# SOLUTION OF AN INVERSE MASS TRANSFER PROBLEM WITH A HYBRIDIZATION OF ARTIFICIAL NEURAL NETWORKS AND LEVENBERG-MARQUARDT METHOD

**Luciana Ferreira Lage**
**Ana Paula Curty Cuco**
**Antônio José da Silva Neto**
Departamento de Engenharia Mecânica e Energia, Instituto Politécnico, IPRJ,
Universidade do Estado do Rio de Janeiro, UERJ,
P.O. Box 97282, 28601-970, Nova Friburgo, RJ, Brazil
lucianaflage@gmail.com, lema_ana@iprj.uerj.br, ajsneto@iprj.uerj.br

**Flavio Moraes Folly**
Centro de Educação Superior a Distância do Estado do Rio de Janeiro – CEDERJ
IPRJ-UERJ - Av. Alberto Rangel S/N° – Pólo de Nova Friburgo, RJ, Brazil
flaviofolly@yahoo.com.br

**Francisco José da Cunha Pires Soeiro**
Departamento de Engenharia Mecânica, Faculdade de Engenharia,
Universidade do Estado do Rio de Janeiro, UERJ, 20550-013, Rio de Janeiro, RJ, Brazil.
soeiro@uerj.br

**Abstract.** *In the present work Artificial Neural Networks (ANN) and a hybridization with the Levenberg-Marquardt method (LM) are used for the solution of an inverse mass transfer problem, which is implicitly formulated as an optimization problem, for the estimation of parameters associated with the adsorption of biomolecules in resin beds.*

*The sensitivity analysis indicates that difficulties may arise in the estimation of one parameter and such situation was confirmed by the high value of the standard deviation associated with the estimation of that specific parameter.*

*The ANN led in most cases to a good fit between the direct problem solution obtained with the Thomas model and the experimental data for lisozyme adsorption, but in the other cases the hybridization ANN-LM yielded an improvement in the solution.*

*Keywords. Biotechnology, Inverse Problems, Mass Transfer, Artificial Neural Networks, Levenberg-Marquardt*

## 1. INTRODUCTION

Due to the relevant applications in the food and pharmaceutical industries, there is a growing demand for the formulation and solution of inverse mass transfer problems (Guiochon, 2002, Silva and Santana, 2000).

Just to give a few examples, Vasconcellos et al. (2003, 2002) Mendes et al. (2005), Folly et al. (2005) and Lage et al. (2006) investigated direct and inverse problems related to the solid-liquid adsorption of biomolecules in resin beds or stirred tanks, and Lugon and Silva Neto (2002) investigated the gas-liquid adsorption in buble columns.

In the present work we are interested in the estimation of adsorption isotherms and mass transfer parameters using experimental data on the concentration of a given substance (biomolecules) measured at the exit of a resin bed. For the direct problem solution we use Thomas model, which provides good results when the effects of axial dispersion are negligible in comparison to the other mass transfer mechanisms (Fellinger, 2003).

For the direct problem solution Thomas' model is used (Thomas, 1944, Folly et al. 2005), and for the solution of the inverse problem, Artificial Neural Networks (ANN) are used (Haykin, 1994, Soeiro and Silva Neto, 2006, Silva Neto and Soeiro, 2005, Soeiro et al., 2004, 2004a).

The experimental determination of adsorption isotherms is an important step for the design of new methods in preparative chromatography (Fellinger, 2003), as well as for the scale-up from laboratory to industrial production level (Seidel-Morgenstein, 2004). For such task the inverse problem of chromatography has provided the best estimates for the isotherm coefficients (Gritti and Guiochon, 2004).

The inverse problem is formulated implicitly, in which we seek to minimize the norm of the squared residues between calculated and measured values of the breakthrough curves, i.e. the time dependent values of the biomolecules concentration at the exit of the adsorption column. For the solution of the inverse problem Artificial Neural Networks (ANN) are used, as well as a hybridization of ANN with the Levenberg-Marquardt method. It is observed that the stochastic method may lead to good solutions by itself, or at least provide good initial guesses for the deterministic method.

The sensitivity analysis which was performed before the inverse problem was solved indicated that difficulties could arise in the estimation of one of the parameters of interest.

## 2. DIRECT PROBLEM FORMULATION AND SOLUTION

Consider an adsorption column composed by a fixed bed of adsorbent resins, in which $h$ represents the column length and $A_c$ its cross section. A mobile phase, composed by a diluted solution of the adsorbate of interest (biomolecule), percolates through the resin bed (fixed phase). The adsorbate is transferred from the bulk of the solution to the vicinity of the resin particles, i.e. mass transfer through the liquid film, and then it diffuses to the interior of the particle pores, being then adsorbed by the solid matrix.

The mathematical model for the chromatography process is based on the mass balance for the two phases; one for the mobile phase that flows through the macro scale porous fixed resin bed, and the other for the resin particles involving the microscale porous solid matrix (Guiochon and Lin, 2003).

### 2.1. Direct Problem Formulation

***Adsorbent mass balance (fixed phase)*** A simplified representation of the mass transfer mechanisms in the solid phase (Santacesaria et al., 1982) considers a time dependent average concentration $\overline{C_i}$ , and the resistances to the mass transfer represented by a global mass transfer coefficient $k_l$ . Being the adsorbate concentration in the bulk of the liquid phase represented by $C$ , the mass balance in the adsorbent spherical particles is written as

$$\varepsilon_i \frac{d\overline{C_i}}{dt} = \frac{3k_l}{R}\left(C - \overline{C_i}\right) - \frac{\partial q_i}{\partial t} \tag{1}$$

where $\varepsilon_i$ is the particle porosity, $q_i$ is the adsorbate concentration in the solid matrix, and $R$ is the radius of the adsorbent particles.

