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1 ORGANIC ACIDS CHROMATOGRAPHY WITH STRONG ANIONIC RESINS

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7 **Purification of organic acids by chromatography with strong anionic resins:**  
8 **investigation of uptake mechanisms**

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1 **Abstract**

2

3 Bio-based organic acids are promising renewable carbon sources for the chemical  
4 industry. However energy-consuming purification processes are used, like distillation or  
5 crystallization, to reach high purities required in some applications. That is why preparative  
6 chromatography was studied as an alternative separation technique. In a previous work  
7 dealing with the purification of lactic, succinic and citric acids, the Langmuir model was  
8 insufficient to explain the elution profiles obtained with a strong anionic resin.

9 Consequently the Langmuir model was coupled with a usual ion-exchange model to take  
10 into account the retention of their conjugate bases (<2%), which are commonly neglected at  
11 low pH (< 1.5). Elution simulations with both uptake mechanisms fitted very well with  
12 experimental pulse tests. Only two parameters were optimized (equilibrium constant of acid  
13 uptake and ion-exchange selectivity coefficient of conjugate base) and their value were  
14 coherent with experimental and resin suppliers' data.

15 These results confirmed that the singular tailing and apparent delay observed with  
16 succinic and citric acids can be explained by the high affinity of succinate and citrate for resin  
17 cationic sites. The model was implemented in a preparative chromatography simulation  
18 program in order to optimize operating parameters of our pilot-scale ISMB unit (Improved  
19 Simulated Moving Bed). The comparison with experimental ISMB profiles was conclusive.

1 **Keywords:** chromatography; modelling; anionic resin; organic acid; sustainable processing.

2

3 **Highlights**

4 • Uptake mechanisms of organic acids with strong anionic resin were investigated.

5 • Langmuir model coupled with ion-exchange model fitted with experimental data.

6 • Singular peak tailing and delay were better explained, particularly for citric acid.

7 • Retention of some organic acids in the dissociated form cannot be neglected.

## 1 1. Introduction

2 In the frame of sustainable development, biomass valorization as a renewable carbon  
3 source for the chemical industry is growing. Indeed, fossil resources are running out in the  
4 medium to long term. Moreover carbon balances have to be improved so as to reduce the  
5 CO<sub>2</sub> level in the atmosphere, whose rapid rise is linked to global warming. In the famous  
6 report of the Pacific Northwest National Laboratory (PNNL) and the National Renewable  
7 Energy Laboratory (NREL)[1], bio-based organic acids are identified as very promising  
8 sources of renewable carbon. Many compounds can be produced from these molecules in the  
9 chemical industry, particularly in the polymer industry. Up to now, the production of bio-based  
10 organic acids keeps small because they are still uncompetitive compared to the  
11 corresponding petroleum-derived products[2]. That is why the reduction of their production  
12 cost is a major concern of the chemical industry.

13 Bio-based organic acids are usually produced by microbial fermentation for the food  
14 industry but further purification techniques are required for other applications which need a  
15 much higher purity, particularly polymer synthesis. Currently, distillation [3-4], esterification  
16 [5-7] and crystallization [8] are commonly used to reach very high purities (> 99.5%)[9].  
17 However, these techniques are energy-consuming and give quite low recovery  
18 rates. Preparative chromatography is a promising solution for downstream processes  
19 because its energy, chemical and water consumptions are generally quite lower and  
20 consequently effluent volumes too. Initially developed for extraction and purification of  
21 complex vegetal mixtures [10], this separation method is spreading in different fields:  
22 biotechnology [11-12], pharmaceutical [13-14] and the sugar industry [15], for instance. Indeed,  
23 the same separation quality may be reached with better yields, lower costs and impacts on  
24 the environment. However, for several years now, the state of the world economy has not  
25 been favorable to industrial investments for the improvement of downstream purification  
26 processes. Moreover, chromatography needs to prove itself for high purity application (>  
27 99.5%) at the industrial scale.

1 In the frame of organic acids purification in fermentation broths, chromatography is often  
2 performed with ion-exchange resin to separate mineral salts, sugars and organic acids. The  
3 eluent is an aqueous solution whose pH can be adjusted with the inorganic acid or base  
4 corresponding to the counter-ions fixed on the resin so as to keep its composition constant.  
5 The separation of compounds is based on affinity differences for the resins. Higher is the  
6 affinity, slower migrates the compound along the resin bed. In the sugar industry, cationic  
7 resins are used to separate sucrose from salts as well as sugars from each other. The  
8 glucose-fructose separation is among the most famous applications of preparative  
9 chromatography. Otherwise, anionic resins are performed for the citric acid purification.  
10 Uptake and slowdown mechanisms are not well known and complex, coupling size  
11 exclusion, ligand exchange, hydrophilic or hydrophobic interactions and ion-exchange [16-  
12 17].

13 In a previous work dealing with the purification of lactic, succinic and citric acids by  
14 chromatography with a strong anionic resin (quaternary ammonium), the Langmuir model  
15 fitted well with the experimental equilibrium isotherms obtained by frontal analysis [18].  
16 However, the corresponding affinity coefficients were significantly lower than those obtained  
17 by pulse tests for succinic and citric acids. Their peaks had a singular tailing and were  
18 delayed compared to simulated ones with the Langmuir model and experimental coefficients  
19 of isotherms. Indeed, the Langmuir model was insufficient to describe the organic acids  
20 retention on the strong anionic resin and frontal analysis gave underestimated affinity  
21 coefficients.

