ADSORPTION OF AROMATIC AMINO ACIDS IN A FIXED BED COLUMN

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Abstract – Phenylalanine (Phe) and tyrosine (Tyr) are two of the twenty amino acids in proteins; they are classified as aromatic amino acids, because both have a benzene ring in their structures. These amino acids are important in the synthesis of several biologically active amines, such as β-endorphin, a neurotransmitter. Amino acids can be separated by ion-exchange chromatography. In this case, it is important that fixed-bed adsorber design adequately predict the breakthrough curve. This work presents a mathematical model for both fluid and porous phases. In the solution proposed for this model the liquid-phase concentration inside the particles is solved analytically and is related to the liquid-phase concentration in the bed using Duhamel's theorem. The solution for liquid-phase concentration in the bed is then solved numerically instead of analytically. The basic mass transfer parameters are from the literature. The results from the model are compared with those obtained experimentally using Phe and Tyr diluted in aqueous solutions in a fixed bed of PVP (poly-4-vinylpyridine) resin.

INTRODUCTION

Around twenty amino acids are found in proteins. Some amino acids are essential, while others are nonessential. Essential amino acids are those that cannot be produced by the body so must be obtained from the diet. Nonessential amino acids can be produced by the body from essential amino acids. Phenylalanine (Phe) is a ringed essential amino acid that is readily available in most food sources, particularly meats and milk products, with lower levels found in oats and wheat germ. It is essential for many bodily functions and is one of the few amino acids that can cross the blood-brain barrier and thus directly affect brain chemistry. Phenylalanine is the precursor of the amino acid tyrosine (Tyr), which cannot be

reconverted, so Phe is essential in the diet. Tyrosine is important to the structure of almost all proteins in the body. Tyr and Phe are also the precursors of several neurotransmitters (Bohinski, 1987), including L-dopa, dopamine, norepinephrine, and epinephrine. Through its effect on neurotransmitters, L-tyrosine may have an effect on several health conditions, including Parkinson's disease, depression, and other mood disorders. Studies have suggested that tyrosine may help people with depression (Gelenberg et al., 1982). Preliminary findings indicate the beneficial effect of Tyr, along with other amino acids, on people affected by dementia, including Alzheimer's disease (Meyer et al., 1977). Because of its role as a precursor to norepinephrine and epinephrine (two of the body's main stress-related hormones) tyrosine may also ease the adverse effects of environmental, psychosocial, and physical stress (Banderet and Lieberman, 1989; Salter, 1989; Neri et al., 1995; Deijen et al., 1999; Shurtleff et al., 1994; Deijen and Orlebeke, 1994; Dollins et al., 1995; Koch, 1996; Chiarone et al., 1990; Alvestrand et al., 1983). Amino acids can be separated experimentally by ion-exchange chromatography, batch ion-exchange chromatography (Dechow, 1990), or a simulated moving bed system (SMB) (Hashimoto et al., 1989; Wu et al., 1998; Cremasco et al., 2000).

An important goal in the design of an adsorber is to predict the sorbate breakthrough curve. Several mathematical models were developed for that curve and analytical solutions can be found in the literature for systems with linear equilibrium (Ruthven, 1984; Carta, 1988). The analytical solution for the complete problem results in an integral expression that is quite difficult to compute numerically (Rasmuson, 1981, 1985) due to the oscillatory nature of the integrand. However, the complex model can be solved numerically using, for example, orthogonal collocation. On the other hand, when the numerical method is used, knowledge of physical adsorption might be lost.

In this paper, a hybrid method is utilized to describe a breakthrough curve for

adsorption in a system containing a single adsorbate at a low concentration. The adsorbate is an aromatic amino acid (Phe or Tyr) diluted in water. The liquid-phase concentration inside the particles is found analytically and it is related to the liquid-phase concentration in the bed using Duhamel's theorem (Rosen, 1952). However, the solution for the liquid-phase concentration in the bed is found numerically instead of analytically.