The mass transfer rate from the solution to the fixed phase is given by Chase (1984)

$$\frac{\partial q}{\partial t} = k_1 C \left(q_m - q\right) - k_2 q \tag{2}$$

where $q$ is the adsorbate concentration, $q_m$ is the maximum adsorbate concentration which the adsorbent may adsorb (maximum adsorption capacity), $k_1$ is the adsorption rate constant and $k_2$ is the desorption rate constant. Further, the dissociation rate constant $k_d$ is defined as

$$k_d = \frac{k_2}{k_1} \tag{3}$$

Considering a very fast adsorption rate on the surface, an equilibrium can be reached $\left(\partial q / \partial t = 0\right)$, (Silva and Santana, 2000), and from Eq. (2) we write

$$\frac{\partial q^*}{\partial t} = k_1 C^* \left(q_m - q^*\right) - k_2 q^* = 0 \tag{4}$$

which leads to the non-linear Langmuir isotherm

$$q^* = \frac{q_m \cdot C^*}{\left(k_d + C^*\right)} \tag{5}$$

Replacing $C^*$ by $\overline{C_i}$ , we obtain from Eqs. (1) and (5),

$$\left(\varepsilon_i + \frac{q_m \cdot k_d}{\left(k_d + \overline{C_i}\right)^2}\right)\frac{d\overline{C_i}}{dt} = \frac{3k_l}{R}\left(C\big|_{r=R} - \overline{C_i}\right) \tag{6}$$

We consider that at the beginning of the process there is no adsorbate in the resin particles. Therefore,

$$\overline{C_i} = 0 \quad \text{for} \quad t = 0 \tag{7}$$

*Column Mass Balance (mobile phase)* A mathematical model which takes into account mass transfer in the liquid film, axial dispersion and a constant flow rate is given by (Guiochon and Lin, 2003)

$$\varepsilon \frac{\partial C}{\partial t} = \varepsilon D_{ax} \frac{\partial^2 C}{\partial x^2} - u_0 \frac{\partial C}{\partial x} - (1 - \varepsilon) \frac{\partial q}{\partial t} \tag{8}$$

where $\varepsilon$ represents the bed porosity, $D_{ax}$ the axial dispersion coefficient, $u$ the constant linear velocity and $x$ represents the axial distance from the entrance of the column, with $0 \le x \le h$.

Using the same assumptions used for the mass balance in the fixed phase, Santacesaria et al. (1982) derived an approximation for the last term of Eq. (8) arriving at

$$\varepsilon \frac{\partial C}{\partial t} = \varepsilon D_{ax} \frac{\partial^2 C}{\partial x^2} - u_0 \frac{\partial C}{\partial x} - \frac{3k_l(1-\varepsilon)}{R}\left(C\big|_{r=R} - \overline{C}_i\right) \tag{9}$$

Here we use the Danckwerts boundary conditions

$$u \cdot C_0 = u \cdot C\big|_{x=0} - D_{ax}\frac{\partial C}{\partial x}\bigg|_{x=0} \quad , \text{for} \quad t > 0 \tag{10}$$

$$\frac{\partial C}{\partial x}\bigg|_{x=h} = 0 \quad , \text{for} \quad t > 0 \tag{11}$$

and the initial condition

$$C = 0 \quad \text{for} \quad t = 0 \text{ , in } \ 0 \le x \le h \tag{12}$$

## 2.2. Direct Problem Solution

For the particular case in which the axial dispersion may be neglected, i.e. $D_{ax} = 0$, and the adsorbate inflow is constant, i.e. $C_0 = constant$, the adsorption problem described in the previous section has an analytical solution (Chase, 1984, Blanch and Clark, 1997, Rice and Do, 1994) and it was first derived by Thomas (1944). The adsorbate concentration in the mobile phase at the exit of the adsorption column, $x = h$, is given by

$$\frac{C}{C_o} = \frac{J(\eta/\sigma, \eta T)}{J(\eta/\sigma, \eta T) + [1 - J(\eta, \eta T/\sigma)\exp(1 - \sigma^{-1})(\eta - \eta T)} \tag{13}$$

where
$$\sigma = 1 + C_o/k_d \tag{14}$$
$$\eta = q_m k_1 h A_c / fl \tag{15}$$
$$T = fl\,t\left(k_d + C_o\right)/ A_c\, q_m\, h \tag{16}$$

$fl$ is the volumetric flow rate through the column, and the function $J(a,b)$ is given by

$$J(a,b) = 1 - e^{-b}\int_0^a e^{-\xi}I_0(2\sqrt{b\xi}\,)\partial\xi \tag{17}$$

where $I_0$ is the modified Bessel function of the first kind and of order zero.

The function $J(a,b)$ may be approximated by an asymptotic series whose two first terms are given by

$$J(a,b) \approx \frac{1}{2}\left[1 - erf(\sqrt{a} - \sqrt{b})\right] + \frac{\exp\left[1 - (\sqrt{a} - \sqrt{b})^2\right]}{2\pi^{\frac{1}{2}}\left[(ab)^{\frac{1}{4}} + b^{\frac{1}{2}}\right]} \tag{18}$$

## 3. INVERSE PROBLEM FORMULATION AND SOLUTION

Following the sensitivity analysis performed by Folly et al. (2005), we are interested in the present work in the simultaneous estimation of the vector of unknowns

$$\vec{Z} = \{k_d, q_m\}^T \tag{19}$$

We consider as experimental data the adsorbate concentration in the liquid phase at the exit of the column, at $x = h$, i.e. $C_{\exp_i} = C_{\exp}(t_i), \quad i = 1,2,\ldots,N$, where $N$ is the total number of experimental data.

As the number of measured data, $N$, is usually much larger than the number of parameters to be estimated, $M = 2$, the inverse problem is formulated implicitly as an optimization problem in which we seek to minimize the squared residues cost function given by

$$Q(\vec{Z}) = \sum_{i=1}^{N} \left[ C_{calc_i}(\vec{Z}) - C_{\exp_i} \right]^2 = \vec{F}^T \vec{F} \tag{20}$$

where $C_{calc_i}(\vec{Z}) = C_{calc}(t_i, \vec{Z})$ represents the calculated values of the concentration obtained with Thomas model, and the elements of the vector of residues $\vec{F}$ are written as

$$F_i = C_{calc_i}(\vec{Z}) - C_{\exp_i} \quad, i = 1,2,\ldots,N \tag{21}$$

This formulation is necessary for the solution of the inverse problem with the Levenberg-Marquardt method. As will be presented next the construction of an Artificial Neural Network for the solution of the inverse problem requires only the knowledge of sets of input parameters $\{k_d, q_m\}$ and the calculated values of the concentration.