22 These results lead us to suspect the impact of conjugate bases (dissociated organic  
23 acids) retention by ion-exchange, despite their very low concentrations. Indeed, the citrate  
24 anion affinity is high for quaternary ammonium anionic resin according to selectivity  
25 coefficients given by resins producers. Usually, this uptake mechanism is not taken into  
26 account because the strong anionic resins are performed at such acid pH (1 to 1.5) that only  
27 0.2% to 0.4% of lactic acid, 0.1% to 0.2% of succinic acid and 1.2% to 2.3% of citric acid are

1 dissociated. Thus, the organic acids dissociation is generally not considered although such  
2 small amount of conjugate bases may have a significant impact if they are strongly retained.

3 The present work aimed at modelling uptake mechanisms on a strong anionic resin. The  
4 Langmuir model, commonly used for the retention of organic acids, was coupled with a usual  
5 ion-exchange model for the retention of conjugate bases. Simulation results were compared  
6 with experimental pulse tests to check the model. The final goal was to improve the accuracy  
7 of a preparative chromatography simulation program in order to optimize the operating  
8 parameters of our pilot-scale ISMB unit (Improved Simulated Moving Bed).

## 9 **2. Chromatography modelling**

### 10 2.1. Mass transfer model

11 The Martin and Synge plate model [19] was chosen to describe the elution of organic  
12 acids through a strong anionic resin bed. In each plate of volume  $V$ , the mobile phase takes  
13 up a volume  $\epsilon V$  and the stationary phase a volume  $(1-\epsilon)V$ , with  $\epsilon$  the bed voidage. Usually,  
14 for preparative chromatography, volumes are expressed in BV (bed volume) [20-22],  
15 corresponding to the ratio of volume to the resin bed volume. Both phases are always  
16 supposed in equilibrium in all plates (nonlinear equilibrium in our case). The axial dispersion  
17 is characterized by the plate number  $N$ .

### 18 2.2. Uptake mechanisms- reactions in stationary phase

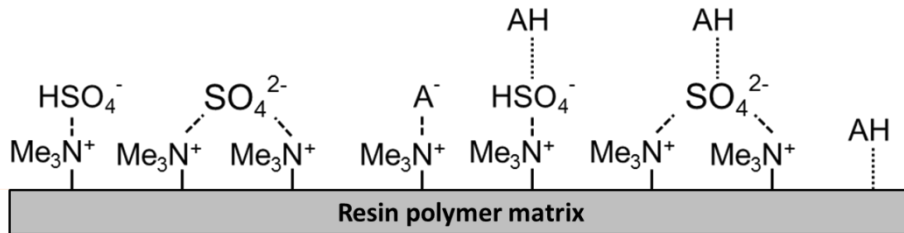
19 The strong anionic resin is a styrene-divinylbenzene resin functionalized with quaternary  
20 ammonium groups  $RMe_3N^+$ . The amount of these cationic sites corresponds to the ion-  
21 exchange capacity  $q_{RMe_3N^+}$  of the resin, expressed in  $\text{mol. L}_{\text{resin}}^{-1}$ . The resin is initially in the  
22 sulfate form, namely with the counteranions  $HSO_4^-$  and  $SO_4^{2-}$  in equilibrium. The proportion of  
23 both forms depends on their concentration in the mobile phase, so on its pH. The  
24 concentrations of hydroxyl anion  $OH^-$  in both phases were considered negligible at  $\text{pH} < 1.5$ .

1 The proposed model was based on two classical uptake mechanisms, with some  
 2 assumptions:

- 3 • Uptake of the organic acid in the dissociated form  $A^-$  by ion-exchange with resin  
 4 counteranions  $HSO_4^-$  and  $SO_4^{2-}$ .
- 5 • Retention of the organic acid in the molecular form AH according to the Langmuir  
 6 model, by weak bonds (hydrogen or van der Waals), on free sites either on  
 7 counteranions  $HSO_4^-$  and  $SO_4^{2-}$  (weak nucleophiles, *cf.* UOP patents [23-24]) or on the  
 8 polymer matrix whose capacity  $q_{mat}$  is also expressed in  $\text{mol. L}_{\text{resin}}^{-1}$ . We supposed that  
 9 the AH retention does not modify the selectivity coefficients of counteranions.

10 Consequently, 6 compounds were considered in the stationary phase:  $HSO_4^-$ ,  $SO_4^{2-}$ ,  $A^-$ ,  
 11 AH-site( $HSO_4^-$ ), AH-site( $SO_4^{2-}$ ) and AH-site(matrix) (figure 1).

