) and a finite difference method to solve differential equations. Uncommon tailing of succinic and citric acid profiles was better predicted. This model still needs to be adjusted and then validated with more experimental data and improved for multi-component simulation.

Chromatography simulation is based on solving mass balances in the mobile phase (convection-diffusion equations) and local exchanges with the stationary phase. It generally results in a non-linear and coupled system of partial differential equations. The classical numerical solving methods are finite element [14–16], finite difference [17,18], or finite volume [19] for the spatial discretization, with an explicit or implicit time scheme. The CE/SE (conservation element/solution element) method, proposed by NASA in 1995 [20], has been applied for simulating explosions [21,22], crystallization [23] and chemical reactions [24,25]. It was first used to simulate chromatography with the Langmuir adsorption model in 2004 [26]. The CE/SE method allows simultaneous treatment of space and time integration. In the case of packed bed chromatography [27], global trials of the CE/SE method showed a better trade-off between accuracy, stability, and calculation speed than traditional methods using an upwind scheme. Compared to conventional approaches, CE/SE method was proved, at equivalent accuracy, to save the CPU time by 77% for the pseudo-linear system of glucose-fructose separation, and by 96% for non-linear enantiomer separation [37].

The present work aims to improve the prediction of the outlet profile of different organic acids and to confirm the role of ion-exchange with strong anionic resin. A more detailed Langmuir adsorption model is proposed based on our previous theoretical work [11], assuming that adsorption is due to a hydrogen bond between organic acids and sulfate anions, as mentioned first in a UOP patent [12]. Experiments were performed first to identify all model parameters (equilibrium constant, mass transfer coefficients, axial dispersion coefficient), then to validate assumptions, and finally to check model prediction. In addition, a continuous column model, solved by the CE/SE method, was developed to more ac-

**Table 1**  
Chemicals used in this work.

	Producer	N °CAS	Purity (%)
Formic acid	Sigma-Aldrich	64–18–6	$> 98$
Succinic acid	Acros organics	110–15–6	99
Citric acid	Acros organics	5949–29–1	99.5
Sulfuric acid	VWR Prolabo	7664–93–9	95
Na <sub>2</sub> SO <sub>4</sub>	Acros organics	7757–82–6	99+

**Table 2**  
Devices used in this work.

Device	Manufacturer	Model
Pump	MasterFlex L/S	7518–10
Column	YMC Europe Ltd.	ECO25
pH/conductivity sensor	Gilson	Verity 1810
UV sensor	Gilson	159 UV–VIS
Fraction collector	Gilson	FC 203B
HPLC	Dionex	Ultimate 3000

curately simulate multi-component separation by chromatography. This new model tackles discrepancies observed in the case of succinic or citric acid separation with strong anionic resin.

## 2. Materials and methods

### 2.1. Experimental setup

The separation of organic acids by chromatography with strong anionic resin was studied using a classical chromatography setup. Experimental devices and chemicals used in this study are detailed in Tables 1 and 2.

The product or the eluent is fed at the top of column by the volumetric pump. The liquid phase flows downwards in the column, while soluble compounds interact with the resin. The output liquid goes through a pH and conductivity sensor, then a UV absorbance analyzer, and finally is sampled by a fraction collector for offline analysis. All sensors and the fraction collector are connected to a computer to monitor pH, conductivity, UV absorbance, and sample collection.

The eluent was a H<sub>2</sub>SO<sub>4</sub> solution at pH 1.5 ( $\approx 0.02$  mol/L) for all experiments. For information, its ionic strength is 0.0314 mol/L. Product pH was also adjusted at 1.5 to limit pH and conductivity variation, and to keep a similar ionic strength during compound elution. The on-line measurement of UV absorbance was used to select samples to analyze by HPLC. The HPLC system (Ultimate 3000, Dionex) is equipped with a refractometer RI-101 (Shodex) at 35 °C. The analytical column is an Aminex HPX-87H (Biorad) connected to a guard column (Micro-Guard cartridge Biorad) kept at 45 °C within an oven. The mobile phase is a 2 mmol/L H<sub>2</sub>SO<sub>4</sub> solution, prepared with Milli-Q water (Direct 8, Millipore).

The flowrate was set at 0.5 BV/h (BV represents the total bed volume, equal to 0.35 L), corresponding to  $3.10^{-4}$  m/s interstitial flow velocity ( $Re_p = 6.6$ ). The internal column diameter was 2.5 cm, and the bed length was 70 cm. A jacketed column linked to a thermostatic bath was used to maintain the temperature at 25 °C. The column was filled with the strong anion resin DIAION UMA 150, functionalized with trimethylamine groups (type 1), manufactured by Mitsubishi Chemical, whose characteristics are summarized in Table 3. The resin is supplied in Cl<sup>−</sup> form, but it was put in sulfate form before running experiments by using the following procedure: 2 BV of 1 mol/L Na<sub>2</sub>SO<sub>4</sub> solution was fed into the column at 1 BV/h, then 8 BV of eluent was fed to wash the bed resin and reach pH equilibrium.

The bed porosity was measured by a pulse test with 10 mL 1 mol/L Na<sub>2</sub>SO<sub>4</sub> solution eluted at 1 BV/h. The porosity was es-

**Table 3**

Main characteristics of the strong anionic resin used in this work (DIAION UMA 150).

Matrix	Styrene-DVB Gel
Functional group	Quaternary ammonium (Type I)
Salt splitting capacity	> 1.4 eq/L
Water content	37–47%
Mean particle size	220–260 $\mu\text{m}$
Uniformity coefficient	< 1.1

timated between 0.39 and 0.41, which corresponds to the range given by the resin manufacturer (Table 3). Finally, the extra-column volume (in tubes, valves, sensors, etc.) was measured by performing a similar pulse test without the chromatography column. It was estimated around 0.05 BV (15 mL). All chromatographic profiles were corrected by removing this extra-column volume from the eluted volume.

## 2.2. Determination of transfer and axial dispersion coefficient

A pulse test consists of injecting a small volume of product (0.05 BV) followed by the eluent at a constant flow rate until all compounds leave the column. It is one of the most common methods used in chromatography to study compound retention and dispersion along the column. A pulse test was chosen in our study to determine physical properties such as adsorption isotherm, mass transfer coefficients, bed porosity and extra-column volume.

During pulse tests, component concentrations at column output are plotted as a function of the eluted volume. The curve obtained is usually called a chromatographic profile, which looks like a peak more or less wide and symmetric. This profile is mainly characterized by its mean retention volume  $V_R$  and its standard deviation  $\sigma$ :

$$V_R = \int_0^\infty V \cdot c \cdot dV / \int_0^\infty c \cdot dV \quad (1)$$

$$\sigma^2 = \int_0^\infty V^2 \cdot c \cdot dV / \int_0^\infty c \cdot dV - V_R^2 \quad (2)$$

where  $V$  is the eluted volume (in BV), and  $c$  is the component concentration in the mobile phase at column output (concentration unit does not matter).

The peak width depends almost on axial dispersion and mass transfer resistance while the component passes through the column. The volume of product fed into the column ( $< 0.05$  BV) is small enough to have a negligible influence on the shape of the pulse test profile. Dead volumes were minimized to limit their influence on dispersion. The global dispersion is usually characterized by the height equivalent to a theoretical plate (HETP) as a function of  $V_R$ ,  $\sigma^2$  and the bed length  $L$ :

$$HETP = \frac{L \cdot \sigma^2}{V_R^2} \quad (3)$$

The van Deemter et al. curve [28] describes the relationship between HETP (inversely proportional to the global dispersion) and the interstitial velocity  $v$  (in  $\text{m} \cdot \text{s}^{-1}$ ). This curve is estimated experimentally by plotting the HETP of component profiles obtained at different flowrates during the pulse test (Fig. 1).

