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A FAD-SMT Model of Large Scale Liquid Adsorption Chromatography

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Abstract. The paper proposes a FAD-SMT model of large-scale liquid chromatography by which a continuous equation of chromatographic separation is decomposed into a convection dispersion partial differential equation and a set of ordinary differential equations. The numerical method for the FAD-SMT model is established. The stability and the convergence condition of numerical solution, and the choice of time and space interval are discussed. The FAD-SMT model is used to simulate liquid adsorption chromatography and cycling adsorption chromatography. Results show that the elution curves calculated by FAD-SMT model are good agreement with the experimental elution curves of the separation of glucose and fructose, the separation of sucrose and reducing sugar and the separation of mannitol and sorbitol. The result of parameter sensitivity analysis shows that the chromatographic elution curves are more sensitive to the changes of the parameter a_i in Langmuir isotherms than to the changes of other parameters in the studied system.

Keywords: large scale chromatography, FAD-SMT model, numerical method

Introduction

The mathematical model of chromatographic process and its numerical method are important tools for simulating and optimizing the chromatographic process. So far several algorithms have been proposed to solve the mathematical models of adsorption column or chromatographic column processes. These models consider not only mass transfer resistance between fluid phase and solid phase but also axial dispersion in fluid phase. Liapis and co-workers (1978, 1980) used orthogonal collocation (OC) method for the discretization of both bulk- and particle-phase equations with boundary condition (B.C.) $\frac{\partial C_i}{\partial x}|_{x=L} = 0$. The resulting ordinary differential equations (ODEs) were solved using a fifth-order Runge-Kutta method. Their methods was applied to front adsorption. Cho and Hegedus (1983) made use of STOP-GO method to model packed bed reactors. By means of STOP-GO method, the packed bed was modeled as a series of mixing cells under the condition of the assumption that the catalyst pellets were exposed to a uniform bulk gas/fluid phase concentration in each of mixing cells and there was no dispersion between the cells. Yu and Wang (1989) tried OC method on finite element for bulk-phase equations and OC method for particle-phase equations. The resulting ODEs and algebraic equations were solved using a differential algebraic equation solver. Mansour (1989) used finite difference method for whole numerical procedure to solve the model of frontal adsorption, using $\frac{\partial C_i}{\partial x}|_{x=L} = 0$. Gu et al. (1990) used the finite element (FE) method for the bulk-phase equations and the OC method for the particle-phase equations. Chen and Hsu (1987) employed the simpler boundary condition $C(t, x \to +\infty) = 0$, and proposed fast Fourier transform to predict breakthrough curves of adsorption. There are also other numerical methods applied to non-linear adsorption column. Poulain and Finlaysonn (1993) made a comparison of eight numerical methods on the basis of their computational efficiency for one dimensional non-linear convection-diffusion problems, but no experimental verification was given. In this work, we present a FAD-SMT model of liquid chromatography processes. On the basis of the FAD-SMT model, the complex partial differential equations describing adsorption chromatographic process will be decomposed into a simple convection diffusion equation and a set of ordinary differential equations. These equations can be easily solved by mature numerical methods.

Model

Consider a chromatographic column packed with spherical and solid adsorbents. Suppose the process is isothermal and there are no concentration gradient in the radial direction of the column and no interference between components. The packed bed chromatographic column can be described by the following set of equations

$$\begin{aligned} &u\frac{\partial C_i}{\partial x} + \frac{\partial C_i}{\partial t} - D_{\mathrm{ax}}\frac{\partial^2 C_i}{\partial x^2} + \frac{1-\varepsilon}{\varepsilon}\rho_s\frac{\partial Q_i}{\partial t} = 0 \\ &\frac{\partial Q_i}{\partial t} = f_i(C_i^*, C_i, t) \qquad i = 1, 2, \ldots, N \qquad (1) \\ &Q_i = g_i(C_i^*) \end{aligned}$$

$$\text{I.C.} \quad \begin{aligned} C_i(0,x) &= 0 \\ Q_i(0,x) &= 0 \end{aligned} \qquad (2)$$

$$\text{B.C.} \quad C_i(t,0) = \begin{cases} C_{0i} & 0 < t \le t_1 \\ 0 & t > t_1 \end{cases} \qquad (3)$$