12



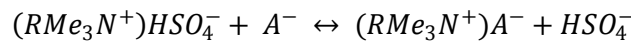
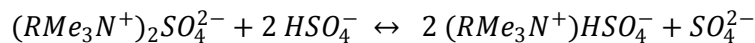
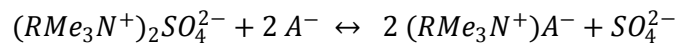
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Figure 1- Illustration of the six compounds considered in the stationary phase

15

16 The ion-exchange reactions correspond to the following equilibria:



17 Since the affinity of counteranions  $HSO_4^-$  and  $SO_4^{2-}$  for resin cationic sites was supposed

18 not influenced by AH uptake, their equilibrium constants can be written as follows:



$$Ke_{A^-/SO_4^{2-}} = \frac{[SO_4^{2-}]q_A^2}{[A^-]^2q_{SO_4^{2-}}} \text{Eq. 1}$$

$$Ke_{HSO_4^-/SO_4^{2-}} = \frac{[SO_4^{2-}]q_{HSO_4^-}^2}{[HSO_4^-]^2q_{SO_4^{2-}}} \text{Eq. 2}$$

$$Ke_{A^-/HSO_4^-} = \frac{[HSO_4^-]q_{A^-}}{[A^-]q_{HSO_4^-}} = \sqrt{\frac{Ke_{A^-/SO_4^{2-}}}{Ke_{HSO_4^-/SO_4^{2-}}}} \text{Eq. 3}$$

1 where  $q_{HSO_4^-}$  and  $q_{SO_4^{2-}}$  represent the  $HSO_4^-$  and  $SO_4^{2-}$  contents in the stationary phase (free or  
2 bound to AH),  $q_A$  - the  $A^-$  content and  $[X]$  the concentration of X in the mobile phase.

3 The ion-exchange equilibrium constants  $K_e$  can be estimated from data of resin  
4 suppliers by equations 5-7. For example, the Dow Chemical Company gives the selectivity  
5 coefficients of anions  $X^-$  for a strong anionic resin in the hydroxide form,  $k_{X/OH}$ , defined as  
6 follows:

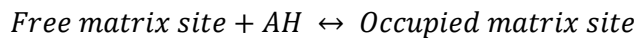
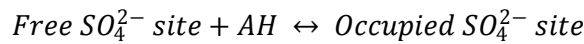
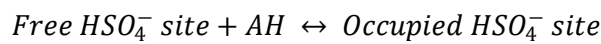
$$k_{X/OH} = \frac{q_{X^-}[OH^-]}{[X^-]q_{OH^-}} \text{Eq. 4}$$

$$Ke_{HSO_4^-/SO_4^{2-}} = \frac{k_{HSO_4/OH}^2}{k_{SO_4/OH}} \text{Eq. 5}$$

$$Ke_{A^-/SO_4^{2-}} = \frac{k_{A/OH}^2}{k_{SO_4/OH}} \text{Eq. 6}$$

$$Ke_{A^-/HSO_4^-} = \frac{k_{A/OH}}{k_{HSO_4/OH}} \text{Eq. 7}$$

7 According to the Langmuir model, the AH uptake reactions on free sites on counteranions  
8  $HSO_4^-$  and  $SO_4^{2-}$  and on the polymer matrix correspond to the following equilibria:



9 The corresponding equilibrium constants  $K_s$  are defined as follows:

$$K_{SAH/HSO_4^-} = \frac{q_{AH-HSO_4}}{[AH]q_{HSO_4}^{free}} \text{Eq. 8}$$

$$K_{SAH/SO_4^{2-}} = \frac{q_{AH-SO_4}}{[AH]q_{SO_4}^{free}} \text{Eq. 9}$$

$$K_{SAH/mat} = \frac{q_{AH-mat}}{[AH]q_{mat}^{free}} \text{Eq. 10}$$

1 where  $q_{AH-HSO_4}$ ,  $q_{AH-SO_4}$  and  $q_{AH-mat}$  represent the AH concentrations bound to uptake sites  
 2 respectively on counteranions  $HSO_4^-$  and  $SO_4^{2-}$  and on the polymer matrix, meanwhile  $q_{HSO_4^-}^{free}$ ,  
 3  $q_{SO_4^{2-}}^{free}$  and  $q_{mat}^{free}$  represent the concentrations of corresponding free uptake sites.

4 Mass balances on the three kinds of uptake sites lead to the following equations:

$$q_{HSO_4^-}^{free} = xq_{HSO_4^-} - q_{AH-HSO_4} \text{ Eq. 11} \quad q_{SO_4^{2-}}^{free} = yq_{SO_4^{2-}} - q_{AH-SO_4} \text{ Eq. 12}$$

$$q_{mat}^{free} = q_{mat} - q_{AH-mat} \text{ Eq. 13}$$

5 where x and y correspond to the uptake capacity of counteranions  $HSO_4^-$  and  $SO_4^{2-}$ ,  
 6 namely the number of molecule that can be retained per counteranion. Indeed, we assumed  
 7 that several molecules can eventually be retained on each counteranion. These numbers are  
 8 not necessarily integers and can be smaller than 1 if one molecule AH occupies several  
 9 counteranions  $HSO_4^-$  or  $SO_4^{2-}$  for steric reasons.