***Levenberg-Marquardt Method (LM).*** The minimization of the cost function $Q(\vec{Z})$ given by Eq. (20) with the Levenberg-Marquardt method consists on constructing an iterative procedure that starts with an initial guess $\vec{Z}^0$, and new estimates are obtained with

$$\vec{Z}^{n+1} = \vec{Z}^n + \Delta\vec{Z}^n, \quad n = 0,1,2,\ldots \tag{22}$$

being the variation $\Delta\vec{Z}^n$ calculated from

$$\Delta\vec{Z}^n = ((J^T)^n J^n + \lambda^n \Gamma)^{-1}(J^T)^n \vec{F}^n \tag{23}$$

where $\lambda$ is the damping parameter, $\Gamma$ represents the identity matrix, and the elements of the Jacobian matrix $J$ are

$$J_{ij} = \frac{\partial C_{calc_i}}{\partial Z_j}, \; i = 1,2,\ldots N \quad \text{and} \quad j = 1,2,\ldots M \tag{24}$$

The iterative procedure of sequentially calculating $\Delta\vec{Z}^n$ and $\vec{Z}^{n+1}$ from Eqs. (23) and (22), is continued until the convergence criterion

$$\left| \Delta Z_j^n \right| < \varepsilon_1 \quad \text{for} \quad j = 1,2,\ldots M \tag{25}$$

is satisfied, where $\varepsilon_1$ is a small number, say $10^{-5}$. The damping factor $\lambda^n$ is varied during the iterative procedure, such that when convergence is achieved its value is close to zero.

***Artificial Neural Networks (ANN).*** In order to solve the inverse mass transfer problem we use here a multi-layer perceptron (MLP) neural network (Haykin, 1994, Bishop, 1995). In Fig. 1 is given a representation of the MLP with the input and output layers, and one hidden layer, for the solution of the inverse mass transfer problem of determining the vector of unknowns $\vec{Z}$, given by Eq. (19), from the knowledge of the measured concentrations (breakthrough curve),

$Y_i$, $i = 1,2,...,N$. By providing $\vec{Y}$ at the input layer we expect that the ANN will provide at the output layer an estimate for $\vec{Z}$.

As real experimental data was not available, we generated sets of synthetic experimental data with

$$Y_i = C_{\exp_i} = C_{calc_i}\left(\vec{Z}_{exact}\right) + \sigma r_i \tag{26}$$

where $C_{calc_i}$ represents the calculated values of the concentration using the exact values of the physico-chemical properties, $\vec{Z}_{exact}$, which in a real application is not available and we want to determine with the inverse problem solution, $\sigma$ simulates the standard deviation of the measurement errors, and $r_i$ is a pseudo-random number generated in the range [-1, 1].

Each neuron $j$, with $j = 1,2,...,N_H$, in the hidden layer performs a linear combination of the input values provided at the input layer

$$p_j = \sum_{i=1}^{N} w_{ji}^{(1)} x_i + w_{j0}^{(1)} = \sum_{i=1}^{N} w_{ji}^{(1)} Y_i + w_{j0}^{(1)}, \quad j = 1,2,...,N_H \tag{27}$$

where $w_{ji}^{(1)}$, $j = 1,2,...,N_H$, $i = 1,2,...,N$ are the weights of the connections between the nodes of the input layer and the neurons of the hidden layer, $N$ is the number of nodes in the input layer, and $N_H$ is the number of neurons in the hidden layer.

The weighted sum $p_j$ given by Eq. (21) is viewed as an excitation to neuron $j$ of the hidden layer, which provides in response

$$q_j = f\left(p_j\right), \quad j = 1,2,...,N_H \tag{28}$$

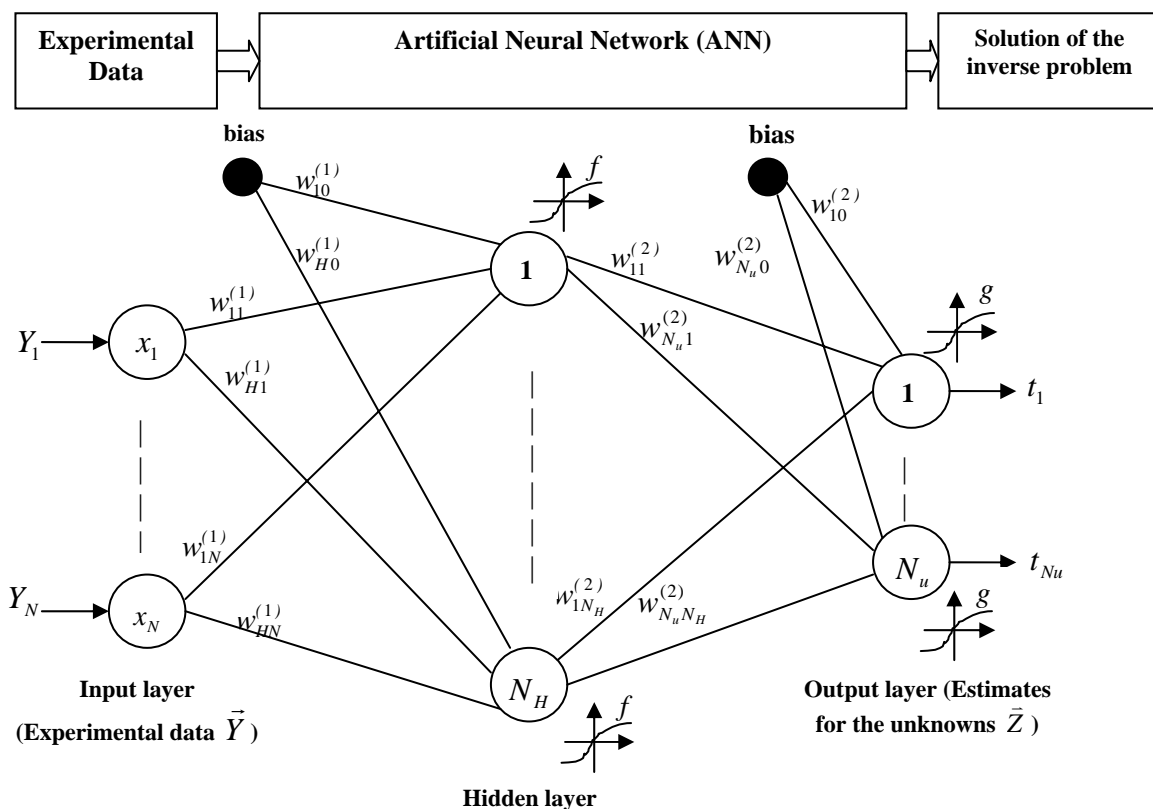where $f(.)$ is an activation function. Various choices for the function $f(.)$ are possible.



