

Inverse and direct modeling applied in the estimation of kinetic parameters of BSA adsorption

D.P. Costa^{1,†}, L.D.T. Câmara¹, M.F. Irizar Mesa², O. Llanes Santiago², D. Curbelo Rodríguez³ and A.J. Silva Neto¹

¹Universidade do Estado do Rio de Janeiro – Instituto Politécnico (UERJ-IPRJ), Departamento de Engenharia Mecânica e Energia

²Instituto Superior Politécnico José Antonio Echeverría (ISPJAE-CUJAE), Departamento de Automática e Computación

³Centro de Inmunología Molecular (CIM)

ABSTRACT

The kinetic modeling applied in the parameters estimation of chromatographic adsorption processes is an important tool in the understanding and improvement of these separation systems. In this work, two kinetic models were utilized in the parameters estimation of BSA adsorption. The correlations between the irreversible kinetic model and the reversible kinetic model with the experimental data were carried out using the Linear Driving Force and the Random Restricted Window (R2W) method, respectively. From both models was possible to achieve a good fit with the experimental data, obtaining parameters with higher accuracy due to the low residues of the cost function.

Key words: adsorption, BSA, chromatography, kinetic modeling

INTRODUCTION

The comprehension about the adsorption mechanisms is an important step for the development and improvement of several adsorption processes involved with the substance studied, such as: separation, purification, decontamination, and others.

In this context, the agitated batch process of adsorption is an important method used for the estimation of equilibrium parameters, which are applied in the processes modeling such as chromatography and Simulated Moving Bed (SMB). The hydrodynamic aspects of such processes become the kinetic modeling an interesting tool for the obtaining parameters that will be incorporated in the equipment design.

The application of an inverse problem methodology for chromatographic systems is a new promising area since the solution of the Inverse Problems has several relevant applications in the engineering field ¹. Other results can be found in ²⁻⁷. In the work of Vasconcellos *et al.* ¹ the inverse problem formulation with the minimization of the square residues cost function was applied in the mass transfer parameters estimation of protein adsorption (Bovine Serum Albumin-BSA).

The optimization method utilized is the same applied by ⁷, the Levenberg-Marquardt. The method in both applications was successful in determining the parameters of non-linear equations.

Some contributions in the application of adsorption kinetic models for the liquid phase can be encountered through the following publications: ⁸⁻¹⁴. An important contribution comes from the work of Chase ⁹, which implemented semi-analytical expressions to model the adsorption phenomena in agitated tanks and chromatographic columns. He considered the kinetic concepts to model the adsorption process as a reversible system with an overall rate of second-order. In a general point of view, the above publications, with exception of the Chase model ⁹, use simplified or empiric expressions for the kinetic models. The advantage of utilizing the concepts of kinetic theory to develop new models, is that the stoichiometry and order, related to the compounds in the adsorption system considered, can be varied and analyzed independently, leading to a better understanding of the involved kinetics phenomenology.

In this work two different kinetic models were applied in the parameters estimation of BSA adsorption on Streamline DEAE. The first and second models are related, respectively, to irreversible and reversible kinetics mechanisms, being utilized the inverse stochastic method (R2W) to correlate the last model with the experimental data.

[†] Corresponding author: dpcosta@iprj.uerj.br

DIRECT MODELING

Irreversible kinetic model (IKM2)

The agitated adsorption techniques to measure kinetic parameters are modeled with following expression for batch process,

$$r_A = \frac{1}{V} \frac{dN_A}{dt} \quad (1)$$

where r_A corresponds to the adsorption rate of component A being proportional to the variation in the moles number of solute A and the tank volume (V) is assumed constant.

The adsorption stoichiometry considered is represented in Fig. 1. It is related to an irreversible kinetic mechanism of the adsorption, i.e., the desorption phenomenon is not considered.