10 For each type of uptake sites, the combination of one mass balance with its corresponding  
 11 equilibrium constant gives the following usual equations of the Langmuir model. They relate  
 12 concentration of AH retained respectively on the three kind of sites to AH concentration in  
 13 mobile phase and total concentration of corresponding sites.

$$q_{AH-HSO_4} = \frac{Ks_{AH/HSO_4^-}[AH](xq_{HSO_4^-})}{1 + Ks_{AH/HSO_4^-}[AH]} \text{ Eq. 14}$$

$$q_{AH-SO_4} = \frac{Ks_{AH/SO_4^{2-}}[AH](yq_{SO_4^{2-}})}{1 + Ks_{AH/SO_4^{2-}}[AH]} \text{ Eq. 15}$$

$$q_{AH-mat} = \frac{Ks_{AH/mat}[AH]q_{mat}}{1 + Ks_{AH/mat}[AH]} \text{ Eq. 16}$$

### 14 2.3. Reactions in mobile phase

15 At low pH (<1.5), organic acids are mainly in the molecular form AH, however the retention  
 16 of the dissociated form  $A^-$  was studied (for polyacids like succinic or citric acids, only the  
 17 monodissociated form was considered). So 5 species were considered in the mobile phase:

- 1  $H^+$ ,  $HSO_4^-$ ,  $SO_4^{2-}$ ,  $AH$  and  $A^-$ . The main reactions are both acid-base equilibria, whose  
 2 equilibrium constants  $K_a$  are defined as follows:



$$K_{a_{AH}} = \frac{[A^-][H^+]}{[AH]} \quad \text{Eq. 17} \qquad K_{a_{HSO_4^-}} = \frac{[SO_4^{2-}][H^+]}{[HSO_4^-]} \quad \text{Eq. 18}$$

- 3 The  $pK_a$  of lactic, succinic and citric acids and hydrogen sulfate at 60°C (operating  
 4 temperature) are respectively 3.86, 4.13, 3.05 and 2.39.

5

#### 6 2.4. Plate mass balances

- 7 The plate content is represented by 11 unknown variables (5 in the mobile phase and 6 in  
 8 the stationary phase) that obey 7 independent equilibrium relations (Eq. 1-2 and 14-18).

- 9 Consequently, 4 mass balances are necessary to solve the system and estimate the content  
 10 of each plate at time “t” from the composition of all plates at time “t-1”.

- 11 *Mass balance of ion-exchange site  $RMe_3N^+$  whatever the time t,*

$$2 q_{SO_4^{2-}}^n + q_{HSO_4^-}^n + q_{A^-}^n = q_{RMe_3N^+} \quad \text{Eq. 19}$$

- 12 *Mass balance of sulfate group  $SO_4$  between t-1 and t:*

$$\begin{aligned} \varepsilon V \left( \frac{d[HSO_4^-]_t^n}{dt} + \frac{d[SO_4^{2-}]_t^n}{dt} \right) + (1 - \varepsilon) V \left( \frac{dq_{SO_4^{2-}}^n}{dt} + \frac{dq_{HSO_4^-}^n}{dt} \right) \\ = Q([HSO_4^-]_t^{n-1} - [HSO_4^-]_t^n) + Q([SO_4^{2-}]_t^{n-1} - [SO_4^{2-}]_t^n) \end{aligned} \quad \text{Eq. 20}$$

- 13 *Mass balance of acids ( $H^+$  element) between t-1 and t (water dissociation negligible):*

$$\begin{aligned} \varepsilon V \left( \frac{d[H^+]_t^n}{dt} + \frac{d[HSO_4^-]_t^n}{dt} + \frac{d[AH]_t^n}{dt} \right) + (1 - \varepsilon) V \left( \frac{dq_{HSO_4^-}^n}{dt} + \frac{dq_{AH-HSO_4^-}^n}{dt} + \frac{dq_{AH-SO_4^{2-}}^n}{dt} + \frac{dq_{AH-mat}^n}{dt} \right) \\ = Q([H^+]_t^{n-1} - [H^+]_t^n) + Q([HSO_4^-]_t^{n-1} - [HSO_4^-]_t^n) + Q([AH]_t^{n-1} - [AH]_t^n) \end{aligned} \quad \text{Eq. 21}$$

- 14 *Mass balance of organic compound A (molecular and dissociated forms) between t-1 and t:*

$$\begin{aligned} & \varepsilon V \left( \frac{d[A^-]_t^n}{dt} + \frac{d[AH]_t^n}{dt} \right) + (1 - \varepsilon) V \left( \frac{dq_{A^-}^n}{dt} + \frac{dq_{AH-HSO_4^-}^n}{dt} + \frac{dq_{AH-SO_4^{2-}}^n}{dt} + \frac{dq_{AH-mat}^n}{dt} \right) \\ & = Q([A^-]_t^{n-1} - [A^-]_t^n) + Q([AH]_t^{n-1} - [AH]_t^n) \end{aligned} \quad \text{Eq. 22}$$

1 In the last three mass balances, the terms on the left-hand side of the equal sign  
 2 correspond respectively to the accumulation terms in the mobile phase and in the stationary  
 3 phase, meanwhile the expressions on the right-hand side correspond to the difference  
 4 between inputs (from the (n-1)<sup>th</sup> plate) and outputs (from the n<sup>th</sup> plate). Q represents the  
 5 flow rate.