One of the most known versions of the van Deemter equation reads as:

$$HETP = A + \frac{B}{v} + C \cdot v \quad (4)$$

This equation considers that the global dispersion has three main causes: the mechanical dispersion ( $A$  term), the molecular diffusion ( $B$  term), and the mass transfer resistance ( $C$  term), as depicted in Fig. 1. The mathematical expressions to obtain the values

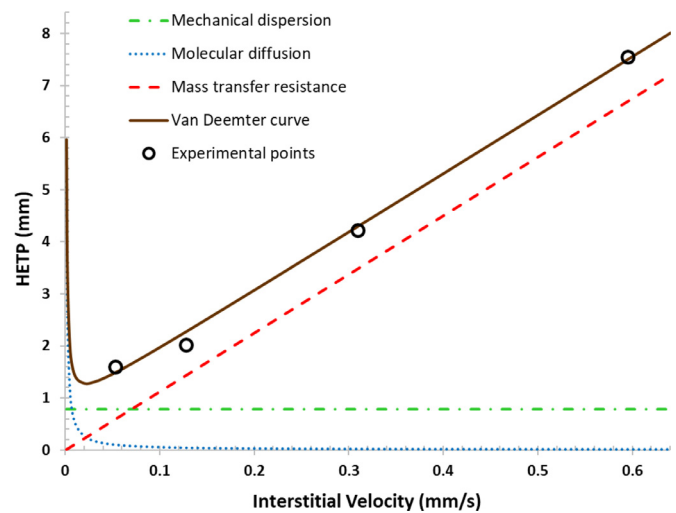


Fig. 1. van Deemter Curve of succinic acid eluted with  $\text{H}_2\text{SO}_4$  solution at pH 1.5 with the system described in materials and methods.

of  $A$ ,  $B$ , and  $C$  are important for prediction purposes. The original article by van Deemter et al. [28] gives the following expressions:

$$A = 2 \cdot \beta \cdot d_p \quad B = 2 \cdot \frac{D_m}{\tau} \quad C = 2 \cdot \left[ \frac{\varepsilon / \alpha}{(1 + F/K_j)^2} \right] \quad (5)$$

where  $\beta$  is a packing factor that equals 1 for a homogeneous packed bed,  $d_p$  is the mean particle diameter (in m),  $D_m$  is the molecular diffusion coefficient (in  $\text{m}^2 \cdot \text{s}^{-1}$ ),  $\tau$  is the bed tortuosity,  $\varepsilon$  is the bed porosity,  $F = \varepsilon / (1 - \varepsilon)$  is the volumetric ratio of mobile phase to stationary phase,  $K_j$  is the linear equilibrium constant (concentration ratio between stationary and mobile phase), and  $\alpha$  is the liquid-side local mass transfer coefficient ( $\text{s}^{-1}$ ).

Within narrow operating conditions of preparative chromatography (flowrate between 0.5 and 2 BV/h), van Deemter curves are almost linear over the whole interstitial velocity range. Thus, the most simple version of van Deemter equation was sufficient to describe experimental results and estimate its coefficients.

From experimental points, the range of  $C$  can be estimated quite accurately by linear regression, then the range of  $\alpha$  can be deduced from previous equation.  $A$  and  $B$  are difficult to estimate separately because of the lack of experimental points in the non-linear part of van Deemter curve. However, in the present modeling work, only axial dispersion coefficient  $D$  is required, and it can be expressed as the sum of molecular diffusion and mechanical dispersion, according to the following equation:

$$D = \frac{D_m}{\tau} + \beta \cdot d_p \cdot v = \frac{A}{2} \cdot v + \frac{B}{2} \quad (6)$$

Thus, the range of  $D$  can be estimated quite accurately from experimental points by fitting the van Deemter equation with the least squares method, while considering the range of  $C$  previously estimated by linear regression.

## 2.3. Physical formulation at the bed level

### 2.3.1. Mass balance

Two types of unidimensional column model are often used to describe the mass transfer inside a chromatography column [13]:

- Continuous models, solved by usual finite methods, where the column is discretized into a large number of very small elements. In this case, the axial dispersion depends on the axial dispersion coefficient  $D$  and the global mass transfer coefficient  $k_a$ .

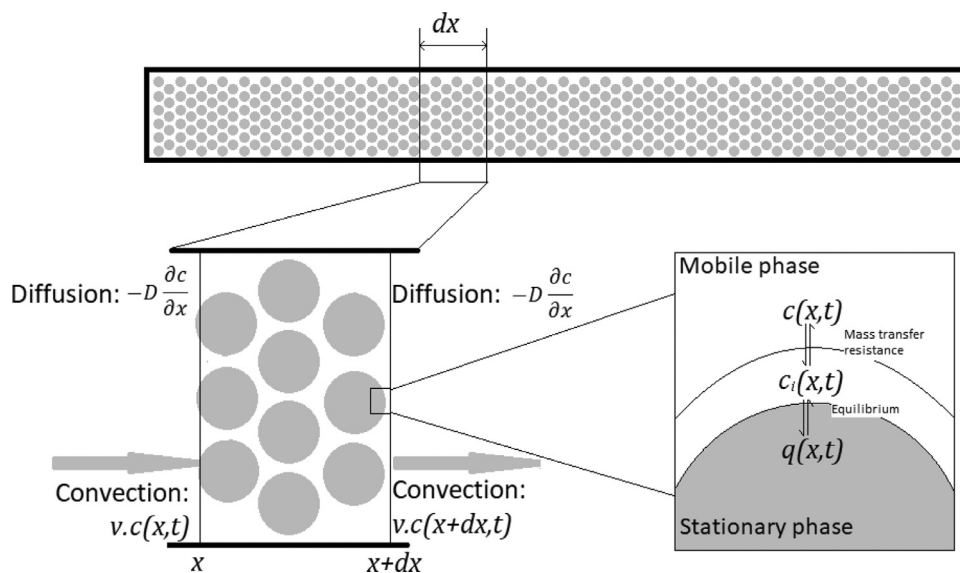


Fig. 2. Mass balance (convection-diffusion equation) and mass transfer model.

- Discontinuous models where the chromatography column is assimilated to a plate column. Each theoretical plate acts as a perfectly stirred reactor. In this case, the axial dispersion becomes an emerging property of the theoretical plate number  $N$ .

Discontinuous models, easy to code and to solve, require low CPU time. However, because the axial dispersion is an indirect effect of the theoretical plate number  $N$ , this model imposes the same axial dispersion for all compounds. Thus, this model is not appropriate for multi-component chromatography simulation if their axial dispersion coefficients  $D$  are not similar. That is the reason why a continuous model was chosen in the present work.

At the level of the chromatography column (Fig. 2), the local 1-D mass balance of one component  $j$  in the mobile phase, for a section of extension  $\partial x$ , can be expressed as two mass balances for liquid side and solid side:

$$\varepsilon \frac{\partial c_j}{\partial t} + \varepsilon v \frac{\partial c_j}{\partial x} = \varepsilon D \frac{\partial^2 c_j}{\partial x^2} + \varepsilon R_j^{a \leftrightarrow b} - (1 - \varepsilon) R_j^{l \leftrightarrow s} \quad (7)$$

$$\frac{\partial q_j}{\partial t} = R_j^{l \leftrightarrow s} \quad (8)$$

where  $c_j$  is the concentration of component  $j$  in the mobile phase (in  $\text{mol.m}^{-3}$ ),  $D$  is the axial dispersion coefficient (in  $\text{m.s}^{-2}$ ),  $v$  is the interstitial velocity (in  $\text{m.s}^{-1}$ ),  $R_j^{a \leftrightarrow b}$  is the mass variation of component  $j$  due to acid-base reactions (in  $\text{mol.m}^{-3}.\text{s}^{-1}$ ),  $R_j^{l \leftrightarrow s}$  is the mass exchange of component  $j$  between the mobile phase and the stationary phase (in  $\text{mol.m}^{-3}.\text{s}^{-1}$ ), and  $q_j$  is the concentration of component  $j$  in the stationary phase (in  $\text{mol.m}^{-3}$ ).

The  $R_j^{a \leftrightarrow b}$  term is due to the acid-base reactions in the mobile phase between  $\text{SO}_4^{2-}$  and  $\text{HSO}_4^-$  anions, organic acid  $\text{HA}$  and its conjugate base  $\text{A}^-$ , and  $\text{H}^+$  cations. When the mobile phase goes through the column, organic acids  $\text{HA}$  can be retained by Langmuir adsorption; meanwhile,  $\text{A}^-$  can be exchanged by  $\text{SO}_4^{2-}$  or  $\text{HSO}_4^-$  anions on resin sites. As the concentration ratio between acid and basic compounds changes in the mobile phase, the acid-base reactions tend to restore equilibrium by transforming the acid into a base or the inverse.