The kinetic mechanism of the adsorption in the Fig. 1 considers the adsorption of 1 (one) mol of solute A (BSA) in 1 (one) mol of active site into the adsorbent (s). The kinetic modeling, in terms of consumption rate of the solute A (r_A) is written in the following form:

$$(-r_A) = k_1 C_A^l C_{A,s}^m \quad (2)$$

where k_1 , C_A and $C_{A,s}$ represent the kinetic constant of adsorption, the concentration of solute A in liquid phase and the concentration of adsorption sites in the solid phase, respectively. For a first order elementary adsorption, the exponents l and m are equal to 1, which corresponds to an overall rate of second order.

With the considerations just described, the Eq. (2) can be solved analytically through the Eq. (1), applying a balance in the moles number of active site of adsorption,

$$C_t = C_s + C_{A,s} \quad (3)$$

in which C_t corresponds to the maximum concentration of adsorption sites, i.e., the sum through the concentration of vacant sites (C_s) and occupied sites by solute A ($C_{A,s}$). Another important balance is related to the concentration of solute A . In the balance of solute A , the initial concentration in the solution (C_{A0}) corresponds to the sum of the initial solute concentration in the solution (C_A) and the adsorbed solute concentration in the solid phase ($C_{A,s}$),

$$C_{A0} = C_A + C_{A,s} \quad (4)$$

The combination of Eqs. (1-4) leads to:

$$\int \frac{dC_A}{C_A(a + C_A)} = -\int k_1 dt \quad (5)$$

in which $a = C_t - C_{A0}$. Performing the integrations in Eq. (5) using the following initial condition,

$$t = 0 \Rightarrow \begin{cases} C_A = C_{A0} \\ C_t = C_s \end{cases} \quad (6)$$

results the final expression of the IKM2¹⁵ kinetic model (irreversible model) which is related to the concentration of solute A , with C_t , C_{A0} and k_1 in the time domain.

$$C_A = \frac{a C_{A0}}{(a + C_{A0}) e^{a k_1 t} - C_{A0}} \quad (7)$$

Reversible kinetic model

The reversible kinetic mechanism can be observed in Fig. 2, in which the parameters k_1 and k_2 correspond to the kinetic constants of adsorption and desorption, respectively.

From Fig. 2, the rate of consumption of the solute A , represented by r_A , is determined by Eq. (8).

$$-r_A = k_1 C_A C_t - k_2 C_{A,s} \quad (8)$$

in which C_A , C_t and $C_{A,s}$ represent the concentration of solute A in the liquid phase, the concentration of active sites of the adsorbent and the concentration of solute A adsorbed in the solid phase, respectively.

The active sites concentration is obtained from the mass balance in the adsorbent,

$$C_t = (q_m - C_{A,s}) \quad (9)$$

in which q_m represents the maximum capacity of adsorption of the solute A (for each initial concentration) on adsorbent.

After such considerations, the reversible kinetic model studied is derived from the rate of variation of BSA concentration into the agitated tank (batch system of adsorption),

$$\frac{dC_A}{dt} = -k_1 C_A (q_m - C_{A,s}) + k_2 C_{A,s} \quad (10)$$

$$\frac{dC_{A,s}}{dt} = k_1 C_A (q_m - C_{A,s}) - k_2 C_{A,s} \quad (11)$$

INVERSE MODELING

Random restricted window (R2W)

The R2W is a basic random algorithm of search that follows the flowchart of Fig. 3¹⁶. The Fig. 4 shows a schematic representation of the R2W algorithm.

The objective of the algorithm is the optimization of the following function Z (Eq. 12) from the determination of the best solution of parameters, ζ_i .

$$Z = f(\zeta_1, \zeta_2, \zeta_3, \dots) \quad (12)$$

Initially, there is a generation of S random seeds related to the parameters above as following the procedure below:

$$\zeta_i = \zeta_{iL} + R(\zeta_{iH} - \zeta_{iL}) \quad (13)$$

in which ζ_{iL} , ζ_{iH} and R represents the lowest value of the parameter, the highest value and the random number, respectively. The procedure from Eq. (13) is repeated for each parameter in the function Z of Eq. (12), that is, for each seed S there is the random estimation for each parameter of the function Z . The random numbers are generated from a uniform random distribution.