6 The proposed model depends on 10 parameters whose value is more or less known  
 7 accurately according to data from resin suppliers, literature or our own experimental results:

- 8 • Plate number: N,
- 9 • Resin ion-exchange capacity:  $q_{RMe_3N^+}$  expressed in mol. L<sub>resin</sub><sup>-1</sup>,
- 10 • Polymer matrix uptake capacity:  $q_{mat}$  expressed in mol. L<sub>resin</sub><sup>-1</sup>,
- 11 • HSO<sub>4</sub><sup>-</sup> uptake capacity: x,
- 12 • SO<sub>4</sub><sup>2-</sup> uptake capacity: y,
- 13 • Equilibrium constant of ion-exchange between A<sup>-</sup> and HSO<sub>4</sub><sup>-</sup>:  $K_{e_{A^-/HSO_4^-}}$ ,
- 14 • Equilibrium constant of ion-exchange between A<sup>-</sup> and SO<sub>4</sub><sup>2-</sup>:  $K_{e_{HSO_4^-/SO_4^{2-}}}$ ,
- 15 • Equilibrium constant of AH uptake on HSO<sub>4</sub><sup>-</sup> counteranions:  $K_{s_{AH/HSO_4^-}}$ ,
- 16 • Equilibrium constant of AH uptake on SO<sub>4</sub><sup>2-</sup> counteranions:  $K_{s_{AH/SO_4^{2-}}}$ ,
- 17 • Equilibrium constant of AH uptake on resin polymer matrix:  $K_{s_{AH/mat}}$ .

## 18 2.5. Numerical methods

19 The finite-difference method with implicit scheme was used to discretize the 3 differential  
 20 equations (eq. 20-22). The Newton-Raphson iterative method was chosen to solve the  
 21 nonlinear system of 4 remaining equations after simplification. The model and its numerical  
 22 solving were computed using the software MATLAB<sup>®</sup>. The initial conditions (concentrations in

1 both phases) need to be given as well as the boundary conditions: composition of the feed  
2 (organic acid solution then eluent) as a function of time.

### 3 3. Results and discussion

#### 4 3.1. Simulation with only the Langmuir model and coefficients of equilibrium isotherms

5 First, the simulations of organic acids elution through a strong anionic resin bed were  
6 performed considering that AH was only retained on the polymer matrix, according to the  
7 Langmuir model. We used the coefficients of equilibrium isotherms obtained previously by  
8 frontal analysis (table 1). So, the elution profiles were only influenced by 3 parameters: the  
9 plate number  $N$ , the polymer matrix uptake capacity  $q_{mat}$  equated to  $q_{max}$  and the equilibrium  
10 constant of AH uptake on resin polymer matrix  $K_{s_{AH/mat}}$  equated to  $K_{s_{AH}}$ .

11

12 **Table 1- Resin uptake capacity  $q_{max}$  and equilibrium constant  $K_{s_{AH}}$  of 3 organic acids estimated by frontal**  
13 **analysis at 60°C for a strong anionic resin [18]**

	$q_{max}$	$K_{s_{AH}}$
	$mol \cdot L_{resin}^{-1}$	$10^{-1} L_{solution} \cdot mol^{-1}$
Lactic acid	$6.8 \pm 2.6$	$1.4 \pm 0.5$
Succinic acid	$2.7 \pm 0.9$	$7.2 \pm 2.5$
Citric acid	$2.5 \pm 0.2$	$9.0 \pm 1.7$

14

15 For lactic and succinic acids, the resin uptake capacity  $q_{max}$  and the equilibrium constant  
16  $K_{s_{AH}}$  have significant error margin because it was not possible to get enough experimental  
17 points in the nonlinear region of equilibrium isotherms [18].

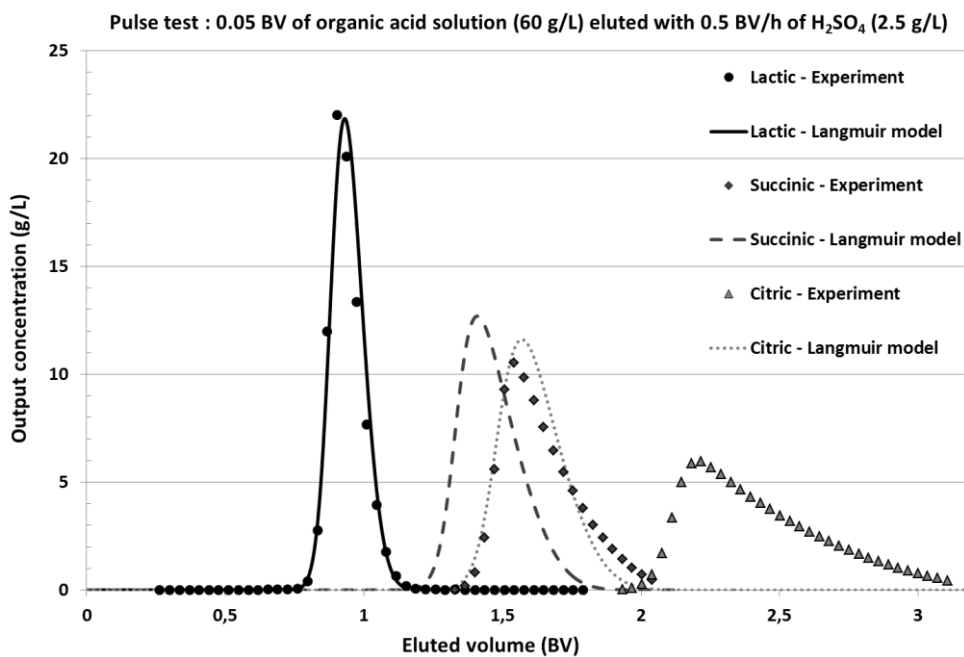
18 According to our previous study [18], the plate number  $N$  was set to 250 for the 3 organic  
19 acids. It corresponds to the experimental value obtained by pulse tests with lactic acid whose  
20 symmetric profile is the most appropriate to characterize axial dispersion. The plate number  $N$