Finally, to avoid any  $R_j^{a \leftrightarrow b}$  term, mass balances in the mobile phase were written for the total content of each organic acid  $\text{A}$  ( $c_A^{\text{tot}} = c_{\text{A}^-} + c_{\text{HA}}$ ), the total sulfate content  $\text{SO}_4$  ( $c_{\text{SO}_4}^{\text{tot}} = c_{\text{SO}_4^{2-}} + c_{\text{HSO}_4^-}$ ) and the total acid content  $\text{H}$  ( $c_{\text{H}}^{\text{tot}} = c_{\text{H}^+} + c_{\text{HA}} + c_{\text{HSO}_4^-}$ ). These

balances are not affected by acid-base reactions. Then, the concentration of each compound can be estimated using the equilibrium constant of each acid-base reaction. Indeed, these reactions are assumed to always be at an equilibrium state because they are considered to be much faster than all other phenomena.

The mass exchange  $R_j^{l \leftrightarrow s}$  between the mobile phase and stationary phase depends on the adopted mass transfer model. With instantaneous mass transfer model, concentrations  $q_j$  in the stationary phase are assumed to be in equilibrium with concentrations  $c_j$  in the mobile phase. In this case, it is not necessary to estimate  $R_j^{l \leftrightarrow s}$  because concentrations  $q_j$  can be deduced directly from concentrations  $c_j$  by solving the equilibrium equations system. With a non-instantaneous mass transfer model, a new equation is needed to estimate  $R_j^{l \leftrightarrow s}$ , which also depends on equilibrium equations between the mobile and stationary phase.

In a previous work [11], the instantaneous mass transfer model was adopted with a discontinuous model, as the influence of mass transfer resistance can be considered directly in the theoretical plate number  $N$  that summarizes the global effect of all dispersion mechanisms.

In the present work, a non-instantaneous mass transfer model was chosen to consider compounds with different mass transfer resistances. Mass transfer resistance between the mobile and stationary phase is driven by molecular diffusion and hydrodynamic properties at the interface (summarized in the Sherwood number, depending on Reynolds and Schmidt numbers). The lumped model was chosen to estimate the mass exchange  $R_j^{l \leftrightarrow s}$  from the global mass transfer coefficient  $k_{aj}$  of component  $j$  (in  $\text{s}^{-1}$ ) between the mobile phase and the stationary phase, due to diffusion inside resin and at its interface [29]:

$$R_j^{l \leftrightarrow s} = k_{aj} \cdot (q_j^{\text{eq}}(c) - q_j) \quad (9)$$

where  $q_j^{\text{eq}}$  represents the theoretical concentration of component  $j$  in the stationary phase (in  $\text{mol.m}^{-3}$ ), which would be in equilibrium with the mobile phase. This equilibrium is calculated from the concentration of all components in the mobile phase by solving all equilibrium equations (adsorption, ion-exchange, and acid-base reactions).

The mass exchange  $R_j^{l \leftrightarrow s}$  can also be expressed at the liquid side, as:

$$R_j^{l \leftrightarrow s} = \alpha_j \cdot (c_j - c_j^i) \quad (10)$$



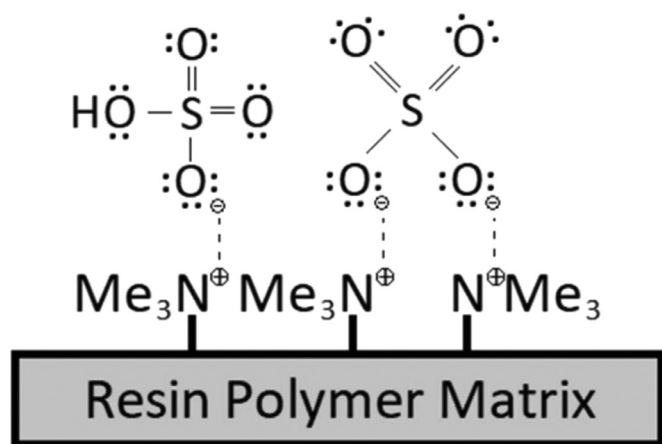


Fig. 3. Representation of the strong anion resin (type 1) in sulfate form.

where  $c_j^i$  is the concentration of the component  $j$  at the interface (in  $\text{mol.m}^{-3}$ ).

Thus,  $k_{aj}$  can be estimated from the  $\alpha_j$  value by assuming a linear equilibrium, whose coefficient  $K_j$  is estimated from the adsorption isotherm of component  $j$  (cf. Section 2.3.2).

$$q_j = K_j * c_j^i \quad q_j^{eq} = K_j * c_j \quad k_a = \frac{\alpha_j \cdot (c_j - c_j^i)}{(q_j^{eq} - q_j)} = \frac{\alpha_j}{K_j} \quad (11)$$

### 2.3.2. Adsorption mechanisms

Counter-anions  $\text{SO}_4^{2-}$  or  $\text{HSO}_4^-$  cover the surface of strong anionic resin in sulfate form (Fig. 3). Their proportion depends on ion-exchange equilibrium and their concentration in the mobile phase. The adsorption mechanism of organic acid on this type of resin is not well documented in the literature. UOP patents [30,31] suggested that the molecular form of organic acid was retained only on counter-anions  $\text{HSO}_4^-$  and  $\text{SO}_4^{2-}$ . Julien et al. [11] developed this hypothesis in their model, assuming that the interaction was probably hydrogen bonding between the acid hydrogen atom of organic acids and the lone electron pairs of sulfate and hydrogen sulfate oxygen atoms.

A Langmuir model is generally used to describe adsorption on chromatography resins, which involves several assumptions [32]:

1. The surface containing adsorption sites is perfectly flat with no corrugation,
2. All adsorption sites are energetically equivalent,
3. Only mono-layer coverage occurs,
4. No interaction occurs between molecules adsorbed on adjacent sites.

As shown in Fig. 3, each  $\text{SO}_4^{2-}$  or  $\text{HSO}_4^-$  contains eight lone electron pairs, so up to eight hydrogen bonds can be theoretically observed on each anion. As an improvement compared to previous works [11], this feature was directly integrated into the adsorption equation in the present work. As a first approximation, the adsorption sites on  $\text{SO}_4^{2-}$  and  $\text{HSO}_4^-$  were assumed to be similar. Thus, instead of writing two adsorption equations for  $\text{SO}_4^{2-}$  and  $\text{HSO}_4^-$  separately, the total concentration of  $\text{SO}_4^{2-}$  and  $\text{HSO}_4^-$  in the stationary phase, called  $q_{\text{SO}_4}^{\text{tot}}$  (in  $\text{mol/L}$ ), was used. In the case of a single component model, the Langmuir equilibrium model for component  $j$  was described as:

$$q_j = \frac{N_{\text{tot}} \cdot q_{\text{SO}_4}^{\text{tot}} \cdot k_{sj} \cdot c_j}{1 + N_j \cdot k_{sj} \cdot c_j} \quad (12)$$

where  $N_{\text{tot}}$  is the number of lone electron pairs on each counter-anion ( $N_{\text{tot}} = 8$ ),  $k_{sj}$  is the adsorption constant of component  $j$ , and

Table 4

Coefficients of the Langmuir equilibrium model for organic acid adsorption on  $\text{HSO}_4^-$  and  $\text{SO}_4^{2-}$  counter-anions.

Organic acids	$N$ estimation	$N$ assumed	$k_s$ (L/mol)
Formic acid	0.25–1.15	0.5 or 1	0.05–0.25 ( $N = 0.5$ ) 0.025–0.125 ( $N = 1$ )
Succinic acid	2.1–11	4 or 8	0.14–0.50 ( $N = 4$ ) 0.07–0.25 ( $N = 8$ )
Citric acid	5.2–10	8	0.14–0.28

$N_j$  is the number of lone electron pairs occupied by each adsorbed molecule.

