

## NUMERICAL SIMULATION OF ADSORPTION COLUMNS: MODEL COMPARISON AND SENSITIVITY ANALYSIS

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**Abstract.** *In the current work we present the mathematical modeling and the solution with the Finite Volume Method of the mass transfer phenomena associated with the adsorption of biomolecules in fixed resin beds. The computational results are validated by the comparison with real experimental data. The calculated breakthrough curves are in good agreement with the measured values of the concentration at the end of the adsorption columns. Results of parametric and sensitivity analysis are also presented indicating that there is a good chance to estimate in future works the resin bead porosity and the value of the saturation concentration in Langmuir's adsorption isotherm.*

**Keywords:** *Mass transfer, Liquid-solid adsorption, Adsorption columns, Langmuir isotherm, Finite Volume Method*

### 1. Introduction

Adsorption processes are widely used in the chemical, biochemical and petroleum industries for both purifications and bulk separations. For the production of pharmaceutical compounds or in the area of fine chemistry and biochemistry, adsorption separation processes have a great importance. A common application is the drying of organic solvents in the liquid phase. Most adsorptive separations are based on the evolution of a mass transfer zone through one or more columns packed with beads or pellets of an appropriate adsorbent material.

Proteins can be separated by some form of chromatography or selective adsorption, and this process may be carried out in a packed column or a stirred tank using a specially chosen adsorbent (Conder and Hayek, 2000). The velocity of the adsorption process is controlled by external diffusion, the effective diffusion in the pores, and the velocity of the adsorption on the active site of the adsorbent. The actual size of each adsorption column is determined from the capacity at breakpoint, that is, from the loading of the adsorbate on the adsorbent up to the point at which breakthrough of the adsorbate is about to occur.

A useful literature related to numerical and experimental studies on protein adsorption kinetics is available. Horstmann and Chase (1989) developed a model describing the kinetics of adsorption of proteins to adsorbents. This model includes the effects of external film mass transfer and pore diffusion. Numerical solution of the governing differential equations was carried out using a finite difference method. Liapis and Rippin (1977) described a multicomponent adsorption equation from a finite bath onto adsorbent particles. This model includes the external film resistance effect and diffusional resistance within the particle. Orthogonal collocation was used to solve the equations for two-component adsorption. Estimates were made of pore and solid diffusion coefficients within carbon particles by using superposition of model prediction onto experimental results. Firouztale *et alii* (1992) employed theoretical models and nonlinear regression analysis to determine the values of liquid film mass transfer and effective pore diffusion coefficient. These values seem to be consistent with values estimated from empirical relations. Conder and Hayek (2000) have used a two-equation model to simulate the protein adsorption on a rigid, silica-based medium. The differential equations were solved using an approach equivalent to that employed by Horstmann and Chase (1989).

Sensitivity analysis may play an important role in validation, optimization, and risk analysis of simulation models. An important requirement in model based parameter estimation is that the sensitivity coefficients should not be of small magnitude, and when more than one parameter are sought to be estimated simultaneously, their sensitivity coefficients must be linearly independent over the experimental time domain (Beck *et alii*, 1985). Similar shapes (time dependence) of sensitivity coefficients for two different parameters indicate that their effects on the model response are similar, being impossible, therefore, to tell them apart. Larger sensitivity coefficients are related to better chances of obtaining a good estimate.

The objectives of the present study are: (i) present the finite volume formulation for a set of differential equations that models the mass transfer phenomena; (ii) compare the numerical results with experimental data; and (iii) perform a sensitivity analysis with respect to the main physico-chemical and process parameters.

## 2. Mathematical Formulation

A model that describes the protein adsorption on macro porous solids was presented by Horstmann and Chase (1989). This model includes the effects of external film mass transfer and pore diffusion as well as an expression for the rate of surface reaction. The assumptions used as the basis of the model can be seen in Horstmann and Chase (1989) and will be briefly listed here to the completeness of the present work: (i) The adsorbent is made of a porous material, into which the solute must diffuse, in a manner described by an effective diffusivity  $D_{eff}$ ; (ii) Mass transfer from the bulk of the liquid to the surface of the adsorbent is governed by a film model characterized by a mass transfer coefficient  $k_s$ ; (iii) The bed is homogeneous, i. e., adsorbent particles are spherical, with uniform size, i. e., radius  $R$ , and density  $\rho$ .