THEORY

Model Hypothesis

In order to obtain the breakthrough curve for the fluid phase, the following assumptions were made:

- the liquid mass flow rate is constant and the cross section is uniform;
- the liquid concentration profile varies very little with radial position in the bed;
- axial dispersion with a constant dispersion coefficient is taken into account;
- resistance of the external mass transfer from the bulk liquid-phase to the resin is assumed to be very small ($Bi \rightarrow \infty$);
- the solid phase (resin) is composed of small spheres of uniform radii;
- the mobile phase is a dilute solution, so Henry´s law can be used to describe sorbate uptake;
- intraparticle diffusion is described by pore diffusion. For a linear isotherm system, the flux due to surface diffusion, if important, can be lumped together with the pore diffusion flux (Ma et al., 1996);
- no chemical reaction occurs;
- the initial concentration inside the column (liquid and resin) is zero.

Applicability of the model will depend on the validity of these hypotheses. In many cases, the experimental conditions can be adequately described by the previous hypotheses, even when they are only approximations.

Mathematical Model

Based on these hypotheses, the following equations are obtained:

- solute mass balance for the solid particles (resin):

$$D_p \cdot \varepsilon_p \cdot \frac{1}{r^2} \cdot \frac{\partial}{\partial r}\left(r^2 \cdot \frac{\partial c}{\partial r}\right) = \varepsilon_p \cdot \frac{\partial c}{\partial t} + \left(1 - \varepsilon_p\right) \cdot \frac{\partial q}{\partial t} \tag{1}$$

$$q = k_p \cdot c \tag{2}$$

where c is the solute concentration in the liquid phase inside the particle pores (volume fraction ε_p) and q is the solute concentration in the resin (volume fraction $1 - \varepsilon_p$);

- solute mass balance for the mobile phase:

$$-E_b \cdot \varepsilon_b \cdot \frac{\partial^2 C}{\partial z^2} + \frac{Q}{A} \cdot \frac{\partial C}{\partial z} + \varepsilon_b \cdot \frac{\partial C}{\partial t} + R_a = 0 \tag{3}$$

where C is the solute concentration in the liquid phase inside the void portions of the fixed bed (volume fraction ε_b) and R_a is the rate of adsorption/desorption of solute by the resin by unit volume of reactor, given by

$$R_a = \frac{3}{R^3} \cdot \left(1 - \varepsilon_b\right) \cdot \frac{\partial}{\partial t}\left[\int_0^R \left[\varepsilon_p \cdot c + \left(1 - \varepsilon_p\right) \cdot q\right] \cdot r^2 \cdot d\, r\right] \tag{4}$$

It is important to observe that C is a function of z and t, while c and q are functions of z, r and t, since each particle will be subject to different external concentrations along the length of the column. Using equation (2), equations (1) and (4) can also be written as

$$D_p \cdot \varepsilon_p \cdot \frac{1}{r^2} \cdot \frac{\partial}{\partial r}\left(r^2 \cdot \frac{\partial c}{\partial r} \right) = \left[\varepsilon_p + k_p \cdot (1 - \varepsilon_p) \right] \cdot \frac{\partial c}{\partial t} \tag{5}$$

$$R_a = \frac{3}{R^3} \cdot (1 - \varepsilon_b) \cdot \left[\varepsilon_p + k_p \cdot (1 - \varepsilon_p) \right] \cdot \frac{\partial}{\partial t} \left[\int_0^R c \cdot r^2 \cdot dr \right] \tag{6}$$

Initial and Boundary Conditions

The initial and boundary conditions that describe a step injection into a chromatographic column are given as follows:

- initial condition:

$$C = 0 \qquad t = 0 \qquad 0 \le z \le L \tag{7}$$

$$c = 0 \qquad t = 0 \qquad 0 \le r \le R \tag{8}$$

- boundary condition:

$$Q \cdot C_e = Q \cdot C - A \cdot E_b \cdot \varepsilon_b \cdot \frac{\partial C}{\partial z} \qquad z = 0 \qquad t > 0 \tag{9}$$

$$-A \cdot E_b \cdot \varepsilon_b \cdot \frac{\partial C}{\partial z} = 0 \qquad z = L \qquad t > 0 \tag{10}$$

$$-D_p \cdot \varepsilon_p \cdot \frac{\partial c}{\partial r} = k_f \cdot (c - C) \qquad r = R \qquad t > 0 \tag{11}$$

$$\frac{\partial c}{\partial r} = 0 \qquad r = 0 \qquad t > 0 \tag{12}$$

Since in this work we are assuming that $Bi \to \infty$, equation (11) reduces to

$$c = C \qquad r = R \qquad t > 0 \tag{13}$$

Correlations for the Model Parameters

The parameters used in the model were calculated using correlations from the literature. The axial dispersion coefficient can be calculated by (Koch and Brady, 1985)

$$\frac{E_b A}{Q d_p} = \varepsilon_b \left[\frac{3}{4} + \frac{\pi^2}{6}(1-\varepsilon_b)\ell n\left(Pe_{M_p}\right) + \frac{1}{Pe_{M_p}} \right] \tag{14}$$

with the molecular mass Peclet number for the particle defined by

$$Pe_{Mp} = \frac{v\, d_p \varepsilon_b}{D_{AB}} \tag{15}$$

and the diffusion coefficient estimated by Wilke and Chang´s equation (1955), for the diluted system

$$\frac{D_{AB}\mu_B}{T} = 7.4\times10^{-8}\frac{(\phi M_B)^{0.5}}{V_{b_A}^{0.6}} \tag{16}$$

with ϕ=2.6 for water, where V_{b_A} is calculated from Le Bas´ volume method (Cremasco, 1998).

The effective diffusion coefficient is calculated from Mackie and Meares (1955)

$$\varepsilon_p D_p = \left(\frac{\varepsilon_p}{2-\varepsilon_p}\right)^2 D_{AB} \tag{17}$$

Strategy for Numerical Resolution

The method used in this paper is similar to the one from Rosen (1952), except that the solution for the PDE for the bed is found numerically instead of analytically. In this work, the liquid-phase concentration inside the particles is found analytically and is related to the liquid-phase concentration in the bed using Duhamel's theorem. However, the solution for liquid-phase concentration in the bed is found numerically instead of analytically. The procedure is described as follows:

The solute concentration in the liquid phase inside the particle pores, c, can be related to the solute concentration in the liquid phase inside the void portions of the fixed bed, C, using Duhamel´s theorem:

$$c = \int_0^t \left[-\frac{\partial u}{\partial \tau}(r, t-\tau) \right] \cdot C \cdot d\tau \tag{18}$$

with

$$-\frac{\partial u(r, t-\tau)}{\partial \tau} = \left. \frac{\partial u(r, \xi)}{\partial \xi} \right|_{\xi = t-\tau} \tag{19}$$

where u is the solution for the problem given by equation (5), initial condition (8), and boundary conditions (12) and (13) with $C = 1$. However, in order to apply equation (18) into equation (6), it is more interesting to work with the average concentration, $\bar{u}$:

$$\bar{u}(t) = \frac{3}{R^3} \cdot \int_0^R u(r,t) \cdot r^2 \cdot dr \tag{20}$$

The analytical solution for u can be found using the method of separation of variables, which results in a Fourier series (Cremasco, 1998). This solution is substituted into equation (20), resulting in

$$\bar{u} = 1 - \frac{6}{\pi^2} \cdot \sum_{n=1}^{\infty} \frac{1}{n^2} \cdot \exp\left(-n^2 \cdot \pi^2 \cdot \theta\right) \tag{21}$$

where

$$\theta = \frac{\varepsilon_p}{[\varepsilon_p + (1-\varepsilon_p) \cdot k_p]} \cdot \frac{D_p \cdot t}{R^2} \tag{22}$$

The series given by equation (21) has fast convergence for large values of t, but it has slow convergence for t approaching zero. Therefore, for very small values of t an asymptotic expression for $\bar{u}$, obtained using the Laplace transform method (Guy et al, 1982), was used:

$$\bar{u} \cong 6 \cdot \sqrt{\frac{\theta}{\pi}} - 3 \cdot \theta \tag{23}$$

which gives accurate results for $0 \le \theta \le 0.05$.