In the case of a multi-component model, the competitive Langmuir equilibrium model for  $m$  components can be described as:

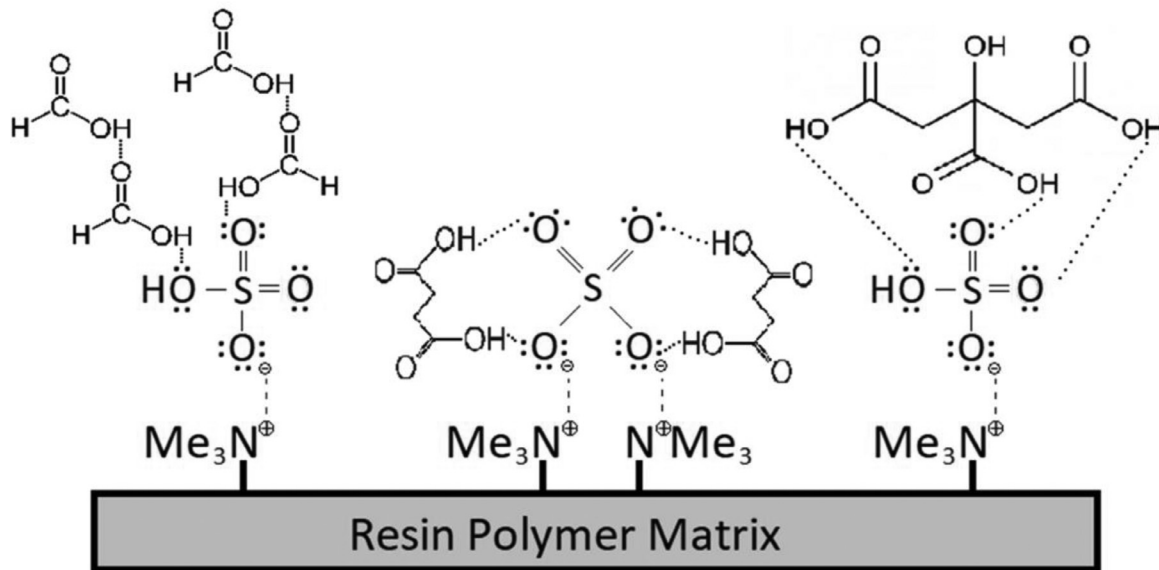
$$q_j = \frac{N_{\text{tot}} \cdot q_{\text{SO}_4}^{\text{tot}} \cdot k_{sj} \cdot c_j}{1 + \sum_{i=1}^m N_i \cdot k_{si} \cdot c_i} \quad (13)$$

The value of  $q_{\text{SO}_4}^{\text{tot}}$  can be estimated from the value of the ion-exchange resin capacity  $q_{\text{max}}$ , which is the concentration of quaternary ammonium groups  $\text{RMe}_3\text{N}^+$ . The resin supplier provides an estimation (ca. 2.3 eq/L where eq corresponds to the equivalent molar charge amount). This value was checked by mixing a given volume of resin in  $\text{OH}^-$  form with a given volume of  $\text{H}_2\text{SO}_4$  solution whose concentration is known. The titration of residual acid concentration in the solution enabled estimating the initial  $\text{OH}^-$  concentration in resin ( $2.1 \pm 0.2$  eq/L).

Equilibrium curves of organic acids were determined by frontal analysis to estimate Langmuir model coefficients ( $N$  and  $k_s$ ) by fitting the model to experimental points. This experimental work is part of another ongoing study on many organic acids to refine their competitive Langmuir adsorption model, and will be the object of another paper. As  $N$  and  $k_s$  values are correlated in the linear zone of equilibrium curves, their estimation can be quite inaccurate when it is impossible to obtain sufficient experimental points in the non-linear zone. Consequently,  $N$  and  $k_s$  are given in Table 4 with their uncertainty range. Because  $N$  represents the number of lone electron pairs occupied by each adsorbed molecule,  $N$  was assumed afterwards to be equal to only rounded values that could be explained physically. When the experimental range of  $N$  can include two possibilities (for formic and succinic acids), two corresponding ranges of the  $k_s$  value were identified.

According to the Langmuir adsorption model and  $N$  estimation from Table 4, formic, succinic, and citric acids seem to occupy a different number  $N$  of lone electron pairs on oxygen atoms of sulfate or hydrogen sulfate counter-anions. The values are rather consistent with their different molecular size and the number of carboxylic acid groups (Fig. 4).

Citric acid occupies more adsorption sites, most likely because of its large molecular size, which hinders access to free lone pairs, and its three carboxylic acid groups that can make H bonds with up to three lone pairs.  $N = 8$  corresponds to only one citric acid molecule per sulfate or hydrogen sulfate counter-anion (all eight lone pairs occupied: H-bond or cluttered). Inversely,  $N = 0.5$  or 1 for formic acid, which is the smallest acid and has only one carboxylic acid group. It corresponds to one or two formic acid molecules per lone pairs (none cluttered and only single H-bonds). The formation of formic acid dimers could explain that up to two molecules can occupy the same adsorption site [33]. Succinic acid is an intermediate case because of its medium size and two carboxylic acid groups.  $N = 4$  or 8 corresponds to one or two succinic acids per sulfate or hydrogen sulfate counter-anions (four or eight lone pairs occupied).  $k_s$  values of formic, succinic, and citric acid



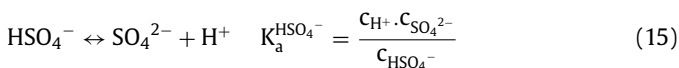
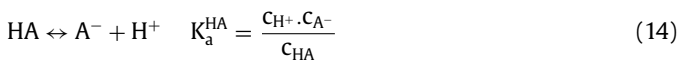
**Fig. 4.** Illustration of organic acid adsorption by hydrogen bonding on  $\text{SO}_4^{2-}$  or  $\text{HSO}_4^-$  counter-anions, which have eight lone electron pairs each.  $N = 0.5$  for formic acid could be explained by dimer conformation, and means that up to 16 molecules could be adsorbed (only 4 of them are represented).  $N = 8$  for citric acid corresponds to one molecule maximum adsorbed on each counter-anion. Indeed, citric acid can form up to 3 hydrogen bonds and the other five free sites could be cluttered.  $N = 4$  for succinic acid corresponds to 2 molecules maximum adsorbed on each counter-anion, because it can form up to 2 hydrogen bonds and could clutter less free sites.

are quite similar and correspond to the strength of the H-bond between their carboxylic acid group and lone electron pairs of sulfate or hydrogen sulfate counter-anions. Their value has been refined further in the present work to remove the possible influence of ion-exchange that may have caused  $k_s$  overestimation.

### 2.3.3. Ion-exchange mechanisms

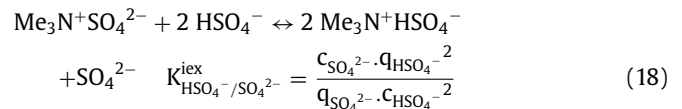
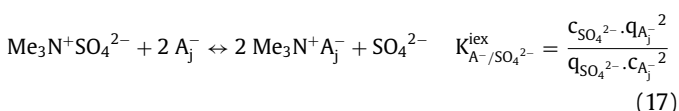
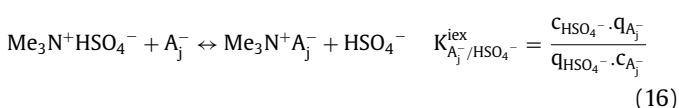
In the present model, ion-exchange was also considered to explain the retention of some organic acids with a particular chromatographic profile (large tailing) with strong anionic resin in sulfate form. Indeed, despite the very low dissociation of organic acids at pH below 2, a small concentration of corresponding organic anions could greatly influence their profile in the case of a very strong affinity for resin ion-exchange sites.

In the mobile phase, organic acid HA and hydrogen sulfate anion  $\text{HSO}_4^-$  can dissociate into its corresponding conjugate base  $\text{A}^-$  or  $\text{SO}_4^{2-}$  and one proton  $\text{H}^+$ . The corresponding acid-base equilibria can be written as follow:



In the present model, usual  $\text{pK}_a$  values of formic, succinic, and citric acids and hydrogen sulfate at 20 °C (operating temperature) were considered: 3.76, 4.16, 3.13, and 1.99, respectively.