We now present the mathematical model developed. The mass balance over a solid particle leads to the differential equation that describes the solute (protein) diffusion inside the particle's pores (adsorbent resin) (Blanch and Clark, 1997)

$$\overbrace{\epsilon_p \frac{\partial C_i}{\partial t}}^I = D_{eff} \overbrace{\left[ \frac{1}{r^2} \frac{\partial}{\partial r} \left[ r^2 \frac{\partial C_i}{\partial r} \right] \right]}^{II} - \overbrace{\frac{\partial q}{\partial t}}^{III} \quad (1)$$

where  $C_i = C_i(r, z, t)$  is the protein concentration in the liquid phase in the interior of the particles pores,  $D_{eff}$  is the effective diffusion coefficient,  $q$  is the protein concentration in the solid particle,  $\epsilon_p$  is the particle porosity, and  $t$  and  $r$  are the temporal and spatial (radial) variables respectively.

Term *I* of Eq. (1) describes the accumulation of adsorbate in the liquid inside the pore, term *II* due to the adsorption at the solid matrix of the resin particle, the change in the concentration with time due to the diffusion in the particle, and term *III*, the net removal of the adsorbate. The initial condition is the following

$$C_i(r, z, t=0) = 0 \text{ for } 0 \leq z \leq L \text{ and } 0 \leq r \leq R \quad (2)$$

and the boundary conditions are

$$\frac{\partial C_i}{\partial r} = 0 \text{ for } t > 0 \text{ and } r = 0 \text{ and } 0 \leq z \leq L \quad (3)$$

$$\epsilon_p D_{eff} \frac{\partial C_i}{\partial r} = k_s (C_b - C_i) \text{ for } t > 0 \text{ and } r = R \text{ and } 0 \leq z \leq L \quad (4)$$

where  $C_b = C_b(z, t)$  is the bulk concentration of protein in the liquid phase. According to Eq. (4) the mass transfer rate through the liquid film is related to  $C_b$  as well as to  $C_i$  at the surface of the particle, i. e.  $r = R$ .

The mass balance in the bulk liquid phase with respect to the protein concentration can be written as (Blanch and Clark, 1997)

$$\overbrace{\frac{\partial C_b}{\partial t}}^I = D_L \overbrace{\frac{\partial^2 C_b}{\partial z^2}}^{II} - u_i \overbrace{\frac{\partial C_b}{\partial z}}^{III} - \overbrace{\left[ \frac{3(1-\epsilon_b)}{R \epsilon_b} D_{eff} \frac{\partial C_i}{\partial r} \right]_{r=R}}^{IV} \quad (5)$$

where  $\epsilon_b$  is the bed porosity,  $D_L$  is the axial dispersion coefficient,  $u_i$  is the interstitial velocity of the flow, that is, the linear velocity of the flow between the resin particles. Term *I* represents the rate of change of the adsorbate concentration in the mobile phase; term *II* represents the axial dispersion; term *III* represents the mass convection; and term *IV* accounts for the uptake of adsorbate by the resin particles. Equation (5) is subjected to the following initial condition

$$C_b = C_0 \text{ when } t = 0 \text{ and } 0 \leq z \leq L \quad (6)$$

and to the following boundary conditions

$$u_i C_0 = u_i C_b - D_L \frac{\partial C_b}{\partial z} \quad \text{for } z = 0 \text{ and } t > 0 \quad (7)$$

$$\frac{\partial C_b}{\partial z} = 0 \quad \text{for } z = L \text{ and } t > 0 \quad (8)$$

Equations (1) and (5) are coupled, that is, one needs to know  $C_b(z, t)$  to solve Eq. (1) and also needs to know  $C_i(r, z, t)$  to solve Eq. (5), therefore these equations cannot be solved separately.

At this point, the set of equations cannot yet be solved because term *III* in Eq. (1) has not been described. The solid-liquid adsorption is governed by this term and there are several models to describe this process. Two models have been used in the present work; both are based on the Langmuir equation. The first model assumes that protein concentration in the adsorbent pore is in local equilibrium with its concentration adsorbed on the inner surface of the pore wall. This hypothesis can be found in many works of this area of knowledge. The first model (Equilibrium Model) equation is therefore

$$q = \frac{q_m C_i}{K_d + C_i} \quad (9)$$

where

$$K_d = \frac{k_d}{k_a} \quad (10)$$

is the dissociation equilibrium constant,  $k_a$  is the association rate constant,  $k_d$  is the dissociation rate constant, and  $q_m$  the Langmuir isotherm equilibrium constant (the maximum adsorption capacity).