Using Duhamel´s theorem and the average concentration $\bar{u}$, an expression for R_a as a

function of C is obtained:

$$R_a = (1-\varepsilon_b)\cdot\left[\varepsilon_p + (1-\varepsilon_p)\cdot k_p\right]\cdot\frac{\partial}{\partial t}\left[\int_0^t \left.\frac{d\,\bar{u}(\xi)}{d\,\xi}\right|_{\xi=t-\tau}\cdot C(z,\tau)\cdot d\tau\right] \tag{24}$$

This expression was used in equation (3), which was solved numerically using a first-order discretization method that avoids both numerical diffusion and numerical instability, based on a combination of implicit and explicit finite differences with a fixed step for Δz and a calculated step for Δt as a function of the column parameters and Δz. The initial and boundary conditions are given by equations (7), (9), and (10). The resulting set of equations is a linear tri-diagonal system in the variables $C(z_i, t_{j+1})$, which was solved with Thomas´s algorithm at each time step, calculating each z profile $C(z_i, t_{j+1})$ from z profiles at previous times.

The main advantage of this approach is that it is easier to compute than the entirely analytical solution (Rosen, 1952). The disadvantage of the analytical solution is that it is quite difficult to calculate, since it is expressed as an integral of an oscillatory function that is very difficult to compute numerically (Rasmuson, 1981, 1985). This difficulty can be avoided with the hybrid approach used here.

The main limitation of the approach used is the fact that Duhamel´s theorem is only applicable to linear PDE with linear initial and boundary conditions. However, the same limitation holds for the entirely analytical solution, since it is based on the same model (Rosen, 1952).

EXPERIMENTAL

The experimental setup is illustrated in Figure 1. The system consists of two Pharmacia P-500 low-pressure pumps, a Pharmacia LCC-500 controller, and a Pharmacia

MV-7 injection valve. A Waters 990 photodiode array detector was used for data acquisition, and the data were processed using the Waters 900 software. A Pharmacia glass column was packed with Reillex™.-HP resin, which is poly-4-vinylpyridine cross-linked with divinylbenzene (PVP), purchased from Reilly Industries, Inc., Indianapolis, USA. The characteristics of the column and resin are shown in Table 1. The amino acids studied were Phe and Tyr, with purities of 98% and 99%, respectively. The partition coefficients were k_p=1.947 for Phe and k_p=3.229 for Tyr (Cremasco et al., 2001).

Breakthrough curves were obtained using injection of aqueous solutions of 0.5 g/l of Phe and of 0.04 g/l of Tyr. All experiments were performed at 1 atm and 25ºC. The feed flow rates were 1.5 ml/min, 2.0 ml/min, and 2.5 ml/min. The effluent was monitored within the range of ultraviolet wavelengths: 260 nm for Phe and 300 nm for Tyr.

RESULTS AND DISCUSSION

To solve the model described above, it is necessary to estimate the free diffusion coefficient value, equation (16). By Le Bas´s volume method, it is possible to estimate the molar volume at boiling point of Phe and Tyr. For Phe, V_{b_A} = 193.4 cm^3/gmol, while for Tyr, this value is V_{b_A} = 200.8 cm^3/gmol. If equation (16) is used at 25° C and infinite dilution is assumed, $D_{AB} = 4.25\times10^{-4}$ cm^2/min for Phe, which is close to the experimental value from Paduano et al. (1990) ($D_{AB} = 4.12\times10^{-4}$ cm^2/min). For Tyr, the value from equation (16) is $D_{AB} = 4.15\times10^{-4}$ cm^2/min.