Figure 1 – Multi-layer perceptron network with one hidden layer for the inverse mass transfer problem.

Each neuron $k$, $k = 1,2,...,N_u$, of the output layer performs a linear combination of the response $q_j$, $j = 1,2,...,N_H$, of the neurons of the hidden layer

$$s_k = \sum_{j=1}^{N_H} w_{kj}^{(2)} q_j + w_{k0}^{(2)}, \qquad k = 1,2,...,N_u \tag{29}$$

where $w_{kj}^{(2)}$, $k = 1,2,...,N_u$, $j = 1,2,...,N_H$, are the weights of the connections between the neurons of the hidden layer and the neurons of the output layer, and $N_u$ is the number of neurons in the output layer, which coincides with the number of unknowns of the inverse problem. Here we have $N_u = 2$ (see Eq. (19)).

The weighted sum $s_k$ given by Eq. (29) is viewed as an excitation to neuron $k$ of the output layer, which provides in response

$$t_k = g(s_k), \qquad k = 1,2,...,N_u \tag{30}$$

where $g(.)$ is an activation function. Various choices for the function $g(.)$ are possible.

Combining Eqs. (27-30) we get

$$t_k = g\left( \sum_{j=1}^{N_H} w_{kj}^{(2)} f\left( \sum_{i=1}^{N} w_{ji}^{(1)} Y_i + w_{j0}^{(1)} \right) + w_{k0}^{(2)} \right), \qquad k = 1,2,...,N_u \tag{31}$$

Considering available the experimental data $Y_i$, $i = 1,2,...,N$, we observe in Eq. (31) that $t_k$, $k = 1,2,...,N_u$, are estimates for the unknowns $Z_k$, $k = 1,2,...,N_u$, obtained by the ANN. But before we can use Eq. (31) we must determine the weight parameters $w^{(1)}$ and $w^{(2)}$.

The determination of the weights $w^{(1)}$ and $w^{(2)}$ is accomplished by presenting a set of patterns (known input $\vec{Y}_{exact}$ and outputs $\vec{Z}_{exact}$) and calculating the weights that provide the best match between the calculated values $\vec{t}$ and the target values $\vec{Z}_{exact}$. The patterns used in this supervised training stage of the ANN were generated by calculating the values $\vec{Y}_{exact}$ from known sets $\vec{Z}_{exact}$ with the Thomas' model described in Section 2.2.

The presentation of a full set of patterns is denominated epoch. After one epoch is completed the set of patterns is presented again, in a different (random) order. After a number of epochs, once the comparison error is reduced to an acceptable level over the whole training set, the training phase ends and the ANN is established. Therefore, in our inverse mass transfer problem the unknowns $\vec{Z}$ (output) can be determined using the experimental data $\vec{Y}$ as the inputs to the ANN (see Fig. 1) and the simple forward sweep described by Eq. (31).

One interesting feature associated with the implementation of the ANN for the solution of the inverse problem was that in the training phase of the ANN we have corrupted the set of patterns with different levels of noise which led to an improvement on the estimated values for the unknowns.

***Hybridization ANN-LM.*** The deterministic LM may not converge if a poor choice is made for the initial guess $\vec{Z}^0$, and if it converges it may lead to a local minimum.

Silva Neto and Soeiro (2003) have used previously a hybridization GA-LM for the solution of inverse problems in heat conduction and radiative transfer, in which the stochastic method is used to generate an initial guess for the deterministic method. The hybridization ANN-LM has also been used for the solution of inverse radiative transfer problems (Soeiro et al., 2004, 2204a, 2006, Silva Neto and Soeiro, 2005)

The same approach is used in the present work for the solution of an inverse problem mass transfer problem as an attempt to estimate the vector of unknowns given by Eq. (19).

## 4. RESULTS AND DISCUSSION

In Table 1 are presented the physico-chemical and process parameters related to real experiments performed by Chase (1984) with the substance lisozyme.

Table 1: Physico-chemical and process parameters for Chase's experiments (1984) with lisozyme.

| Parameter | Value |
|---|---|
| $h$ - column height (cm) | 10.4 |
| $A_c$ - column cross section (cm$^2$) | 0.785 |
| $fl$ - volumetric flow rate (ml/min) | 1.0 |
| $C_0$ - adsorbate concentration at the column inlet | 0.1 mg/ml |
| $q_m$ - maximum adsorption capacity | 14 mg/ml |
| $k_d$ - dissociation rate constant | 0.025 mg/ml |
| $k_1$ - adsorption rate constant | 0.20 ml/mg.min |

The values of $k_1$, $k_d$ and $q_m$ shown in Table 1 were obtained by Chase (1984) using a batch experiment with the Langmuir isotherm.

In Fig. 1 are shown the sensitivity coefficients for the parameters $k_1$, $k_d$ and $q_m$ which are defined as

$$X_{k_1}(t) = k_1 \frac{\partial C_{calc}(t)}{\partial k_1}, \; X_{k_d}(t) = k_d \frac{\partial C_{calc}(t)}{\partial k_d} \text{ and } X_{q_m}(t) = q_m \frac{\partial C_{calc}(t)}{\partial q_m} \qquad (32a\text{-}c)$$

From Fig. 1 it can be observed that using Thomas model and the experimental data obtained by Chase (1984) for lisozyme, it is not possible to estimate $k_1$. Therefore, in all computations whose results will be presented next it has been considered a fixed value $k_1 = 0.20 \; ml/mg \cdot \min$. Difficulties may be observed in the estimation of $k_d$ due to the low sensitivity of the model to that parameter, and good estimates may be obtained for the parameter $q_m$. This has been confirmed by Folly et al. (2005), as well as by the results obtained with the present work.
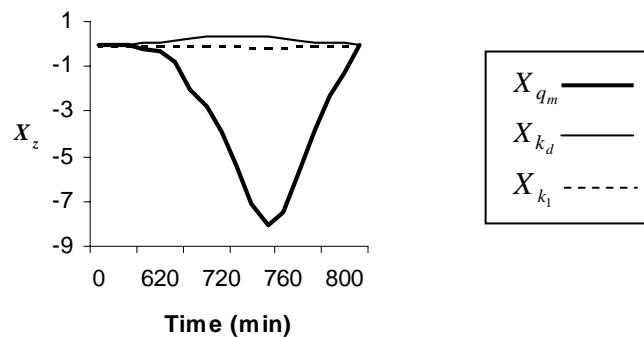


Figure 1: Sensitivity coefficients with respect to parameters $k_1$, $k_d$ and $q_m$ Folly et al. (2005).