After the initial procedure of random estimative of the parameters (step 1 in the flowchart), we have the determination of the profile of function Z . In this work the function Z was represented by a reversible kinetic model (Eqs. 10 and 11).

The step 2 in the flowchart corresponds to the comparison between the simulation results from the reversible kinetic model and the experimental data. This comparison was carried out of the squared residues function Q ,

$$Q = \sum_{i=1}^n (C_{exp} - C_{sim})^2 \quad (14)$$

with the terms C_{exp} , C_{sim} and n corresponding to, respectively, the experimental concentration, the concentration from the simulation and the number of points for the same event (number of experimental points in the range of time). In step 2 we have a vector of residues from the number of seeds generated. For each seed we have a comparison between the model and the experimental data, having the determination of the squared residue Q .

The step 3 corresponds to the determination of the seed S that leads to the lowest value of residue Q , i.e., the solution that provides the best fit between the experimental data and the simulation results. The best solution of seed S is utilized in step 4.

In the step 4 there is a restriction of the search around the solutions of the parameters encountered for the seed with the lowest residue. The search restriction is determined by the factor range of search (δ) which establishes the domain of search near the best solutions of parameters of Eq. (12). The new range of search is determined by

$$\zeta_{iL} = \zeta_i^* - \delta \cdot (\zeta_i^*) \quad \zeta_{iH} = \zeta_i^* + \delta \cdot (\zeta_i^*) \quad (15)$$

in which ζ_i^* corresponds to the best solution of the parameter i encountered in the previous step. For each parameter ζ_i^* of the

seed there is the determination of a new range of search utilizing the same range of search (δ).

The final step 5 is reached for the cases which is not assumed a new phase of search ($\psi=0$) or the number of phases is achieved. For the cases which are assumed a number of phases, the algorithm returns to the step 1 with the range of search restricted, i.e., the same number of random seeds are generated in the new restricted domain for each of the parameters. This procedure leads to a high concentration of estimations over a small range, in which the chance to obtain the best solution is high.

RESULTS AND DISCUSSIONS

Irreversible kinetic model (IKM2)

From Figs. 5 and 6 can be seen the good correlation between the IKM2 model and the experimental data for two different initial concentrations of BSA.

In this case was applied the basic Linear Driving Force ¹⁶, due to the simplicity of such model in the estimation of only one parameter, the kinetic constant of the adsorption (k_1).

Table 1 shows the maximum capacity of adsorption for each initial concentration (q_m) of BSA (total number of BSA molecules adsorbed on the active sites of the adsorbent), the kinetic constant of adsorption (k_1) and the cost function of square residues (Q). The maximum capacity of adsorption for each initial concentration is easily obtained through the difference between the initial (C_{A0}) and equilibrium concentration (C_{eq}).

From the results shown can be observed that there is an increase in the value of q_m with the increase in the initial concentration, being this behavior typical of the Langmuir isotherm. Also, there is an increase in the kinetic constant of adsorption with the increase in the value of C_{A0} . The value of the cost function was higher for the case with high concentration, indicating that in this case the agreement with the experimental data was less satisfactory with compared to the other one.

Reversible kinetic model

In the reversible model two kinetic constants were estimated at the same time, the kinetic constant of adsorption (k_1) and the kinetic constant of desorption (k_2), utilizing the R2W to provide the correlations with the experimental data.

From Figs. 7 and 8 can be seen the excellent performance of the reversible model for both initial concentrations studied.

Table 2 presents the simulation results along with the values of the cost function (Q). Compared to the IKM2 model, also the high value of (Q) comes from the high concentration case, indicating a less satisfactory fit for this concentration.