The second model (Kinetic Model) equation is described by

$$\frac{\partial q}{\partial t} = \overbrace{k_a C_i (q_m - q)}^I - \overbrace{k_d q}^{II} \quad (11)$$

where  $k_a$  and  $k_d$  are, respectively, association and dissociation rate constants. Term *I*, in Eq. (11), describes the adsorption rate in the resin particles, determined by the concentration of the product in the pore liquid,  $C_i$ , and the concentration of free sites in the resin,  $q_m - q$ . Term *II*, in Eq. (11), describes the desorption rate from the resin particles determined by the concentration of the absorbed product,  $q$ .

At this point, the problem formulation has been completed and the attention will now be turned to the solution methodology.

### 3. Solution Methodology

In the present work Eqs. (1) and (5) have been solved numerically using the Finite Volume Method (Patankar, 1980; Ferziger and Peric, 1996). In this methodology, the first step is to divide the solution domain in small non-overlapping control volumes, whose faces are aligned with the coordinate lines. Next, the equations are integrated along each one of these control volumes yielding a set of algebraic equations. The concentration derivatives along the faces of the control volumes are approximated using piecewise linear profiles, and after rearrangements all algebraic equations are cast into the following formula

$$A_p B_p = A_e B_e + A_w B_w + S_p \quad (12)$$

where  $B$  may be  $C_b$  or  $C_i$ , depending whether the domain corresponds to the fluid film or to the porous matrix, respectively. The subscript  $P$  refers to each specific control volume whose neighbors are at **East**, **West**;  $S_p$  is a source term. Equation (12) is non-linear because the coefficients “ $A$ ” and “ $B$ ” depend upon the concentration itself. For a given iteration the coefficients were lagged by one iteration, i. e., they were evaluated using the concentration value from the previous iteration. Additionally,  $S_p$  was linearized following the procedure suggested by Patankar (1980). In order to achieve convergence with the numerical scheme the linearization of the source term as well as the use of relaxation factors played a crucial role. For each iteration, Eqs. (1) and (5) were solved separately and alternatively.

Equation (1) was solved twice and Eq. (5) was solved four times. Detailed information about this numerical procedure can be found in Vasconcellos *et alii* (2003) or Mendes (2004).

To solve Eq. (1) it is necessary to evaluate  $\partial q/\partial t$  term numerically. Using the Finite Volume Method such term is evaluated as following

$$\int_{Volume} \int_{time} \frac{\partial q}{\partial t} dt dV \cong (q_p - q_p^0) \Delta V_p \frac{dy}{dx} \quad (13)$$

where the superscript “0” means quantities evaluated at the previous time level and  $\Delta V_p$  is the volume of the control volume. When the Kinetic Model is used to model the solid-liquid adsorption phenomenon then the value of  $q_p$  in Eq. (13) is determined using the Runge-Kutta-Fehlberg method (Galassi *et alii*, 2003). When the Equilibrium Model is used to model the solid-liquid adsorption phenomenon Eq. (13) becomes

$$\int_{Volume} \int_{time} \frac{\partial q}{\partial t} dt dV \cong \left( \frac{q_m (C_i)_p}{K_d + (C_i)_p} - \frac{q_m (C_i)_p^0}{K_d + (C_i)_p^0} \right) \Delta V_p \quad (14)$$

where  $(C_i)_p$  is the value of  $C_i$  (unknown) and  $(C_i)_p^0$  is the value of  $C_i$  evaluated in the previous time level.

### 3. Results

All results presented herein were obtained for the Lysozyme - Sepharose CL-6B and the process parameters are shown in Table 1.