Organic anions  $\text{A}_j^-$  can replace  $\text{HSO}_4^-$  or  $\text{SO}_4^{2-}$  counter-anions on quaternary ammonium ion-exchange sites. Ion-exchange reactions correspond to the following equilibria:



where  $K_{\text{X}^-/\text{Y}^-}^{\text{ie}}$  is the ion-exchange coefficient of anions  $\text{X}^-$  by anions  $\text{Y}^-$  on resin sites.

In the stationary phase, the concentration of ion-exchange sites  $q_{\text{max}}$  is always conserved:

$$q_{\text{max}} = 2 \cdot q_{\text{SO}_4^{2-}} + q_{\text{HSO}_4^-} + \sum_j q_{\text{A}_j^-} \quad (19)$$

All corresponding equilibrium constants can be deduced from resin manufacturer data listed in the appendices [34,35], which provides the value of  $K_{\text{X}^-/\text{OH}^-}^{\text{eq}}$  between many anions  $\text{X}^-$  and  $\text{OH}^-$ .

### 2.4. Computational strategy

As detailed in the introduction, several computational methods could be used to solve the system of equations in space and in time. The CE/SE method was chosen in the present work for its ability to deal with space and time integrals simultaneously. The integral is calculated between normal mesh points and intermediate mesh points, and it takes two integrals to move one step forward in space or time.

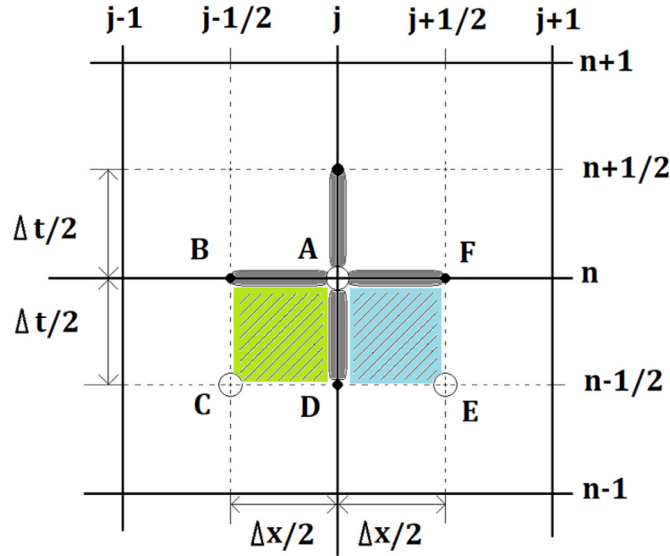
This method is based on Gauss's divergence theorem [36]. In the case of a 1D space model, it is also called Green's theorem. For a partial differential equation (PDE) like:

$$\frac{\partial u}{\partial t} + \frac{\partial f}{\partial x} = p \quad (20)$$

Green's theorem tells us that the line integral along a closed curve  $\partial C$  of a function equals the integral of the derivative over the corresponding plane region  $\partial D$ :

$$\oint_{\partial C} (-u \cdot dx + f \cdot dt) = \iint_{\partial D} \left( \frac{\partial u}{\partial t} + \frac{\partial f}{\partial x} \right) \cdot dx \cdot dt = \iint_{\partial D} p \cdot dx \cdot dt \quad (21)$$

Fig. 5 shows the space and time discretization used and the mesh points where all variables are estimated. By definition, the



**Fig. 5.** The SE (solution element, AB and other 3 sides of squares starting from point A) and CE (conservation element, rectangles ABCD and ADEF) at position  $j$  and time  $n$ . Values at point A are calculated from points C and E at  $n-1/2$ ; values at C or E are obtained from points at time  $n-1$  via the CE and SE at the point at time  $n-1/2$  (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

solution element SE ( $j, n$ ) is the gray space-time interior region centered at point A ( $j, n$ ). It includes a horizontal line segment, a vertical line segment, and their immediate neighborhood points (B, D, F). In this solution element, we chose to approximate  $u$  and  $f$  values by a first-order Taylor formula from its center point A ( $j, n$ ):

$$u^*(x, t) \sim u_j^n + u_{xj}^n \cdot (x - x_j) + u_{tj}^n \cdot (t - t_n) \quad (22)$$

$$f^*(x, t) \sim f_j^n + f_{xj}^n \cdot (x - x_j) + f_{tj}^n \cdot (t - t_n) \quad (23)$$

where  $u_{xj}^n$  and  $f_{xj}^n$  correspond to the space derivative of  $u$  and  $f$  at the mesh point ( $j, n$ ), and  $u_{tj}^n$  and  $f_{tj}^n$  correspond to the time derivative of  $u$  and  $f$  at the mesh point ( $j, n$ ).

A zero-order Taylor formula was chosen to approximate the source term  $p$ , which means that  $p$  was treated as a constant in each solution element:

$$p^*(x, t) \sim p_j^n \quad (24)$$

The conservation element CE ( $j, n$ ) corresponds to the rectangle FADE (blue) and ABCD (green), where the source term  $p$  was consequently considered equal at mesh points A, B, D, and F, but different at mesh points C ( $p_{j-1/2}^{n-1/2}$ ) and E ( $p_{j+1/2}^{n-1/2}$ ).

Finally, Green's theorem applied within the rectangle FBCE (blue + green) by approximating  $u$ ,  $f$  and  $p$  leads to the following explicit equation that enabled  $u_j^n$  to be estimated from values of  $u$ ,  $f$  and  $p$  at the previous semi-time step:

$$u_j^n = \frac{1}{2} \left[ u_{j+1/2}^{n-1/2} + u_{j-1/2}^{n-1/2} \right] - s_{j+1/2}^{n-1/2} + s_{j-1/2}^{n-1/2} + \frac{\Delta t}{4} \cdot \left( p_{j+1/2}^{n-1/2} + p_{j-1/2}^{n-1/2} \right) \quad (25)$$

where

$$s_{j\pm 1/2}^{n-1/2} = \left( \frac{\Delta t}{2 \cdot \Delta x} \right) \cdot f_{j\pm 1/2}^{n-1/2} + \left( \frac{\Delta x}{8} \right) \cdot u_{xj\pm 1/2}^{n-1/2} + \left( \frac{\Delta t^2}{8 \cdot \Delta x} \right) \cdot f_{tj\pm 1/2}^{n-1/2} \quad (26)$$

In the case of chromatography convection-diffusion equation, the CE/SE method can be applied to solve the mass balance in the mobile phase by defining:

$$f = v \cdot c - D \cdot \frac{\partial c}{\partial x} \quad u = c \quad p = -\frac{(1 - \varepsilon)}{\varepsilon} \cdot k_a \cdot (q^{eq} - q) \quad (27)$$

**Table 5**

Operating conditions of single component pulse tests.

	Formic acid	Succinic acid	Citric acid
Sample volume (BV)	0.035	0.02	0.02
Concentration (mol/L)	0.75	0.27	0.55
Eluent	pH 1.5 H <sub>2</sub> SO <sub>4</sub> (0.02 mol/L)		
Flowrate (BV/h)	0.5		

As a consequence,  $f$ ,  $u_t$ ,  $f_x$ , then  $f_t$  can be deduced from  $u_x$  at the mesh point ( $j, n$ ):

$$f = v \cdot u - D \cdot u_x \quad f_x = \frac{\partial f}{\partial u} \cdot \frac{\partial u}{\partial x} = \left( v \cdot \frac{\partial u}{\partial u} - D \cdot \frac{\partial u}{\partial u \partial x} \right) u_x \sim v \cdot u_x \quad (28)$$

$$u_t = p - f_x \text{ (Eq. 20)} \quad f_t = \frac{\partial f}{\partial u} \cdot \frac{\partial u}{\partial t} = \left( v \cdot \frac{\partial u}{\partial u} - D \cdot \frac{\partial u}{\partial u \partial x} \right) u_t \sim v \cdot u_t \quad (29)$$

This set of equations prove that only  $u$  and  $u_x$  are needed to solve Eq. (25). There are many possibilities to calculate the derivative  $u_x$  from  $u$ . In the present model, it was calculated by using a modified harmonic mean [37]:

$$u_x = \frac{|u_x^+|u_x^- + |u_x^-|u_x^+}{|u_x^+| + |u_x^-|} \quad u_x^- = (u_j^n - u_{j-1}^n)/\Delta x \quad u_x^+ = (u_{j+1}^n - u_j^n)/\Delta x \quad (30)$$

where  $u_x^-$  and  $u_x^+$  are the partial derivatives on the left and right sides, respectively. The modified harmonic mean equals zero when  $u_x^-$  and  $u_x^+$  have opposite signs and equals the traditional harmonic mean when  $u_x^-$  and  $u_x^+$  have the same sign.