The values of the cost function (Q), applying the R2W routine into the reversible model, were a little smaller than those obtained from the Linear Driving Force method applied in the IKM2 model (Table 1), indicating the potential of the R2W method in the estimation of multiple parameters.

CONCLUSIONS

In this work, both kinetic models applied were effective in the correlation of adsorption data of Bovine Serum Albumin (BSA). The models provided excellent agreement with the experimental data for all concentrations studied, being possible the estimation of kinetic constants with satisfactory accuracy. The application of the R2W method was very satisfactory, because, this method estimated two kinetic parameters (k_1 and k_2) at same time in the reversible kinetic model, leading to lower values of the cost function (Q). The higher values of the cost function for the cases of high concentration of BSA suggest in the future an statistical analysis of the experimental points, in which could be possible to reach values of equivalent to those obtained with the lower concentrations. This procedure can lead to kinetic parameters with higher accuracy, providing reliable parameters for the project and characterization of the equipments of separation. The use of experimental data in a high range of concentration probably will affect positively the estimation of parameters due to the possibility of deep statistical analysis of the experiments.

ACKNOWLEDGEMENTS

The authors acknowledge the financial and technical support provided by CNPq (Conselho Nacional de Desenvolvimento Científico e Regional), FAPERJ (Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro) and CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior).

REFERENCES

1. VASCONCELLOS, J.F.V.; SILVA NETO and SANTANA, C.C.: "An Inverse Mass Transfer Problem in Solid-Liquid Adsorption Systems": *Inverse Problems in Engineering*, vol. 11, No. 5, pp. 391-408, 2003.
2. VASCONCELLOS, J.F.V.; SILVA NETO, A.J.; SOEIRO, F.J.P. and SANTANA, C.C.: "Parameter Estimation in Adsorption Columns with Stochastic Global Method": *presented in 4th Internete national Conference on Inverse Problems*, Rio de Janeiro, Brazil, 2002.
3. VASCONCELLOS, J.F.V.; SILVA NETO and SANTANA, C.C.: "An Inverse Mass Transfer Problem of Parameter Estimation in Adsorption Columns": *presented in 5th World Congress on Computational Mechanics*, Vienna, Austria, 2002.
4. LUGON JR, J.; SILVA NETO, A.J. and SANTANA, C.C.: "An Inverse Mass Transfer Problem in Gas Liquid Adsorption in Columns of Bubble and Foam": *presented in Inverse Problems in Engineering Symposium*, Texas, United States of America, 2001.
5. DENISOV, A.M.: "Inverse Problems of Absorption Dynamics, Proceedings of Minisymposium on Inverse Problems in Medicine" (invited lecture): *presented in Brazilian Congress on Applied and Computational Mathematics*, Santos, Brazil, 2000.
6. FELINGER, A.; ZHOU, D. and GUIOCHON, G.H.A.: "Determination of the Single Component and Competitive Adsorption Isotherms of the 1-Indanol Enantiomers by Inverse Method": *Journal of Chromatography A*, vol. 1005, pp. 35-49, 2003.
7. FOLLY, F.M.; SILVA NETO, A.J. and SANTANA, C.C.: "An Inverse Mass Transfer Problem for the Characterization of Simulated Moving Bed Adsorption Columns": *presented in 5th International Conference on Inverse Problems in Engineering*, Cambridge, United Kingdom, 2005.
8. THOMAS: "Heterogeneous Ion Exchange in Flowing System": *Journal of American Chemical Society*, vol. 66, pp. 1664-1668, 1944.
9. CHASE, H.A.: "Prediction of the Performance Affinity Chromatography": *Journal of Chromatography*, vol. 297, pp. 179-202, 1984.
10. SARKAR, D. and CHATTORAJ, D.K.: "Activation Parameters for Kinetics of Protein Adsorption at Silica Water Interface": *Journal of Colloid and Interface Science*, vol. 157, pp. 219-226, 1993.
11. HAMANDI, N.K.; SWAMINATHAN, S. and CHEN, X.D.: "Adsorption of Paraquat Dichloride from Aqueous Solution by Activated Carbon Derived by Adsorbents from Used Tires": *Journal of Hazardous Materials B*, vol. 112, pp. 133-141, 2004.
12. OTERO, M.; GRANDE, C.A. and RODRIGUES, A.E.: "Adsorption of Salicylic Acid onto Polymeric Adsorbents and Activated Charcoal": *Reactive and Functional Polymers*, vol. 60, pp. 203-213, 2004.
13. GULEN, J.; AROGUZ, A.Z. and DALGIN, D.: "Adsorption Kinetics of Azinphosmethyl from Aqueous Solution onto Pyrolyzed Horseshoe Sea Crab Shell from Atlantic Ocean": *Bioresource Technology*, vol. 96, pp. 1169-1174, 2005.
14. AROGUZ, A.Z.: "Kinetics and Thermodynamics of Adsorption of Azinphosmethyl from Aqueous Solution onto Pyrolyzed (at 600°C) Ocean Peat Moss (Sphagnum sp.)": *Journal of Hazardous Materials*, 2006.
15. CÂMARA, L.D.T.; SANTANA, C.C. and SILVA NETO, A.J.: "Kinetic Modeling of Proteins Adsorption with a Methodology of Error Analysis": *Journal of Separation Sciences*, vol. 30, pp. 688-692, 2007.
16. CÂMARA, L.D.T.; SANTANA, C.C. and SILVA NETO, A.J.: "Kinetic Modeling Through the Inverse Problem Methodology Applied to Salicylic Acid Adsorption in Polymeric and Activated Charcoal Adsorbents": *presented in 11th Brazilian Congress of Thermal Sciences and Engineering*, Curitiba, Brazil, 2008, Paper CIT06-0643.
17. CÂMARA, L.D.T. and SILVA NETO, A.J.: "Inverse Stochastic Characterization of Adsorption Systems by a Random Restricted Window (R2W) Method": *presented in International Conference on Engineering Optimization*, Rio de Janeiro, Brazil, 2008.