Table 1. Test case data used in simulation (Kempe *et alii*, 1999)

Parameter	Symbol	Value
Inlet concentration	$C_0$	$7.14 \times 10^{-3} \text{ mol/m}^3$
Flow rate	—	$1.67 \times 10^{-8} \text{ m}^3/\text{s}$
Column diameter	—	0.01 m
Column length	$L$	0.104 m
Bed porosity	$\epsilon_b$	0.39
Resin particle porosity	$\epsilon_p$	0.75
Resin particle radius	$R$	50 $\mu\text{m}$
Axial dispersion	$D_L$	$5.75 \times 10^{-8} \text{ m}^2/\text{s}$
Mass transfer rate	$k_s$	$6.9 \times 10^{-6} \text{ m/s}$
Effective diffusion coefficient	$D_{eff}$	$5.3 \times 10^{-11} \text{ m}^2/\text{s}$
Maximum adsorption capacity	$q_m$	1.22 $\text{mol/m}^3$
Adsorption rate coefficient	$k_a$	0.286 $\text{m}^3/(\text{mol.s})$
Desorption rate coefficient	$k_d$	$5.0 \times 10^{-4} \text{ s}^{-1}$

#### 3.1 Validation

The validation of the scheme described herein was performed by comparing the results obtained here with the experimental data available in Chase (1984). In Fig. 1 is shown a comparison between the results of the present work and those of Chase (1984), for four column lengths: 14 mm, 27 mm, 41 mm and 104 mm, using both the Equilibrium Model, Eq. (9), and the Kinetic Model, Eq. (11), to describe the solid-liquid adsorption phenomena. The dimensionless value of  $C_b/C_0$  is evaluated at  $z = L$  for all results presented in this work. It is observed a good agreement between the results of both models and the experimental data, but the results of each model were slightly different. The mass transfer front is somewhat faster when Eq. (9) is used.

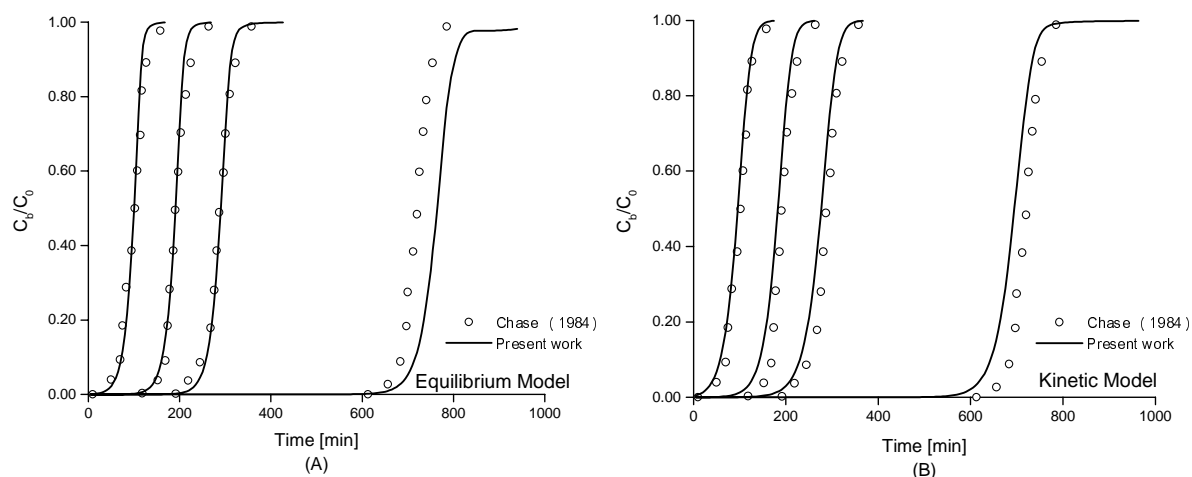


Figure 1 – Comparison of experimental data and numerical solution for the dimensionless concentration of Lysozyme - Sepharose CL-6B. (A) - Equilibrium Model, (B) - Kinetic Model

In Fig. 2 is shown the dimensionless concentration of Lysozyme - Sepharose CL-6B along the column height for different times. All curves in this figure were not exactly as they should be, i. e., it was expected a sharp mass transfer fronts. It was used WUDS (Raithby and Torrence, 1974) to interpolate the convective term and this is not the best strategy to capture sharp fronts with a relatively small number of nodes. In future works more accurate interpolation method will be employed.