where $g_i(C_i^*)$ is the function describing the isotherm for i component. It can be linear or non-linear. $f_i(C_i^*, C_i, t)$ is rate expression which describes the mass transfer between fluid phase and solid phase. The differences in rate theory models are mainly due to the differences in describing the interface mass transfer. In the mathematical modeling of chromatographic separation processes an option is to model a system as realistically as possible taking into account the individual resistance to mass transfer to give what are known as distributed parameter models. However, the mathematics involved can be complex, and in some circumstances an option may be to use simplified rate equation for the liquid/solid interface mass transfer, essentially combining the resistance to mass transfer to give what are known as lumped parameter models. For these simplified models the assumption should be made that the liquid film diffusion is the rate controlling step. The interface mass transfer equation then becomes simple functions of time and position only and are no longer controlled, for example, by momentary rate of intraparticle diffusion, which is dependent on the shape of unsteady concentration profile within the particle. In this work, the assumption is also made that isotherms can be linear or Langmuir, and the interface mass transfer rate can be described by lumped parameter model with linear driving force (shown as Eq. (4)).

$$\frac{\partial Q_i}{\partial t} = k_i(C_i - C_i^*) \qquad (4)$$

FAD-SMT Model

The establishment of FAD-SMT model is on the basis of the principle that a complicated transfer process is made up of two or more simple processes. The transfer process in the packed-bed of chromatographic column is considered to be synthesized by following two processes, (1) fluid flowing, adsorbate dispersion in fluid phase and (2) adsorbate transfer between fluid and solid phases. According to the assumption above, the complicated partial differential equations (1)–(3), which describe large scale chromatographic separation, can be decomposed to a simply partial differential convection dispersion equation and a set of ordinary differential equations. Here is assumption in details.

In the packed-bed of chromatographic column, suppose that the transfer process is made up of following two processes:

1. During *dt* time duration, fluid flows and adsorbate axial dispersion takes place in fluid phase but fluid/solid interface mass transfer does not happen, which is called as “Flow and Axial Dispersion process” (i.e., FAD).
2. In the fictitious *dt* time duration, no fluid flows (i.e., $u = 0$, $D_{\mathrm{ax}} \cong 0$), and adsorbate transfer takes place between fluid phase and solid phase, which is called as “Stop and Mass Transfer process” (i.e., SMT).

For FAD, the behavior of the adsorbate in packed-bed can be described by following partial differential equation:

$$\begin{aligned} u\frac{\partial C_i}{\partial x} + \frac{\partial C_i}{\partial t} - D_{\mathrm{ax}}\frac{\partial^2 C_i}{\partial x^2} &= 0 \\ C_i(0,x) &= 0 \\ C_i(t,0) &= \begin{cases} C_{0i} & 0 < t \le t_1 \\ 0 & t > t_1 \end{cases} \end{aligned} \qquad (5)$$

For SMT, at any position x, the mass transfer between liquid phase and solid phase can be described by the following set of ordinary differential equations:

$$\begin{aligned} \frac{dQ_i}{dt} &= f_i(C_i^*, C_i, t) \\ \frac{dC_i}{dt} &= -\frac{1-\varepsilon}{\varepsilon}\rho_s \frac{dQ_i}{dt} \\ Q_i(0,x) &= 0 \end{aligned} \tag{6}$$

Suppose that the processes proceed on FAD → SMT → FAD → SMT→ FAD → SMT ... until the processes stop. Terminal concentration of adsorbate in FAD is initial concentration in SMT, and then the terminal concentration SMT is the initial concentration in next FAD.

Numerical Solution of FAD-SMT Model

The numerical solution of Eq. (5) is performed by using Lax-wendroff differential formula shown as Eq. (7).

$$\begin{aligned} &C_j^{n+1} - C_j^n + \frac{a}{2}\left(C_{j+1}^n - C_{j-1}^n\right) - \left(\frac{a}{2} + \varphi\right) \\ &\times \left(C_{j+1}^n - 2C_j^n + C_{j-1}^n\right) = 0 \\ &n = 0, 1, 2, 3, \ldots, \; j = 1, 2, 3, \ldots, M \end{aligned} \tag{7}$$

where $\alpha = \Delta t \cdot u/\Delta x$, $\varphi = \Delta t \cdot D_{\text{ax}}/\Delta x^2$, and $M = L/\Delta x$.