AUTHORS

Diego Pinto Costa, graduated in Mechanical Engineering, Master's in Computational Modeling, master student at Universidade do Estado do Rio de Janeiro (UERJ-IPRJ), P.O. Box 97.282, 28601-970, (+55 22) 2533-2322, dpcosta@iprj.uerj.br, Rio de Janeiro, Brazil.

Leôncio Diógenes Tavares Câmara, graduated in Chemical Engineering, Master in Chemical Engineering, Doctor in Chemical Engineering, teacher and researcher of the

Department of Mechanical Engineering and Energy at Universidade do Estado do Rio de Janeiro (UERJ-IPRJ), P.O. Box 97.282, 28601-970, (+55 22) 2533-2322, dcamara@iprj.uerj.br, Rio de Janeiro, Brazil.

Mirtha Irizar Mesa, graduated in Electronics Engineering, Master in Applied Informatics, Doctor in Technical Sciences, teacher of the Department of Automation and Computers at Technical University of Havana, (+53 7) 2663-329, mirtha@electronica.cujae.edu.cu, Havana, Cuba.

Orestes Llanes Santiago, graduated in Electrical Engineering, Master in Automatic Control, Philosophy Doctor in Applied Sciences, teacher and researcher of the Department of Automation and Computers at Technical University of Havana, (+53 7) 2663-329, orestes@electronica.cujae.edu.cu, Havana, Cuba.

David Curbelo Rodríguez, graduated in Chemical Engineering, Master in Biotechnological Processes, Philosophy Doctor in Technical Sciences, Director of Manufacturing for Therapeutic Antibodies at Center of

Molecular Immunology (CIM), P.O. Box 16040, david@cim.sld.cu, Havana, Cuba.