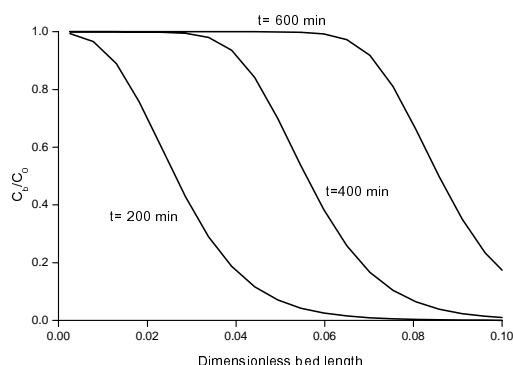


Figure 2 - Dimensionless concentration of Lysozyme - Sepharose CL-6B along the column height for three different times

### 3.2 Parameter Analysis

A parameter analysis was performed in order to evaluate the influence of the effective diffusion coefficient,  $D_{eff}$ , axial dispersion coefficient,  $D_L$ , association rate constant,  $k_a$ , and the resin particle diameter,  $R$ , on the calculated values of the dimensionless concentration at the end of the adsorption column as a function of time. The calculated breakthrough curves for a wide range of values for  $D_{eff}$ ,  $D_L$ ,  $k_a$  and  $R$  are presented in Figs 3(a) – (d), respectively.

Depending on the operating conditions for the chromatographic separation such as pH and ionic strength, the diffusivity of the protein can vary significantly (Kempe *et alii*, 1999). In order to obtain the results shown in Fig. 3(D) the value of the dissociation equilibrium constant,  $K_d$ , was kept constant.

From the results shown in Fig. 3 we observe that the calculated values of the dimensionless concentration at the end of the adsorption column were almost insensitive to  $D_L$  and  $k_a$ .

This subject is further investigated with the sensitivity analysis presented in the next section.