In Table 2 are shown the results obtained with the ANN method, as well as with the hybridization ANN-LM. It was considered a total number of 21 test cases but in Table 2 are shown the results for only four cases. One of the test cases selected is related to Chase's experimental data (Chase, 1984) and the other three represent a broad range of variation of the parameters of interest. The level of noise corresponds to the noise artificially inserted in the patterns used for the ANN training. The hybridization consists in using the estimates obtained with ANN, $\vec{Z}_{ANN}$, as the initial guess for the Levenberg-Marquardt method, i.e. $\vec{Z}_{LM}^0 = \vec{Z}_{ANN}$.

Table 2: Estimates for $k_d$ and $q_m$ for lisozyme using the ANN method, the hybridization ANN-LM, and Chase's experimental data (1984).

| Method | | ANN | | | ANN-LM | | |
|---|---|---|---|---|---|---|---|
| Noise | Test-Case | $k_d$ (mg/ml) | $q_m$ (mg/ml) | $Q$ [Eq. (20)] | $k_d$ (mg/ml) | $q_m$ (mg/ml) | $Q$ [Eq. (20)] |
| 0% | 1 | 0.0198 | 13.2002 | 2.2083x10$^{-4}$ | 0.0200 | 13.2002 | 5.9478x10$^{-9}$ |
| | 12 | 0.0363 | 14.3002 | 8.7062x10$^{-6}$ | 0.0365 | 14.2999 | 6.8471x10$^{-9}$ |
| | 17 | 0.0445 | 14.9006 | 3.1505x10$^{-4}$ | 0.0440 | 14.9004 | 1.2466x10$^{-7}$ |
| | 21 | 0.0221 | 14.0912 | 0.1237 | 0.0451 | 14.2117 | 0.0211 |

Table 2 (Continuation): Estimates for $k_d$ and $q_m$ for lisozyme using the ANN method, the hybridization ANN-LM, and Chase's experimental data (1984).

| Method | | ANN | | | ANN-LM | | |
| Noise | Test-Case | $k_d$ (mg/ml) | $q_m$ (mg/ml) | $Q$ [Eq. (20)] | $k_d$ (mg/ml) | $q_m$ (mg/ml) | $Q$ [Eq. (20)] |
|---|---|---|---|---|---|---|---|
| 1% | 1 | 0.0214 | 13.1877 | $8.6047 \times 10^{-6}$ | 0.0201 | 13.1896 | $3.7872 \times 10^{-4}$ |
| | 12 | 0.0362 | 14.3592 | $5.76924 \times 10^{-3}$ | 0.0369 | 14.3051 | $4.9353 \times 10^{-5}$ |
| | 17 | 0.0431 | 14.9810 | $01.4919 \times 10^{-2}$ | 0.0432 | 14.8719 | $2.4697 \times 10^{-4}$ |
| | 21 | 0.0395 | 14.0839 | $2.2107 \times 10^{-2}$ | 0.0420 | 14.1108 | $1.9450 \times 10^{-2}$ |
| 3% | 1 | 0.0266 | 12.2859 | 0.2019 | 0.0425 | 12.9063 | $4.0347 \times 10^{-2}$ |
| | 12 | 0.0346 | 14.4627 | $4.4205 \times 10^{-2}$ | 0.0368 | 14.2971 | $1.1351 \times 10^{-3}$ |
| | 17 | 0.0414 | 15.0334 | $5.8851 \times 10^{-2}$ | 0.0438 | 14.8899 | $3.0664 \times 10^{-4}$ |
| | 21 | 0.0068 | 17.5899 | 0.8705 | 0.0024 | 18.8351 | $1.2038 \times 10^{-2}$ |
| 5% | 1 | 0.0192 | 13.0654 | $3.8384 \times 10^{-2}$ | 0.0219 | 13.068 | $3.5052 \times 10^{-3}$ |
| | 12 | 0.0351 | 13.6334 | 0.6600 | 0.0514 | 14.8187 | $5.8252 \times 10^{-2}$ |
| | 17 | 0.0436 | 14.5103 | 0.1661 | 0.0428 | 14.8073 | $1.4931 \times 10^{-3}$ |
| | 21 | 0.0303 | 14.6805 | 0.5742 | 0.0354 | 14.0803 | $3.3026 \times 10^{-2}$ |
| 8% | 1 | 0.0174 | 13.9508 | 0.3892 | 0.0190 | 13.2317 | $1.3382 \times 10^{-2}$ |
| | 12 | 0.0374 | 14.3773 | $2.3650 \times 10^{-2}$ | 0.0350 | 14.2682 | $9.7210 \times 10^{-3}$ |
| | 17 | 0.0395 | 15.0041 | $5.3445 \times 10^{-2}$ | 0.0443 | 14.9315 | $2.7835 \times 10^{-3}$ |
| | 21 | 0.0274 | 13.9981 | $4.9931 \times 10^{-2}$ | 0.0438 | 14.1659 | $1.9864 \times 10^{-2}$ |

From the results shown in Table 2, when compared to the value shown in Table 1, one observes that indeed the estimates for $k_d$ seem to be poor. A much better result is obtained for the estimates for $q_m$. Nonetheless, as both parameters $k_d$ and $q_m$ are being estimated simultaneously, it is expected that the quality of the estimates for $q_m$ are affected by the low sensitivity of the model to the parameter $k_d$.

The control parameters used in the ANN implementation are shown in Table 3. In this work the Neural Network Toolbox of the software MATLAB 6.5.1 (Mathworks, Inc.) was used with the following neuron model in the backpropagation network: 17 elements in the input vector (corresponding to the number of points where concentration is measured), log-sigmoid (logsig) transfer function between the input layer and the hidden layer (with 34 elements) and a linear transfer function (purelin) in the output layer (with 2 elements in the output vector, which are the unknowns of the formulated inverse problem). The number of epochs required in the training stage of the ANN varies with the convergence goal previously specified which on its turn depends on the test case under consideration.