Antônio José da Silva Neto, graduated in Mechanical Engineering, Master in Mechanical Engineering, Philosophy Doctor in Mechanical Engineering, teacher and researcher of the Department of Mechanical Engineering and Energy at Universidade do Estado do Rio de Janeiro (UERJ-IPRJ), P.O. Box 97.282, 28601-970, (+55 22) 2533-2322, ajsneto@iprj.uerj.br, Rio de Janeiro, Brazil.

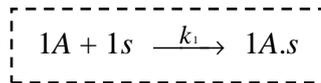


Figure 1. Representation of the adsorption stoichiometry, IKM2 model (irreversible mechanism).

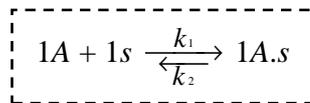


Figure 2. Representation of the adsorption stoichiometry (reversible mechanism).

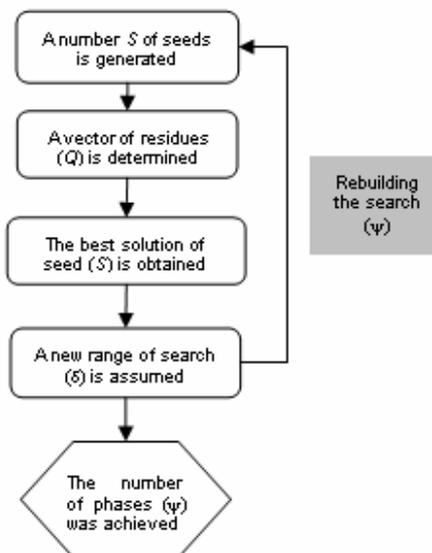


Figure 3. Flowchart of the R2W algorithm.

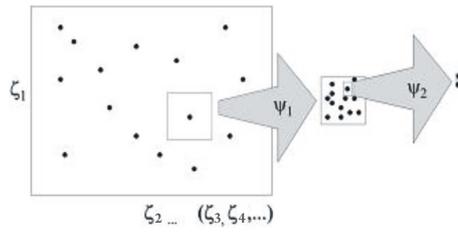


Figure 4. Schematic representation of the R2W domain search restriction.

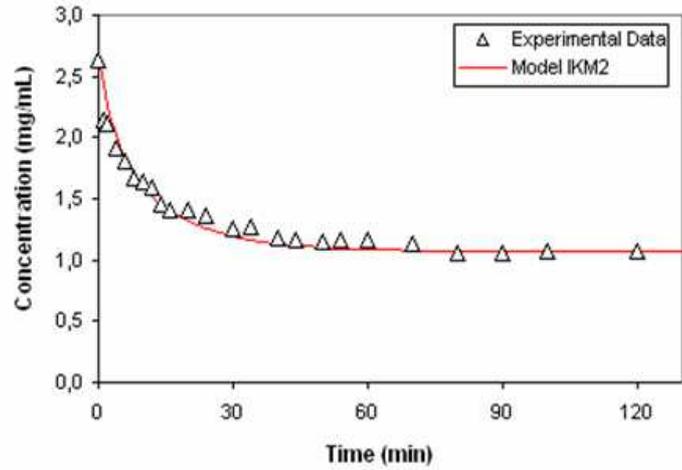


Figure 5. Correlation between the IKM2 model (red line) and the experimental data (points) of the BSA adsorption on Streamline DEAE. Where $C_{A0} = 2,628$ mg/mL