The effective diffusion coefficients for Phe and Tyr are calculated by equation (17), using the values of D_{AB} from equation (16). In this case, D_p=1.10×10^{-4} cm^2/min for Phe and

$1.07\times10^{-4}\,\mathrm{cm^2/min}$ for Tyr, which are close to the values in from Cremasco et al. (2001) (D_p=$1.02\times10^{-4}\,\mathrm{cm^2/min}$ for Phe and $1.01\times10^{-4}\,\mathrm{cm^2/min}$ for Tyr).

The theoretical values for the diffusion coefficient and effective diffusion coefficient were used to describe the breakthrough curves. Other values used in the modeling are shown in Table 1. The resulting theoretical curves for 1.5ml/min, 2.0ml/min, and 2.5ml/min are compared with those of the experimental method. Figures 2 and 3 show a comparison between experimental adsorption curves and those from the model proposed in this paper.

It can be observed that the calculated values agree well with the experimental ones. This is even more interesting considering that mass transfer parameters were estimated from correlations but not fitted, i.e., no fitting method was used to adjust the parameters in this work. Therefore, the method has a good predictive capability since it required only previously available data to obtain good results.

However, there is a difference between the calculated and the experimental values, particularly in Figure 3, that needs to be explained. The area above the breakthrough curve given by

$$\int_0^{\infty}\left[1-\left(C/C_0\right)\right]_{z=L}\cdot dt=\frac{V}{Q}\cdot\left\{\varepsilon_b+\left(1-\varepsilon_b\right)\cdot\left[\varepsilon_p+\left(1-\varepsilon_p\right)\cdot k_p\right]\right\} \tag{25}$$

is related to the adsorption capacity of the column. In Figure 3, for example, it is clear that the areas for the experimental and calculated curves are not the same. It can be seen from equation (25) that this area does not depend on the mass transfer parameters (E_b, D_p, D_{AB}). Also, numerical tests and comparison with the analytical value given by the right hand side of equation (25) indicated that the difference between calculated and experimental values in the breakthrough curves was not due to the numerical method used. Therefore, this difference is very likely due to some of the other parameter values used in the simulations (V, Q, ε_b, ε_p, k_p), which may have been incorrectly determined in the experiments.

All calculations were performed in a Pentium 150 MHz with 16 Mbytes RAM, using Fortran 77. The number of intervals in the axial direction was 300, while the number of time intervals is shown in Table 2. The computational time was less than 10 seconds for each case. The precision of the numerical approach can be improved with more intervals, but that requires longer computational times. For the examples tested, it was not necessary to use a more refined grid of points.

CONCLUSIONS

A hybrid approach for solving the model for fixed-bed biosorption was proposed. The hybrid approach has the advantage of being easier to apply than the purely analytical solution. Results indicate that the method was efficient and easy to apply, solving the problem in a very short computational time. The numerical results described well the experimental data in the breakthrough curves for two amino acids and three different flow conditions, using only estimated parameters from the literature.

The performance of the model with the proposed method for solving it, using the parameters from correlations, indicates that it can be a useful tool for predicting breakthrough curves. Although the mathematical model has some limitations, it can be applied to a variety of situations, as long as the model hypotheses are satisfied.

REFERENCES

Alvestrand, A., Ahlberg, M., Forst, P. and Bergstrom, J., Clinical Results of Long-term Treatment with a Low Protein Diet and a New Amino Acid Preparation in Patients with Chronic Uremia. Clin. Nephrol., vol. 19, pp. 67-73 (1983).

Banderet, L.E. and Lieberman, H.R., Treatment with Tyrosine, a Neurotransmitter Precursor,

Reduces Environmental Stress in Humans. Brain Res. Bull., vol. 22, pp. 759-62 (1989).

Bohinski, R.C., Modern Concepts in Biochemistry. 5th Ed., Allyn and Bacon, Boston (1987).