Thus, only one variable  $u$  is needed to solve the system, which is calculated via Eq. (25) with an explicit scheme. Starting from points at time step  $n$ , Eqs. (22)–(30) allow us to move to time step  $n + 1/2$ . Points at time  $n + 1$  are then calculated in the same way as points at time  $n + 1/2$ .

Meanwhile, the mass balance in the stationary phase can be solved separately by a 1st order finite-difference method, at each mesh point ( $j, n$ ):

$$\frac{q_j^n - q_j^{n-1}}{\Delta t} = k_a \cdot (q^{eqn} - q_j^n) \quad (31)$$

Boundary conditions are used to obtain values of first and last mesh points, as proposed by Chuanyi et al. [37]:

$$\frac{\partial c_1^n}{\partial x} \sim \frac{c_2^n - c_1^n}{\Delta x} = \frac{v}{D} (c_1^n - c_{feed}) \quad (32)$$

$$\frac{\partial c_{jend}^n}{\partial x} \sim \frac{c_{jend}^n - c_{(jend-1)}^n}{\Delta x} = 0 \quad (33)$$

### 3. Results and discussion

#### 3.1. Influence of Langmuir and ion-exchange coefficients

A tailing can be observed in the chromatography outlet profile of some organic acids with a strong anionic exchange resin. Theoretically, this could be due to a high value of their adsorption affinity  $k_s$  or ion-exchange coefficient  $K^{lex}$ . Fig. 6A and 6B show the impact of values  $k_s$  and  $K^{lex}$  on the outlet profile during the single component pulse test simulation of citric acid with parameters of Tables 4, 5 and 7. In Fig. 6A,  $K^{lex}$  is fixed at 1, a negligible value, to study only the influence of  $k_s$  on the profile shape and position. Then, the influence of  $K^{lex}$  is depicted in Fig. 6B. Pulse tests

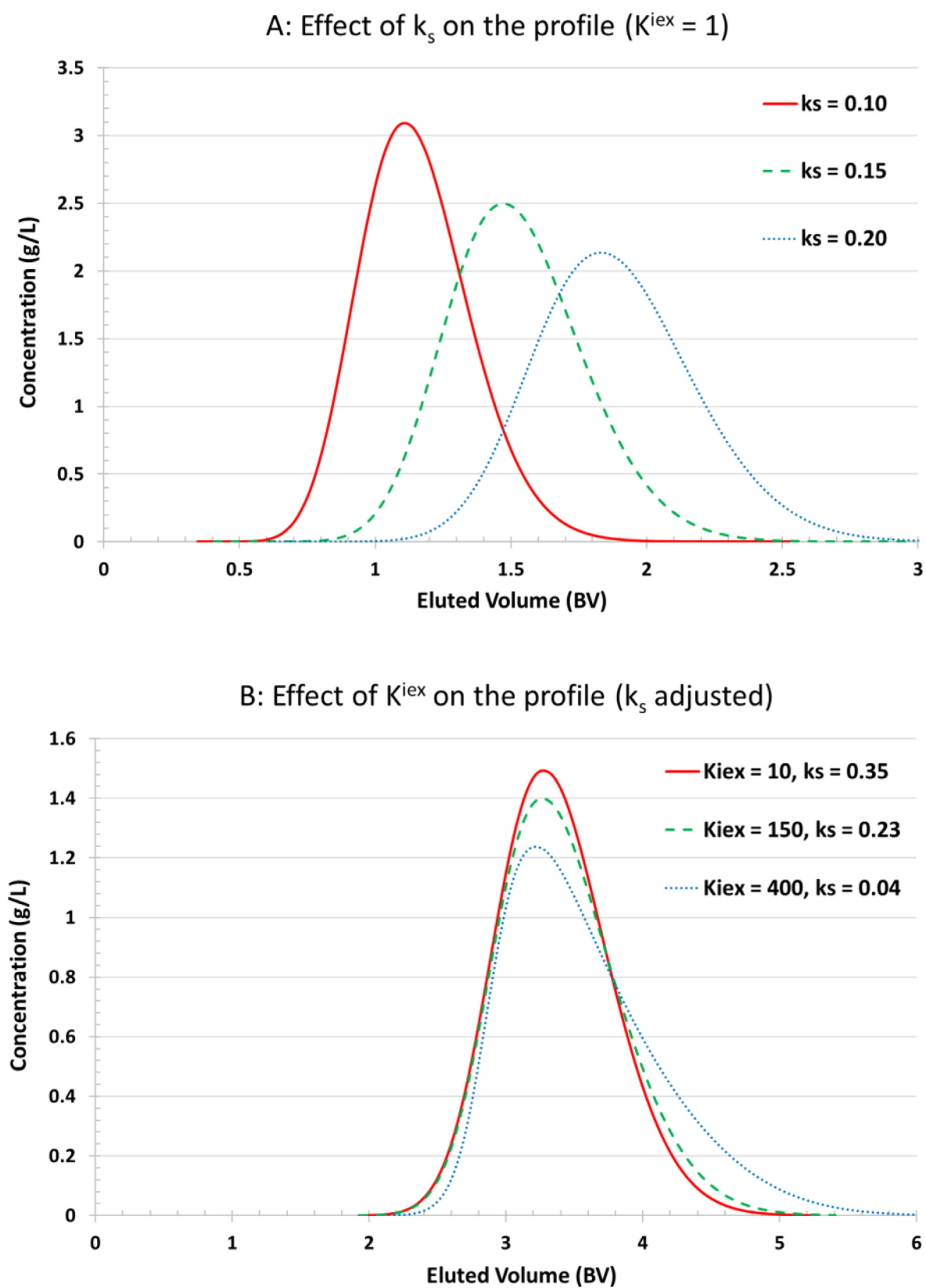


Fig. 6. Influence of  $k_s$  (Fig. 6A on the top) and  $K^{iex}$  (Fig. 6B at the bottom) on organic acid outlet profile.



**Table 6**  
Comparison of  $K^{iex}$  and  $k_s$  estimations of formic, succinic and citric acids.

Organic acid	$K^{iex}$ identified from pulse test	$K^{iex}$ supplier	$k_s$ estimated from equilibrium curves	$k_s$ identified from pulse test simulations
Formic acid	$15 \pm 10$	5	0.05–0.25 ( $N = 0.5$ ) 0.025–0.125 ( $N = 1$ )	0.2–0.25 ( $N = 0.5$ or 1)
Succinic acid	$900 \pm 100$	Not given	0.14–0.50 ( $N = 4$ ) 0.07–0.25 ( $N = 8$ )	0.26–0.28 ( $N = 4$ or 8)
Citric acid	$300 \pm 50$	250	0.14–0.28 ( $N = 8$ )	0.12–0.14 ( $N = 8$ )

**Table 7**  
Values of  $k_a$  and  $D$  of formic, succinic and citric acids.

Organic acid	$k_a$ van Deemter ( $10^{-3} \text{ s}^{-1}$ )	$k_a$ adjusted ( $10^{-3} \text{ s}^{-1}$ )	$D$ van Deemter ( $10^{-7} \text{ m}^2/\text{s}$ )	$D$ used ( $10^{-7} \text{ m}^2/\text{s}$ )
Formic acid	31–35	45	1–1.1	1
Succinic acid	7.5–9.5	8	0.68–1.4	0.8
Citric acid	2.8–3.4	5.6	4–5	4

with different values of  $K^{iex}$  were simulated. As the objective was to highlight the effect of  $K^{iex}$  only on the profile shape, the value of  $k_s$  was adjusted for each value of  $K^{iex}$  to obtain the same retention volume.

As expected, Fig. 6A shows that the higher is the adsorption coefficient  $k_s$ , the higher is the retention volume. However, the value of the coefficient  $k_s$  barely changes the profile shape and its relative symmetry. In comparison, Fig. 6B shows that  $K^{iex}$  significantly impacts the profile shape by increasing its tailing.