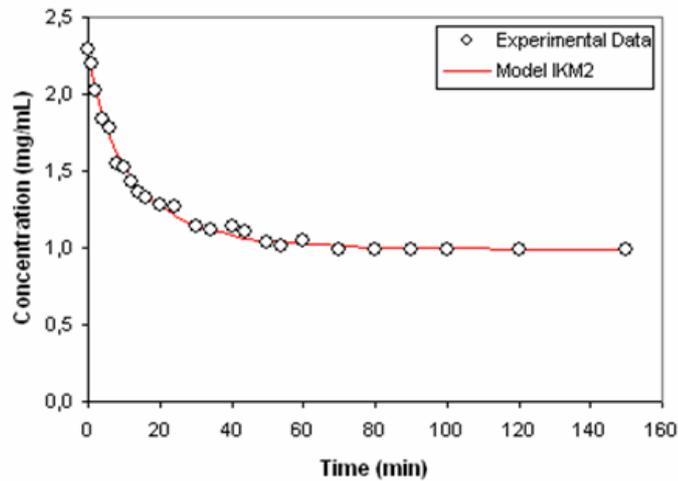


Figure 6. Correlation between the IKM2 model (red line) and the experimental data (points) of the BSA adsorption on Streamline DEAE. Where $C_{A0} = 2,287$ mg/mL.

Table 1. Parameters estimated from the application of IKM2 kinetic model.

C_{A0} (mg/mL)	q_m (mg/mL)	k_1 (mL/mg.min)	Q
2,628	1,564	$5,40 \times 10^{-2}$	$1,89 \times 10^{-1}$
2,287	1,304	$4,80 \times 10^{-2}$	$2,52 \times 10^{-2}$

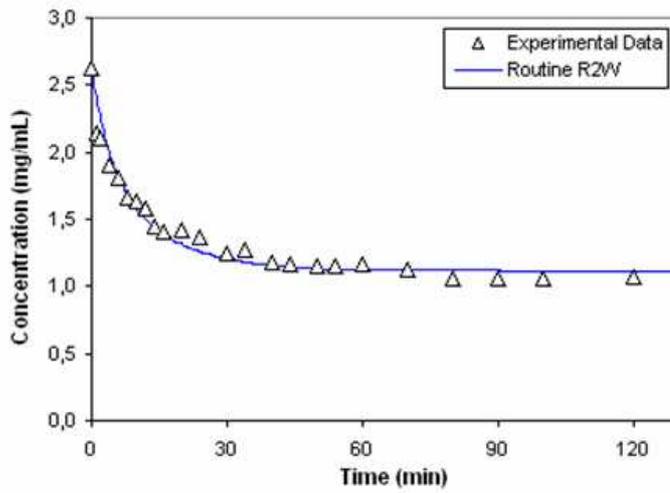


Figure 7. Correlation between the R2W routine (blue line) and the experimental data (points) of the BSA adsorption on Streamline DEAE. Where $C_{A0} = 2,628$ mg/mL

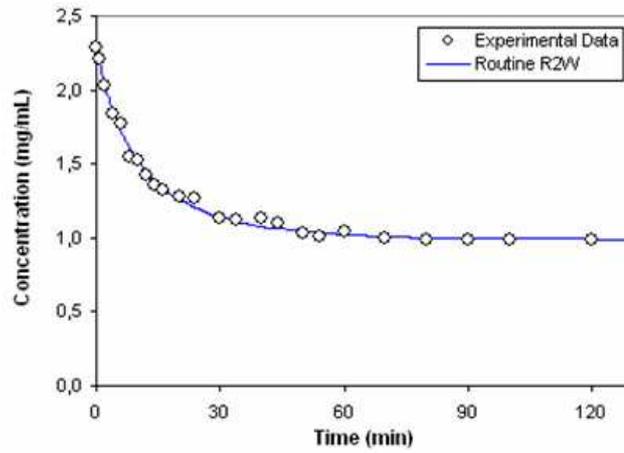


Figure 8. Correlation between the R2W routine (blue line) and the experimental data (points) of the BSA adsorption on Streamline DEAE. Where $C_{A0} = 2,287$ mg/mL

Table 2. Parameters estimated from the application of R2W routine with reversible model.

C_{A0} (mg/mL)	q_m (mg/mL)	k_1 (mL/mg.min)	k_2 (min^{-1})	Q
2,628	1,564	$2,89 \times 10^{-2}$	$1,06 \times 10^{-3}$	$1,62 \times 10^{-1}$
2,287	1,304	$2,43 \times 10^{-2}$	$1,45 \times 10^{-4}$	$2,48 \times 10^{-2}$