Carta, G., Exact Analytic Solution of a Mathematical Model for Chromatographic Operations. Chem. Eng. Science. vol. 43, no. 10, pp. 2877-2883 (1988).

Chiaroni, P., Azorin, J.M. and P. Bovier, A Multivariate Analysis of Red Blood Cell Membrane Transports and Plasma Levels of L-Tyrosine and L-Tryptophan in Depressed Patients before Treatment and after Clinical Improvement. Neuropsychobiol, vol.23, pp. 1-7 (1990).

Cremasco, M.A., Fundamentals of Mass Transfer, (in Portuguese). Unicamp Publisher, Campinas, Brazil (1998).

Cremasco, M.A., Hritzko, B.J. and Wang, N.-H. L., Separation of Two Amino Acids in a Four-column Simulated Moving Bed: An Experimental Study, Procedings of XIII Brazilian Chemical Engineering Meeting, CD ROM, Águas de São Pedro, Brazil (2000).

Cremasco, M. A., Hritzko, B. J., Xie, Y. and Wang, N.-H. L., Parameters Estimation for Amino Acids Adsorption in a Fixed Bed by Moment Analysis. Brazilian J. of Chem. Engineering, vol.18, no.2, pp. 181-194 (2001).

Dechow, F.J., Separation and Purification Techniques in Biotechnology. Noyes Publication, NJ (1990).

Deijen, J.B. and Orlebeke, J.F., Effect of Tyrosine on Cognitive Function and Blood Pressure under Stress. Brain Res. Bull., vol. 33, pp. 319-23 (1994).

Deijen, J.B., Wientjes, C.J. and Vullinghs, H.F., Tyrosine Improves Cognitive Performance and Reduces Blood Pressure in Cadets after One Week of a Combat Training Course. Brain Res. Bull., vol. 48, pp. 203-209 (1999).

Dollins, A.B., Krock, L.P. and Storm, W.F., L-Tyrosine Ameliorates some Effects of Lower Body Negative Pressure Stress. Physiol. Behav., vol. 57, pp. 223-30 (1995).

Gelenberg, A.J., Gibson, C.J. and Wojcik, J.D., Neurotransmitter Precursors for the Treatment of Depression. Psychopharmacol Bull., vol. 18, pp. 7-18 (1982).

Guy, R.H., Hadgraft, J., Kellaway, I.W. and Taylor, M.J., Calculations of Drug Release Rates from Spherical Particles. International Journal of Pharmaceutics, vol. 11, pp. 199-207 (1982).

Hashimoto, K., Yamada, M., Adachi, S. and Shirai, Y., A Simulated Moving-bed Adsorber with Three Zones for Continuous Separations of L-Phenylalanine and NaCl, J. Chem. Eng. of Japan, vol. 22, no. 4, pp. 432-434 (1989).

Koch, D.L. and Brady, J.F., Dispersion in Fixed Beds, J. Fluid Mech., vol. 154, pp. 399-427 (1985).

Koch, R., Tyrosine Supplementation for Phenylketonuria Treatment. Am. J. Clin. Nutr., vol. 64, pp. 974-975 (1996).

Ma, Z., Witley, R.D. and Wang, N.-H.L., Pore and Surface Diffusion in Multicomponent Adsorption and Liquid Chromatography Systems. AIChE J., vol. 42, no. 5, pp. 1244-1262 (1996).

Mackie, J.S. and Meares, P., The Diffusion of Electrolytes in a Cation-exchange Resin Membrane. Proc. Roy. Soc. London, Serie A, vol. 267, pp. 498-506 (1955).

Meyer, J.S., Welch, K.M.A. and Deshmuckh, V.D., Neurotransmitter Precursor Amino Acids in the Treatment of Multi-infarct Dementia and Alzheimer's Disease. J. Am. Ger. Soc., vol. 7, pp. 289-98 (1977).