1 was considered equal for all species. Indeed, the study of axial dispersion (Van Deemter  
2 curves) in this work showed that the molecular diffusion is negligible compared to the  
3 mechanical dispersion and the influence of mass transfer limitation, which were quite similar  
4 between compounds in our experimental operating conditions.

5 These conditions were applied in the model so as to compare with experimental results:  
6 0.05 BV of 60 g.L<sup>-1</sup> organic acid solution, whose pH was adjusted to 1.4 with sulfuric acid,  
7 were eluted with a 2.5 g.L<sup>-1</sup> sulfuric acid solution. The temperature was 60 °C and the flow  
8 rate was 0.5 BV.h<sup>-1</sup>.

9 For lactic acid, the simulation results are quite close to the experimental ones (figure 2).  
10 So, the lactic acid uptake mechanisms by a strong anionic resin can be well fitted with only  
11 the Langmuir model. However, this model is insufficient to simulate elution of succinic and  
12 citric acids. Indeed, the simulation gives much earlier and narrower peaks than the  
13 experiments, particularly for citric acid. Another uptake mechanism must then be responsible  
14 for the delay and peak tailing observed experimentally and should be taken into account.

15



16

1 **Figure 2 - Comparison of experimental pulse test profiles with simulated ones considering the Langmuir**  
2 **model with experimental coefficients of equilibrium isotherms**

3  
4 3.2. Simulation with taking into account the retention of the dissociated form  $A^-$

5 Simulations of organic acids elution were performed with the proposed model which takes  
6 into account the retention of the molecular form AH according to the Langmuir model and the  
7 retention of the dissociated form  $A^-$  by ion-exchange with resin counteranions.

8 To simplify, as a start, we considered that the molecular form AH was retained only on  
9 free uptake sites of counteranions  $HSO_4^-$  and  $SO_4^{2-}$  according to UOP patents [23-24].  
10 Moreover, we supposed that the equilibrium constants of AH uptake on both counteranions  
11 were equal. They were estimated first from the experimental equilibrium constant  $K_{S_{AH}}$  (table  
12 1), then optimized by fitting simulation results to experimental profiles (least squares  
13 method). They were expected lower than  $K_{S_{AH}}$  since it includes also the contribution of ion-  
14 exchange in retention.

15 According to the supplier, the ion-exchange capacity  $q_{RMe_3N^+}$  is about  $1.35 \text{ mol. L}_{\text{bed}}^{-1}$ ,  
16 equivalent to  $2.4 \text{ mol. L}_{\text{resin}}^{-1}$ . The uptake capacities of counteranions  $HSO_4^-$  and  $SO_4^{2-}$ ,  $x$  and  
17  $y$ , were supposed equal and defined from the experimental uptake capacity  $q_{max}$  (table 1). For  
18 instance,  $q_{max}$  of lactic acid is twofold to threefold higher than  $q_{RMe_3N^+}$ , so  $x$  and  $y$  were  
19 supposed equal to 2 (table 3). It could be related to both nucleophile carbonyl groups of  
20 counteranions  $HSO_4^-$  and  $SO_4^{2-}$  while lactic acid gets only one electrophile hydroxyl group. It  
21 means that 2 molecules of lactic acid can be retained on each counteranion. For succinic and  
22 citric acids,  $x$  and  $y$  were supposed equal to 1 (table 3).

23 The selectivity coefficients  $k_{X/OH}$  were first estimated from data of the Dow Chemical  
24 Company (table 2), then optimized by fitting simulation results to experimental profiles (least  
25 squares method).

26

1 **Table 2- Selectivity coefficients of some anions (compared with OH<sup>-</sup>) on a strong anionic resin**  
 2 **(Data from Dow Chemical Company)**

	HSO <sub>4</sub> <sup>-</sup>	SO <sub>4</sub> <sup>2-</sup>	Citrate*	Formate	Acetate	Propionate
<b>k<sub>X/OH</sub></b>	85	150	220	4.6	3.2	2.6

3 \* Valence not mentioned

4  
 5 The plate number N was still set to 250 for the 3 organic acids. Values of simulation  
 6 parameters for the 3 organic acids were gathered in the table 3.