To summarize, the retention volume depends on both  $K^{iex}$  and  $k_s$  while the profile tail is influenced almost solely by  $K^{iex}$ . Indeed, very high  $k_s$  values could also lead theoretically to significant profile tailing, but these values would not be consistent with experimental retention volume, which corresponds to a  $k_s$  ranging between 0 and 0.3 L/mol.

The impact of ion-exchange constant  $K^{iex}$  depends on the pH of the liquid phase and the pKa of the organic acid. When the pH is much lower than pKa ( $\text{pH} < \text{pKa} - 2$ ), organic acids are mainly in molecular form. In this case, a very small proportion is dissociated into the anionic form, and the peak is less sensitive to the value of  $K^{iex}$ .

### 3.2. Identification of Langmuir and ion-exchange coefficients

In the present study,  $K^{iex}$  was estimated to reproduce the experimental profile tailing obtained for formic, succinic, and citric acids, starting from the resin supplier's estimation. Meanwhile,  $k_s$  was adjusted to fit the experimental retention volume. Initially,  $k_s$  was set to the experimental value estimated previously from equilibrium curves, considering different possible  $N$  values (Table 4). Fig. 7 shows experimental mono-component pulse tests that were used to refine estimations of  $k_s$  and  $K^{iex}$  given in Table 6. The operating conditions of these pulse tests are detailed in Table 5.

The mean value of  $D$  obtained from the van Deemter curve was used for simulation. Only the value of  $k_a$  was slightly adjusted to fit better the peak left front (Table 7).

In Table 6, the identified ranges of  $K^{iex}$  correspond quite well to the supplier's data for formic and citric acids.  $k_s$  ranges identified from pulse test simulations were not influenced by different possible  $N$  values considered for each organic acid. Indeed, the denominator ( $1 + N.k_s.c$ ) of the Langmuir equation remained close to 1 because of weak component concentration during pulse test simulations. For formic and succinic acids, the  $k_s$  range estimated from pulse test simulation is consistent with its range identified from equilibrium curves, for  $N = 0.5$  and 4, respectively. Meanwhile, the  $k_s$  range of citric acid identified from pulse tests lies at the bottom of its range estimated from equilibrium curves. Thus, 0.5, 4 and 8

were considered afterward as the unique, consistent  $N$  values for formic, succinic and citric acids, respectively. For citric acid, the slight  $k_s$  overestimation from equilibrium curves can be explained by the strong influence of ion-exchange (illustrated by the significant tailing of the citric acid profile, cf. Fig. 7).

### 3.3. Analysis of ion-exchange effect on the chromatography profile

Fig. 7 presents simulation curves of pulse tests for different organic acids, to compare the Langmuir adsorption model with the hybrid model, which considers that organic acid can be retained by Langmuir adsorption but also by ion-exchange.

Both models can predict the experimental results for formic acid. This is not surprising as its tailing is negligible, and its profile is almost symmetrical. The formic acid profile is marginally influenced by ion-exchange due to its very low  $K^{iex}$  ( $< 30$ ). Moreover, it is much less dissociated into anions than citric acid because of its higher pKa (3.76 vs. 3.13). Thus, at pH 1.5, only 0.5% formic acid is dissociated, making the ion-exchange effect even more negligible.

In comparison, succinic acid has the highest pKa (4.16) but also the highest  $K^{iex}$  according to Table 6 ( $900 \pm 100$ ). Therefore, despite a low proportion dissociated into anions (0.2% at pH 1.5), the strong retention of succinate anion on resin ion-exchange sites can explain its slight profile tailing.

Finally, the citric acid profile has the largest tailing because of its lower pKa (3.13) and quite high  $K^{iex}$ . Indeed, citric acid is the most dissociated into anions (2.3% at pH 1.5) and citrate anions are strongly retained by ion-exchange.

Fig. 7 confirms that the tailing of succinic and citric acid profiles cannot be reproduced by the Langmuir adsorption model. In contrast, the hybrid model is in good agreement with experimental results. It confirms that organic anions retention by ion-exchange must be considered to make predictive simulation, even if they are poorly dissociated at  $\text{pH} = 1.5$ .

## 4. Multi-component pulse test prediction

To confirm that the hybrid model is more predictive than the model with only Langmuir adsorption, a pulse test with a mixture of formic acid and succinic acid was both simulated and carried out (Fig. 8). Table 8 gives parameter values used in both models, whose ranges were estimated previously from experimental data analysis (Tables 6 and 7).

Experimental profiles depicted in Fig. 8 correspond to a pulse test performed with 10 mL pH 1.5 solution, composed of 0.65 mol/L formic acid and 0.267 mol/L succinic acid, eluted with pH 1.5  $\text{H}_2\text{SO}_4$  solution at 0.5 BV/h, using the same setup described above.

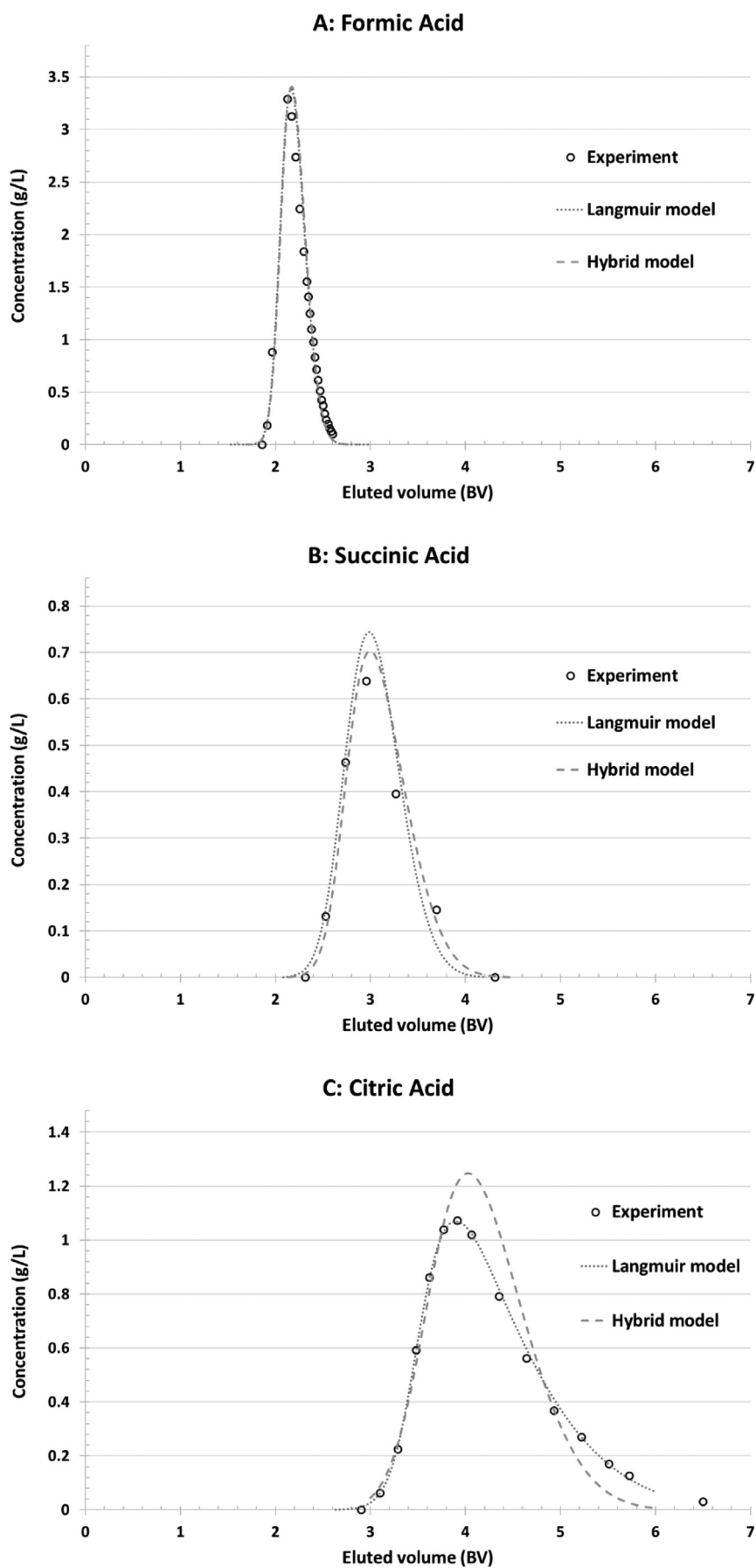


Fig. 7. Influence of ion-exchange on outlet profile of formic (Fig. 7A), succinic (Fig. 7B) and citric acids (Fig. 7C).