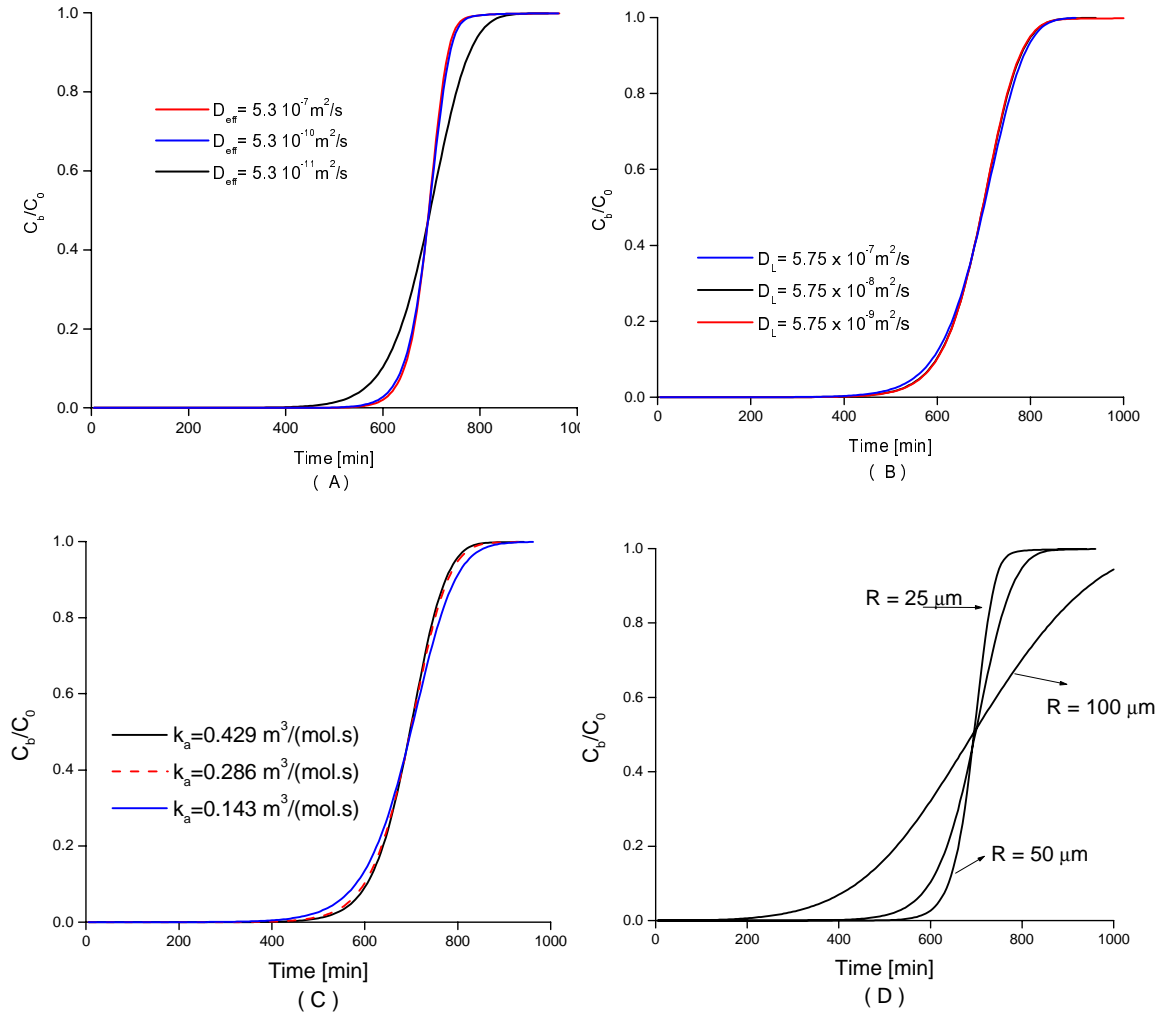


Figure 3 – Parameter analysis. Calculated breakthrough curves as a function of:  
 (A) effective diffusion coefficient, (B) axial dispersion coefficient,  
 (C) association rate constant, and (D) resin particle diameter

### 3.3 Sensitivity Analysis

In the present work we want to analyze the scaled sensitivity coefficients

$$X_s(t) = \beta_s \frac{\partial C_b(t)}{\partial \beta_s} \text{ for } s = 1, 2, \dots, Np \quad (15)$$

where  $\beta_s$  are the physico-chemical properties or process parameters,  $Np$  is the total number of parameters and  $C_b(t)$  is the calculated value of the concentration at the end of the adsorption column.

From Eq. (15) we observed that the scaled coefficients have all the same units, i. e., protein concentration, and then a direct comparison is possible.

In order to calculate the sensitivity coefficients we have used a central Finite Difference approximation

$$\frac{\partial C_b(t)}{\partial \beta_s} = \frac{C_b(\beta_1, \beta_2, \dots, \beta_s + \Delta\beta_s, \dots, \beta_{Np}) - C_b(\beta_1, \beta_2, \dots, \beta_s - \Delta\beta_s, \dots, \beta_{Np})}{2\Delta\beta_s} \quad (16)$$

In Figs. 4 and 5 are presented the calculated values of the scaled sensitivity coefficients for the parameters  $D_{eff}$ ,  $k_s$ ,  $q_m$ ,  $k_d$ ,  $\epsilon_b$  and  $\epsilon_p$ , considering adsorption columns with  $L = 41$  mm (Fig. 4) and  $L = 104$  mm (Fig. 5). In Figs.

4(A) and 5(A) are represented the sensitivity coefficients of higher magnitude and in Figs. 4(B) and 5(B) are represented those of lower magnitude.

From those results we observe that the highest sensitivity of the mass transfer phenomena discussed in this work is associated with the resin bed porosity,  $\epsilon_b$ , and the saturation value in Langmuir's adsorption isotherm,  $q_m$ .