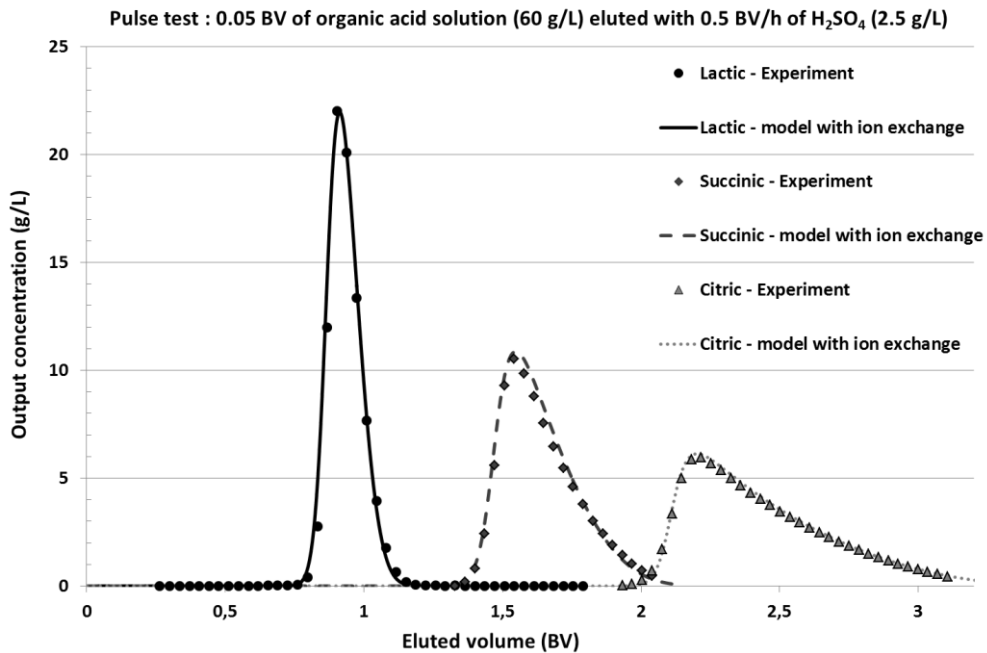
7  
 8 **Table 3 - Optimized parameters for simulation of lactic, succinic and citric acids elution with the proposed**  
 9 **model which also takes into account A<sup>-</sup> ion-exchange**

		Lacticacid	Succinicacid	Citricacid
<i>N</i>	—	250	250	250
<i>q<sub>RM<sub>e3</sub>N<sup>+</sup></sub></i>	<i>mol. L<sub>resin</sub><sup>-1</sup></i>	2.4	2.4	2.4
<i>k<sub>A/OH</sub></i>	—	2.5	330	110
<i>k<sub>H<sub>2</sub>SO<sub>4</sub>/OH</sub></i>	—	85	85	85
<i>k<sub>SO<sub>4</sub>/OH</sub></i>	<i>L<sub>resin</sub> · L<sub>solution</sub><sup>-1</sup></i>	150	150	150
<i>K<sub>S<sub>AH</sub>/H<sub>2</sub>SO<sub>4</sub></sub></i>	<i>L<sub>solution</sub> · mol<sup>-1</sup></i>	0.225	0.82	0.70
<i>K<sub>S<sub>AH</sub>/SO<sub>4</sub><sup>2-</sup></sub></i>	<i>L<sub>solution</sub> · mol<sup>-1</sup></i>	0.225	0.82	0.70
<i>x</i>	—	2	1	1
<i>y</i>	—	2	1	1

10  
 11 The figure 3 shows that the proposed model fitted very well the experimental profiles with  
 12 coherent value for each parameter compared to experimental and resin supplier's data. The  
 13 delay and peak tailing observed mainly with succinic and citric acids can be reproduced with  
 14 this model.



1



2

3 **Figure 3 - Comparison of experimental pulse test profiles and simulations ones considering the Langmuir**  
4 **model combined with ion-exchange of conjugate bases**

5

6 It confirms that the retention of the dissociated organic acids by ion-exchange with resin  
7 counteranions must be considered despite of the very low dissociation of the acid at acidic pH  
8 (0.1 to 2%). Indeed, the conjugate base of some organic acids, like citrate, can have a very  
9 high affinity for resin cationic sites, so the organic acid can be much more retained than  
10 expected. Moreover, it shows that assumptions added in this simulation to simplify the model  
11 were acceptable.

### 12 3.3. Implementation in a ISMB chromatography simulation program

13 This uptake model was developed in order to improve simulation of preparative  
14 chromatography like ISMB (Improved Simulated Moving Bed) that is currently used at pilot  
15 scale in our laboratory. We aimed at predicting the ISMB performance more accurately with  
16 strong anionic resins and optimizing operating parameters according to the wanted recovery  
17 rates and purities.