Table 3: Control parameters used in the ANN method.

| Control Parameter | Value |
|---|---|
| Output vector $\left(N_u\right)$ | 2 elements |
| Input vector $\left(N\right)$ | 17 elements |
| Patterns | 400 |
| Goal for convergence | from $10^{-2}$ up to $10^{-6}$ |

In Figs. 2-6 are shown the corrupted, experimental and calculated breakthrough curves, being the latter computed with the estimated values for $k_d$ and $q_m$ obtained with either ANN or ANN-LM and the Thomas model. These results were selected because the hybridization ANN-LM led to a better fit of the model to the experimental data.
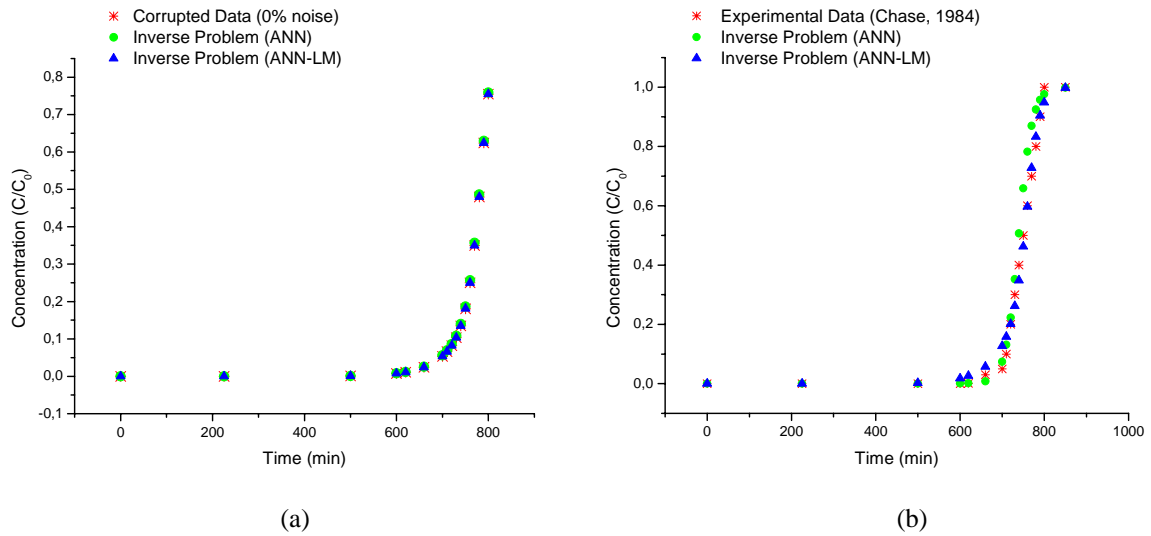
(a)



(b)

Figure 2: Corrupted, Experimental (Chase, 1984) and calculated breakthrough curves for lisozyme, with ANN method and hybridization ANN-LM

(a) Test-Case 17 with 0 % noise in the training set data. (b) Tes-Case 21 with 0 % noise in the training set data.
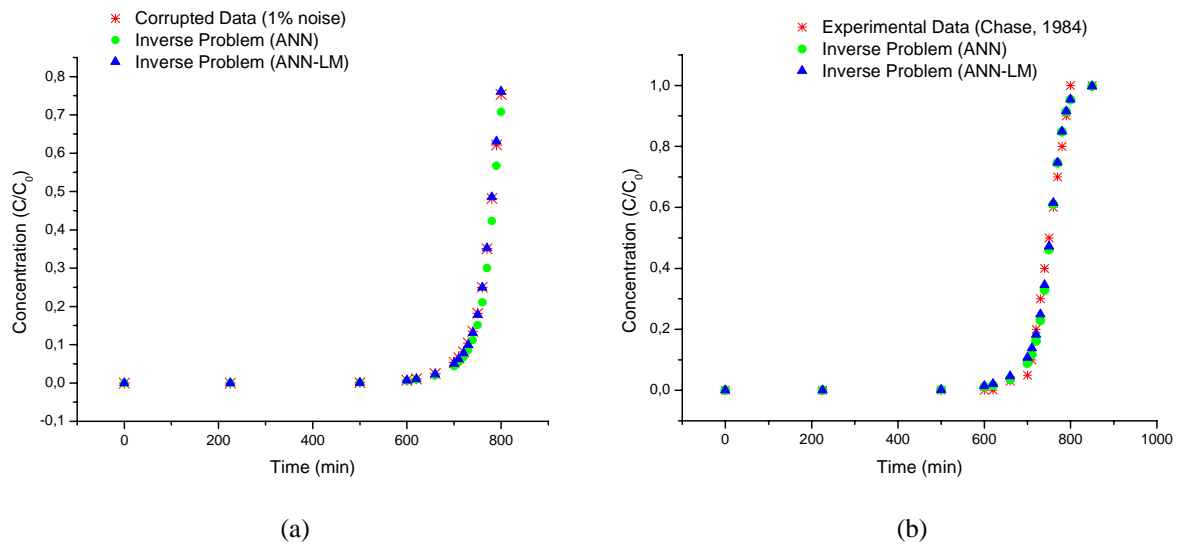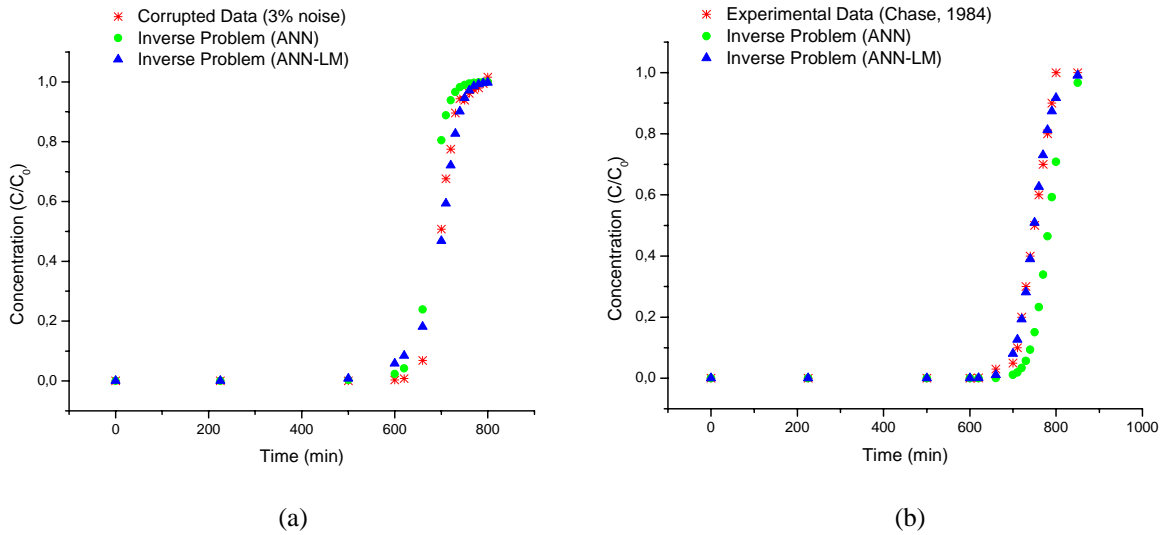