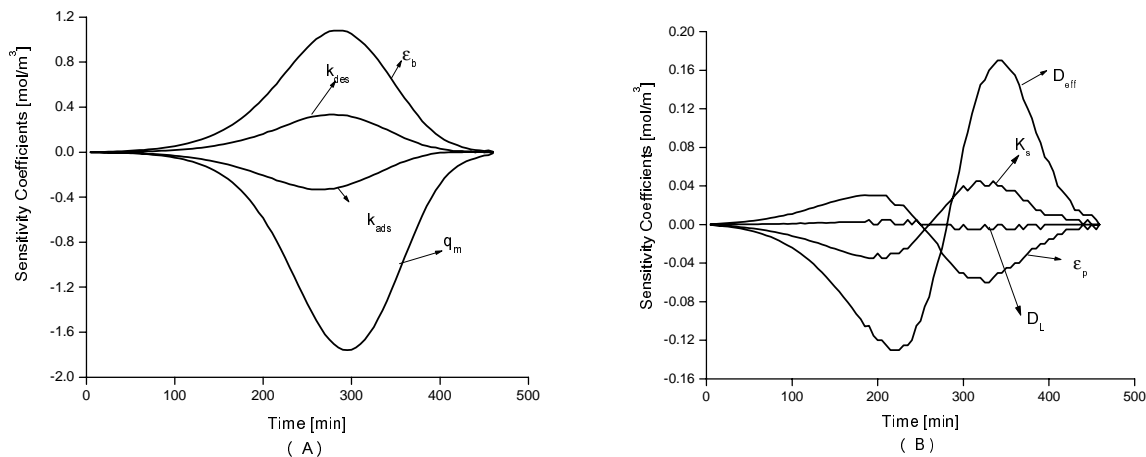


Figure 4 – Scaled sensitivity coefficient for a column of length  $L = 41$  mm .  
( A ) sensitivity coefficient of higher magnitude, ( B ) sensitivity coefficient of lower magnitude

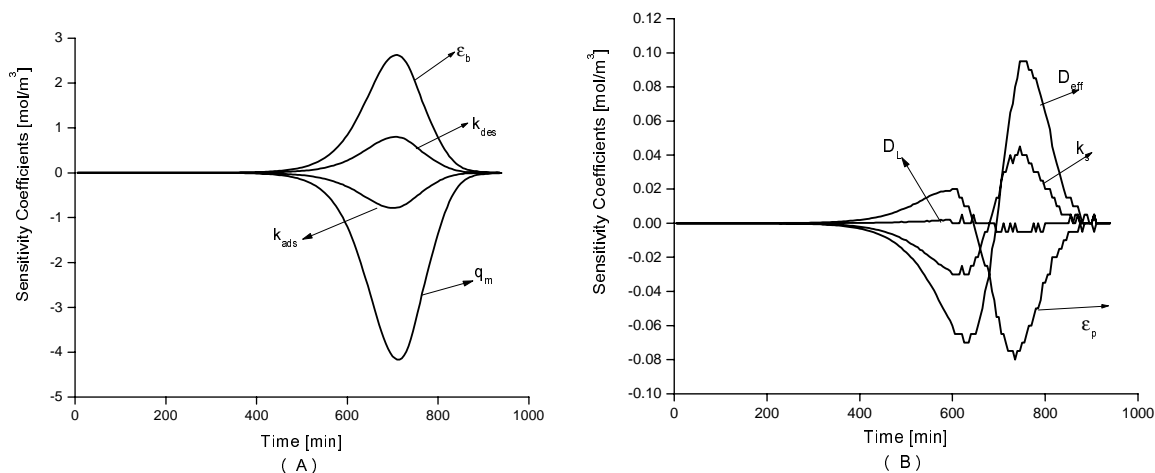


Figure 5 – Scaled sensitivity coefficient for a column of length  $L = 104$  mm .  
( A ) sensitivity coefficient of higher magnitude, ( B ) sensitivity coefficient of lower magnitude

In future works we will formulate and solve inverse mass transfer problems in order to estimate physic-chemical properties and/or process parameter using the computational model presented herein and experimental data.

An important requirement in parameter estimation is that the sensitivity coefficients should not be of small magnitude. Larger sensitivity coefficients are related to better chances of obtaining good estimates. Besides that, when two or more parameters are estimated simultaneously, their sensitivity coefficients must be linearly independent (Beck *et alii*, 1985).

Similar shapes, i. e., similar time dependence, of the sensitivity coefficients for two or more parameters indicate that their effects on the computational model response are similar, being, therefore, impossible to identify each parameter separately.

#### 4. Conclusion

In the present work we have presented the results obtained for the simulation of the liquid-solid adsorption phenomenon in resin beds. The Finite Volume Method was used and the results were compared with real experimental

data available in the literature. The computational results are in good agreement with the experimental data. It was also performed a parametric analysis which is in good agreement with the results published by other authors.

At last a sensitivity analysis was performed indicating that there are good chances to estimate the resin bed porosity and the saturation value of the concentration in Langmuir's adsorption isotherm, using experimental data on the concentration measured at the end of the adsorption column. In future works we will formulate and solve such inverse mass transfer problems.

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