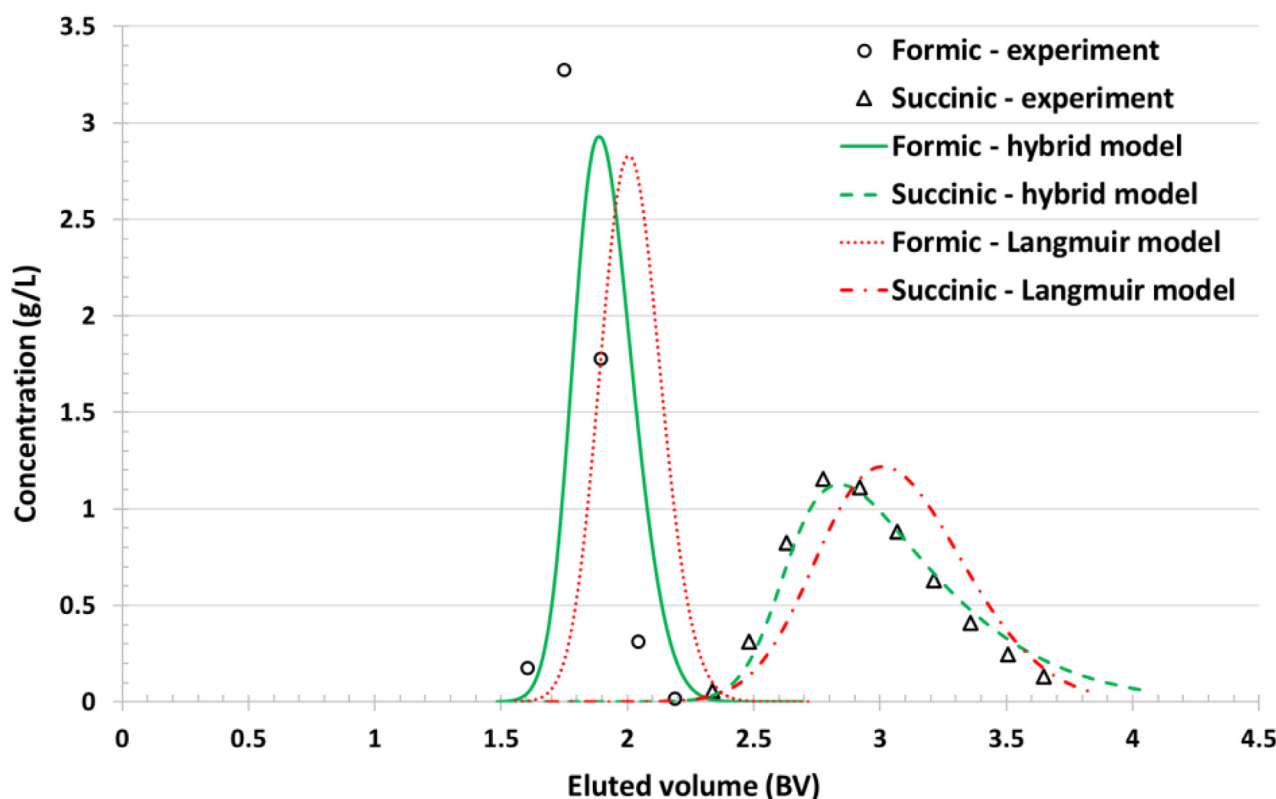


Fig. 8. Multi-component pulse test to compare predictions of a model with only Langmuir adsorption to the hybrid model, which also considers ion-exchange.

**Table 8**  
Parameters used for multi-component pulse test simulation.

Model	Organic acid	$N$	$k_s$ (L/mol)	$K^{icx}$	$k_a$ (s <sup>-1</sup> )	$D$ (10 <sup>-7</sup> m <sup>2</sup> /s)
Hybrid model (adsorption + ion-exchange)	Formic acid	0.5	0.24	25	0.045	1
	Succinic acid	4	0.26	800	0.008	0.5
Langmuir model (only adsorption)	Formic acid	0.5	0.25	0	0.045	1
	Succinic acid	4	0.44	0	0.008	0.5

Fig. 8 confirms clearly that the hybrid model predicts the chromatographic profile of both organic acids much better. More specifically, the hybrid model is able to predict the significant tailing of the succinic acid profile, unlike the Langmuir model. Moreover, the mean retention volume of formic acid is better predicted by the hybrid model, even though there is still a slight difference (0.1 BV) compared to experimental points.

The slight discrepancies observed can be due to assumptions and simplifications in the present hybrid model. For example, all adsorption sites were considered equivalent. To be more accurate, adsorption sites on the upper side of  $SO_4^{2-}$  and  $HSO_4^-$  counter-anions should be considered more accessible than sites closer to the resin matrix (Fig. 4). In addition, some studies [38,39] showed that the original Langmuir competitive equation is not suitable for multi-layer adsorption. Thus, a more accurate model considering different types of adsorption sites might be an interesting approach to better predictions of multi-component mixture separation by chromatography.

## 5. Conclusion

Strong anionic resins are often used in sulfate form in chemical or food and feed industries to separate organic acids by chromatography. However their retention mechanisms are not well known and must be better understood to improve model prediction. In this work, a hybrid model was developed and used to ex-

plain elution profiles of succinic and citric acids, which display unusual tailing. Compared to classic Langmuir adsorption models, it also considers the effect of organic acid dissociation into anions that can be retained on resin ion-exchange sites. The model was solved with the CE/SE method.

Estimation of adsorption equilibrium coefficient ( $N$  and  $k_s$ ) were consistent with organic acids adsorption by hydrogen bonding between the hydrogen atom of their carboxylic acid group and one lone electron pair of oxygen atoms of sulfate or hydrogen sulfate counter-anions. Present results confirm that the tailing of succinic and citric acid profiles is mainly caused by ion-exchange of their very low dissociated fraction, even at low pH (< 1.5). Therefore organic acid dissociation and ion-exchange must be considered to develop a predictive model for succinic and citric acids. The hybrid model prediction was successfully validated in the case of a multi-component pulse test.

This hybrid model is currently implemented in a multi-column chromatography simulation program to predict and optimize the performance of simulated moving bed technologies. It is also useful to design new multi-fraction processes.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## CRediT authorship contribution statement

**Wuyang Zhong:** Conceptualization, Methodology, Data curation, Writing – original draft. **Patrick Perre:** Supervision, Visualization, Investigation, Writing – review & editing. **Fanny Duval:** Data curation. **Julien Lemaire:** Methodology, Data curation, Visualization, Writing – review & editing.

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## Appendices

SBA (strong base anion) resins selectivity coefficients [34,35].

Anion	Type 1	Type 2
$\text{HSiO}_3^-$	<1.0	<1.0
$\text{OH}^-$	1.0	1.0
$\text{F}^-$	1.6	0.3
$\text{CH}_3\text{CH}_2\text{COO}^-$	2.6	0.3
$\text{CH}_3\text{COO}^-$	3.2	0.5
$\text{HCOO}^-$	4.6	0.5
$\text{H}_2\text{PO}_4^-$	5.0	0.5
$\text{IO}_3^-$	5.5	0.5
$\text{HCO}_3^-$	6.0	1.2
$\text{Cl}^-$	22	2.3
$\text{NO}_2^-$	24	3
$\text{BrO}_3^-$	27	3
$\text{HSO}_3^-$	27	3
$\text{CN}^-$	28	3
$\text{HSO}_4^-$	35	9
$\text{Br}^-$	50	6
$\text{NO}_3^-$	65	8
$\text{ClO}_3^-$	74	12
Phenate	110	27
$\text{SO}_4^{2-}$	150	/
$\text{I}^-$	175	17
$\text{SeO}_4^{2-}$	280	/
Citrate	220	23
$\text{ClO}_4^-$	>500	/
$\text{CrO}_4^{2-}$	1700	/
$\text{C}_6\text{H}_5\text{SO}_3^-$	>500	75

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