(a)



(b)

Figure 3: Corrupted, Experimental (Chase, 1984) and calculated breakthrough curves for lisozyme, with ANN method and hybridization ANN-LM

(a) Test-Case 17 with 1 % noise in the training set data. (b) Test-Case 21 with 1 % noise in the training set data.

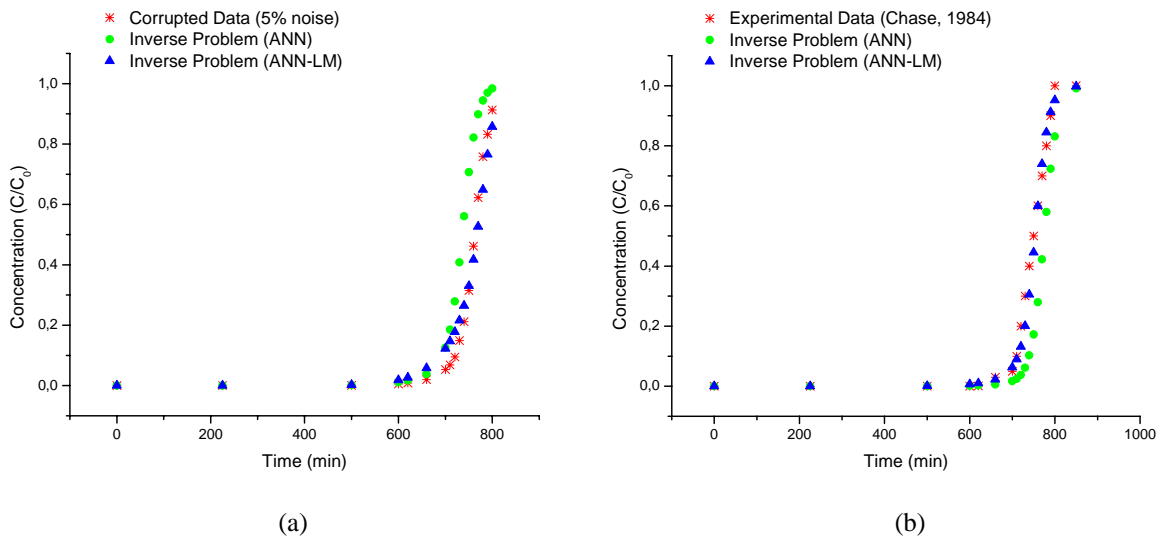(a)                                                                          (b)

Figure 4: Corrupted, Experimental (Chase, 1984) and calculated breakthrough curves for lisozyme,
with ANN method and hybridization ANN-LM

(a) Test-Case 1 with 3 % noise in the training set data. (b) Test-Case 21 with 3 % noise in the training set data.



(a)                                                                          (b)

Figure 5: Corrupted, Experimental (Chase, 1984) and calculated breakthrough curves for lisozyme,
with ANN method and hybridization ANN-LM

(a) Test-Case 12 with 5 % noise in the training set data. (b) Test-Case 21 with 5 % noise in the training set data.
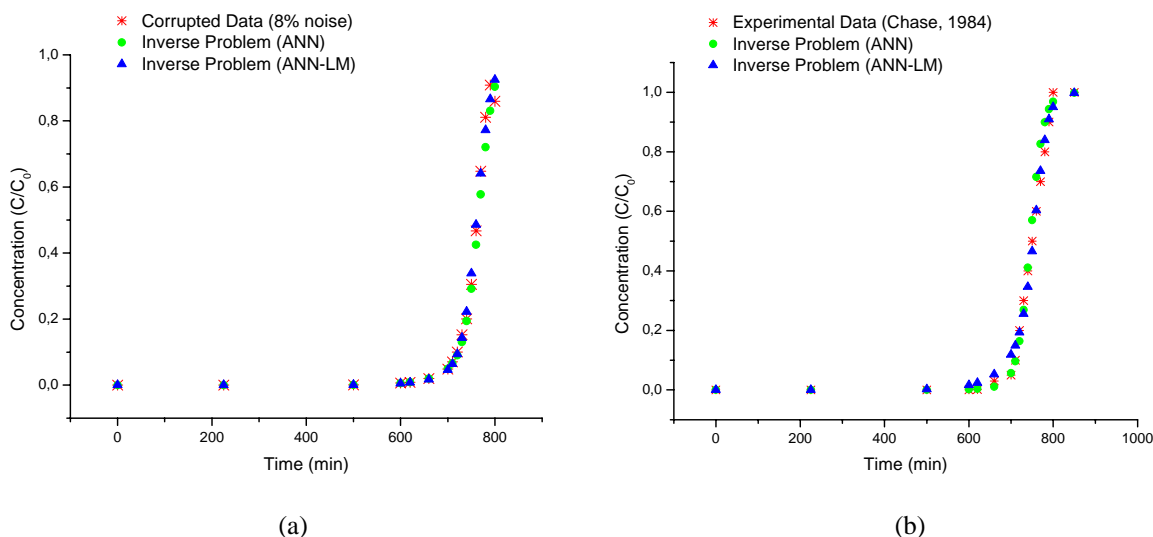
(a)                                    (b)

Figure 6: Corrupted, Experimental (Chase, 1984) and calculated breakthrough curves for lisozyme,
with ANN method and hybridization ANN-LM

(a) Test-Case 12 with 8 % noise in the training set data. (b) Test-Case 21 with 8 % noise in the training set data.