Neri, D.F., Wiegmann, D. and Stanny, R.R., The Effects of Tyrosine on Cognitive Performance During Extended Wakefulness. Aviat. Space Environ. Med., vol. 66, pp. 313-319 (1995).

Paduano, L., Sartori, R., Vitagliano, V. and Constantino, L., Transport and Thermodynamics Properties of (D.L) Norleucine-Water and (L) Phenylalanine-Water, at 25^{o}C. J. Mol.

Liq., vol. 47, pp. 193-202 (1990).

Rasmuson, A., Exact Solution of a Model for Diffusion and Transient Adsorption in Particle and Longitudinal Dispersion in Packed Beds, AIChE J., vol. 27, no. 6, pp. 1032-1035 (1981).

Rasmuson, A., Exact Solution of a Model for Diffusion in Particles and Longitudinal Dispersion in Packed Beds: Numerical Evaluation, AIChE J., vol. 31, no. 3, pp. 518-519 (1985).

Rosen, J.B., Kinetics of a Fixed Bed System for Solid Diffusion into Spherical Particles. The J. of Chem. Physiscs, vol. 20, no. 3, pp. 387-394 (1952).

Ruthven, D.M., Principles of Adsorption and Adsorption Process. Wiley-Interscience, New York (1984).

Salter, C.A., Dietary Tyrosine as an Aid to Stress Resistance among Troops. Mil. Med., vol. 154, pp. 144-146 (1989).

Shurtleff, D., Thomas, J.R. and Schrot, J., Tyrosine Reverses a Cold-induced Working Memory Deficit in Humans. Pharmacol. Biochem. Behav., vol. 47, pp. 935-941 (1994).

Spiegel, M.R., Fourier Series, Schaum´s Outline Series, McGraw-Hill Book Company, New Yourk (1974).

Spiegel, M.R., Theory and Problems of Laplace Transforms, Schaum´s Outline Series, McGraw-Hill Book Company, New York (1986).

Wilke, C.R. and Chang, P., Correlation of Diffusion Coefficients in Dilute Solution, AIChE J., vol. 1, pp. 264-270 (1955).

Wu, D.-J, Xie, Y., Ma, Z. and Wang, N.-H.L., Design of Simulated Moving Bed Chromatography for Amino Acids Separations. Ind. Eng. Chem. Res., vol. 37, pp. 4023-4035 (1998).

NOMENCLATURE

A	- cross-transversal area of the column;	L^2
c	- solute concentration in the mobile phase inside of the particle;	ML^{-3}
C	- solute concentration at the elution;	ML^{-3}
C_0	- solute concentration at the eluted peak;	ML^{-3}
D	- fixed bed diameter;	L
d_p	- average particle diameter;	L
D_p	- effective pore diffusion coefficient;	L^2T^{-1}
E_b	- axial dispersion coefficient;	L^2T^{-1}
k_p	- partition coefficient;	-
L	- length of the column;	L
q	- solute concentration in the porous phase;	ML^{-3}
Q	- injection flow rate;	L^3T^{-1}
r	- radial position;	L
R	- particle radius;	L
t	- time;	T
v	- interstitial velocity;	LT^{-1}
v_0	- superficial velocity;	LT^{-1}
V	- total volume of the column ($A \cdot D$);	L^3
z	- axial position.	L

Greek letters

ε_b	- bed porosity;	-
ε_p	- particle porosity;	-
ν	- solution cinematic viscosity.	L^2T^{-1}

Tables

Table 1: Bed and resin characteristics (Cremasco et al., 2000).

L (cm)	D (cm)	ε	d_p (cm)
12.5	1.5	0.37	0.036

Table 2: Number of time intervals (N) for M=300.

Q (ml/min)	1.5	2.0	2.5
Tyr	80	70	60
Phe	60	50	45

Figure captions

Figure 1: Fixed-bed experimental setup for elution curves.

Figure 2: Comparison between experimental and simulated breakthrough curves for Tyr.

Figure 3: Comparison between experimental and simulated breakthrough curves for Phe.