1 An ISMB unit is composed of 4 columns in series filled with the stationary phase. The  
2 ISMB process consists in changing sequentially position of inputs (feed and eluent) and  
3 outputs (extract enriched with the more retained component, succinic acid, and raffinate  
4 enriched with the less retained, salts and lactic acid). An operating step is composed of four  
5 different sub-steps, where each column corresponds to one zone:

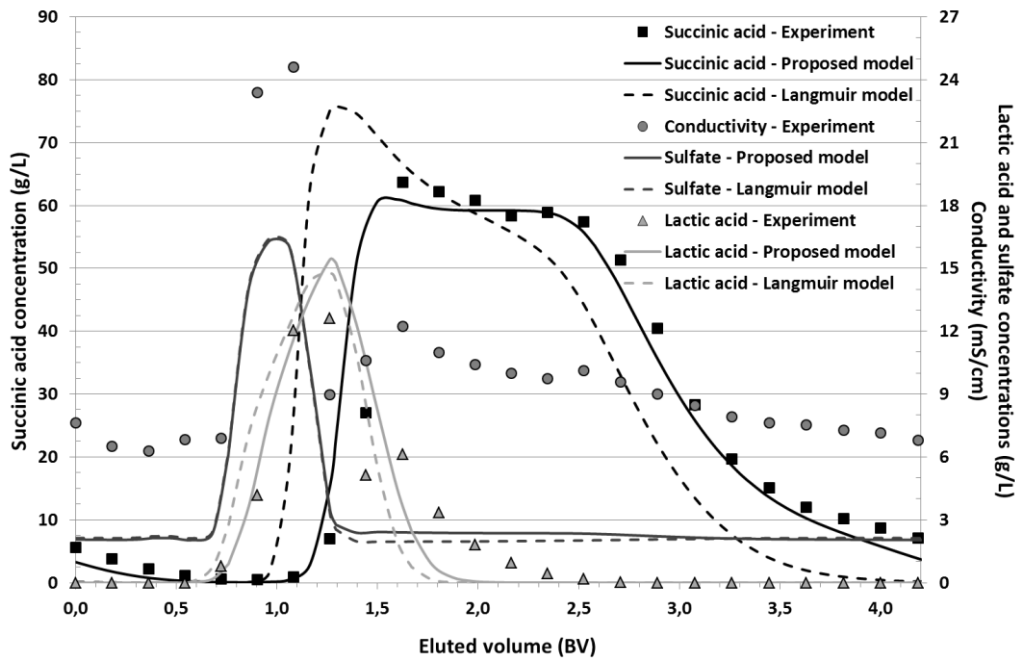
- 6 1) Feed input in the zone 3 and raffinate output from the zone 3.
- 7 2) Eluent input in the zone 1 and extract output from the zone 1.
- 8 3) Eluent input in the zone 1 and raffinate output from the zone 3.
- 9 4) Recirculation loop with all zones connected in series.

10 After one step, each zone is shifted by one column: the zone 1 becomes the zone 2, the  
11 zone 2 becomes the zone 3, etc. So, a cycle is performed after 4 steps. ISMB performance  
12 depends on different volumes eluted during these four sub-steps.

13 ISMB simulations were performed with the Langmuir model whose coefficients were  
14 optimized previously from an experimental pulse test at pilot scale, then with the model  
15 developed whose coefficients were also optimized in the same way. The feed was mainly  
16 composed of sulfatesalts (16 g/L), succinic acid (65 g/L) and lactic acid (14 g/L) while the  
17 eluent was a 2.5 g/L sulfuric acid solution.

18 The figure 4 shows that the proposed model fitted better ISMB experimental profiles than  
19 the Langmuir model. The accuracy of ISMB simulation with strong anionic resin was  
20 improved by taking into account the retention of dissociated organic acids by ion-exchange,  
21 despite their very low concentrations.

22



1  
2 **Figure 4 - Comparison of experimental ISMB profiles with simulated ones, first with the model which is**  
3 **developed, then with the Langmuir model only**

4  
5 **4. Conclusion**

6 Preparative chromatography is an efficient separation technique which is spreading in  
7 different industrial fields. For several years now, anionic resins have been performed for the  
8 citric acid purification, however uptake mechanisms are still not well known. In a previous  
9 work [18], peaks corresponding to succinic and citric acids exhibited singular tailing and  
10 delay which could not be explained only by the Langmuir model.

11 The uptake mechanisms supposed in the proposed model are relevant to explain the  
12 characteristic elution profiles of some organic acids obtained in pulse tests. To sum up, we  
13 assume that the acid molecular form can be retained on resin counteranions or polymer  
14 matrix while the dissociated form can be fixed to cationic sites by ion-exchange. Usually, the  
15 organic acids dissociation is not considered at such low pH (<1.5), but we proved that even a  
16 very small proportion of dissociated form can have a significant impact when it is strongly  
17 retained. This is the reason why the Langmuir model is sufficient for lactic acid because of

1 the low affinity of lactate but insufficient for citric acid since citrate affinity is very high for  
2 quaternary ammonium anionic resins.

3 The developed model was implemented in a preparative chromatography (ISMB)  
4 simulation program in order to optimize the operating parameters of our pilot-scale unit and  
5 improve estimation of its performance. Experimental ISMB profiles confirmed that the  
6 proposed model was better than the Langmuir model to describe the organic acids retention  
7 on strong anionic resins.

8 Next, a plug flow reactor model will be used to take into account different axial dispersions  
9 of compounds. Moreover, it would be interesting to further investigate so as to support the  
10 assumptions which were made to simplify the model and eventually to refine it.

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14

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