## 5. CONCLUSIONS

In the present work it is observed that the hybridization of a deterministic (LM) with an stochastic (ANN) method may lead to a better fit of a model used for the direct problem solution to real experimental data available for a mass transfer problem involving solid-liquid adsorption. Nonetheless, the sensitivity analysis performed before the inverse problem is solved shows that difficulties may arise in the estimation of one mass transfer parameter, the dissociation rate constant $k_d$.

The estimates for the maximum adsorption capacity, $q_m$, are much better, but it may be affect by the poor sensitivity of the direct model to the parameter $k_d$.

In a future work the authors will investigate the estimation of parameters $k_d$ and $q_m$ separately.

As the direct problem solution is analytical, and very fast to compute, the approach described in the present work for the solution of the inverse mass transfer problem is not computationally intensive, and therefore CPU time requirement is not an issue.

### 6. Acknowledgements

### 7. REFERENCES

Bishop, C. M., 1995, "Neural Networks for Pattern Recognition", Ed. Clarendon Press.
Blanch, H.W. and Clark, D.S., 1997, "Biochemical Engineering", Ed. Marcel Dekker, New York.
Chase, H.A., 1984, "Prediction of the Performance of Preparative Affinity Chromatography". Journal of Chromatography, Vol. 297, pp. 179-202.
Fellinger, A., Cavazzini, A. and Guiochon, G., , 2003, "Numerical determination of the competitive isotherm of enantiomers", Journal of Chromatography A, 986, pp. 207-225.
Folly, F. M., Silva Neto, A.J. and Santana, C.C., 2005, "An Inverse Mass Transfer Problem for the Characterization of Simulated Moving Beds Adsorption Columns". Proc. 5th International Conference on Inverse Problems in Engineering: Theory and Practice, Cambridge, UK.
Guiochon, G. and Lin, B., 2003 "Modeling for Preparative Chromatography". Ed. Academic Press, UK.
Guiochon, G., 2002, "Preparative Liquid Chromatography (Review)". Journal of Chromatography, Vol. 965, pp. 129-161.

Gritti, F. and Guiochon, G., 2004, "Effect of the ionic strength of the solution and the nature of its ions on the adsorption mechanism of ionic species in RPLC-III. Equilibrium isotherms and overload band profiles on Kromasil-$C_{18}$", Journal of Chromatography A, 1047, pp. 33-48.

Haykin, S., 1994, "Neural Networks: A Comprehensive Foundation", Ed. Prentice Hall, Inc..

Lage, L. F., Cuco, A. P. C., Folly, F. M., Soeiro, F. J. C. P. and Silva Neto, A. J., 2006, "Stochastic and Hybrid Methods for the Solution of an Inverse Mass Transfer Problem", Proc. III European Conference on Computational Mechanics, Lisbon, Portugal.

Lugon Jr., J., Silva Neto, A.J. and Santana, C. C., 2002, "Estimation of Gas-Liquid Adsorption Isotherms Using an Inverse Problem Approach". TEMA – Tendências em Matemática Aplicada e Computacional, Vol. 3, No. 2, pp. 161-170. In Portuguese.

Mendes, M. C. S., Silva Neto, A. J. and Vasconcellos, J. F. V., 2005, "Numerical Simulation of Adsorption Columns: Model Comparison and Sensitivity Analysis", Proc. 18th International Congress of Mechanical Engineering, ABCM, Ouro Preto, Brazil.

Rice, G. R. and Do, D. D., 1994, "Applied Mathematics and Modeling for Chemical Engineers", Ed. John Wiley & Sons, New York.

Santacesaria, E., Morbidelli, M., Servida, A., Storti, G. and Carrã, S., 1982, "Separation of xylenes on y zeolites-2. Breakthrough Curves and their Interpretation", Ind. Eng. Chem. Process Des. Dev., Vol. 21, pp. 446-451.

Seidel-Morgenstein, A., 2004, Experimental determination of single solute and competitive adsorption isotherms. *Journal of Chromatography A,* 1037, 255-272.

Silva Neto, A.J. and Soeiro, F.J.C.P., 2003, "Solution of implicitly formulated inverse heat transfer problems with hybrid methods", 2nd MIT Conference on Computational Fluid and Solid Mechanics, Cambridge, USA.

Silva Neto A. J. and Soeiro, F. J. C. P., 2005, "Inverse problem of space dependent albedo estimation with artificial neural networks and hybrid methods", Proc. 18th International Congress of Mechanical Engineering, COBEM, ABCM, Ouro Preto, Brazil

Silva, F.R.C. and Santana, C.C., 2000, "Adsorption of Inulinases in Ion Exchange Columns". Appl. Biochem. Biotech, Vol. 84-86, pp. 1063-1078.

Soeiro, F. J. C. P. and Silva Neto, A. J., 2006, "Solution of Inverse Radiative Transfer Problems in Two-Layer Media with Artrificial Neural Networks", Proc. 14th Inverse Problems in Engineering Seminar, Ames, USA.

Soeiro, F. J. C. P., Soares, P. O. and Silva Neto, A. J., 2004, "Solution of Inverse Radiative Transfer Problems with Artificial Neural Networks and Hybrid Methods", Proc. 13th Inverse Problems in Engineering Seminar, Cincinnati, USA, pp. 163-169.

Soeiro, F. J. C. P., Soares, P. O., Campos Velho, H.F. and Silva Neto, A. J., 2004a, "Using Neural Networks to Obtain Initial Estimates for the Solution of Inverse Heat Transfer Problems", Proc. Inverse Problems, Design and Optimization Symposium, vol. I, pp. 358-363, Rio de Janeiro, Brazil.

Thomas, H., 1944, "Heterogeneous Ion Exchange in Flowing System", J. Am. Chem. Soc., Vol. 66, pp. 1664-1668.

Vasconcellos, J.F.V., Silva Neto, A.J. and Santana, C.C., 2003, "An Inverse Mass Transfer Problem in Solid-Liquid Adsorption Systems". Inverse Problems in Engineering, Vol. 11, No. 5, pp. 391-408.

Vasconcelos, J.F.V., Silva Neto, A.J., Santana, C.C. and Soeiro, F.J.C.P., 2002, "Parameter Estimation in Adsorption Columns with a Stochastic Global Optimization Method". Proc. 4th International Conference on Inverse Problems in Engineering: Theory and Practice, Angra dos Reis, Brazil, Vol. II, pp. 227-234.