Stability condition:

$$\Delta x \geq (\Delta t^2 u^2 + 2\Delta t D_{\text{ax}})^{0.5}. \tag{8}$$

The truncation error of Eq. (7) is $O(\Delta t^2 + \Delta x^2)$. When Eq. (7) is used to solve Eq. (5) numerically, it is necessary to make an aproximation $c_M^n \cong c_{M-1}^n$.

The numerical solution for Eq. (6) is proceeded on the ODE's numerical method. For example, modified Euler method can be used if Eq. (6) is linear or weak non-linear, and Gear's stiff method can be used if Eq. (6) is strong non-linear. Stability condition of the numerical solution for Eq. (6) is as follows:

$$\begin{aligned} \frac{\partial f}{\partial Q} &\leq 0 \\ -B\frac{\partial f}{\partial C} &\leq 0 \end{aligned} \tag{9}$$

Convergence condition is as follows:

$$\begin{aligned} \left|\frac{\Delta t}{2} \cdot \frac{\partial f}{\partial Q}\right| &< 1 \\ \left|B\frac{\Delta t}{2} \cdot \frac{\partial f}{\partial C}\right| &< 1 \end{aligned} \tag{10}$$

where $B = \frac{1-\varepsilon}{\varepsilon}\rho_s$. It is very important to chose time interval Δt and axial increment Δx reasonably so as to calculate the elution curves of chromatography accurately. On the one hand Δt chosen must be satisfied with Eq. (10) to ensure numerical convergence, and on the other hand Δx must be chosen to satisfy Eq. (8) after Δt has been determined to avoid numerical instability. However, it is noted that the Eq. (8) is inequality, and not of all Δx which satisfy the Eq. (8) in value could make numerical solution accuracy because the truncation error of the Lax-wendroff differential formula is $O(\Delta t^2 + \Delta x^2)$ and then calculation error increases with the increase of Δx. In this work, select $\Delta t = 6$ s, and then by using computer, Δx was calculated and then optimized automatically so that it can satisfy the Eq. (8) and make (Input-Output)/Input minimum theoretically.

If the adsorption rate model, Eq. (4) is not represented with the linear driving force or the influence of coexistence of adsorbates on adsorption isotherm and mass transfer kinetics are taken into account, the function $f_i(C_i^*, C_i, t)$ in Eq. (1) or Eq. (6) would become a complex function. Nevertheless, no matter how Eq. (6) is complex, it is always a set of ordinary differential equations, and it can be solved by some mature numerical methods.

Results and Discussion

Sensitivity Analysis of Thermodynamic and Dynamic Parameters

The purpose of sensitivity analyses of parameters a_i, b_i, k_i and D_{ax} is to identify qualitatively the effect of these parameters on chromatography separation process according to the root-mean-square error β_i% between experimental and theoretical elution curves. Firstly, make one of these parameters a_i, b_i, k_i and D_{ax} increase or decrease by 10%, then put it in Eq. (1) and calculate chromatographic elution curve $C_i(t, L)$, and finally find out the root-mean-square error β_i% produced by the change of this parameter by using Eq. (11). Where $C_i(t, L)_{\text{expt.}}$ is the experimental elution curve

Table 1. The sensitivity analysis result of parameters.

a_s	b_s	k_s	a_r	b_r	k_r	D_{ax}	β_s	$\beta_r\%$
2.198	2.34	0.1382	1.55	3.94	0.37	0.85	8.5	8.21
2.198*	2.34	0.1382	1.55	3.94	0.37	0.85	13.0	15.43
2.198*	2.34	0.1382	1.55	3.94	0.37	0.85	13.0	18.44
2.198	2.34	0.1382	1.55	3.94*1	0.37	0.85	8.5	8.70
2.198	2.34	0.1382	1.55	3.94*0	0.37	0.85	8.7	8.67
2.198	2.F3	0.1382*	1.55	3.94	0.37	0.85	9.7	8.82
2.198	2.34	0.1382*	1.55	3.94	0.37	0.85	8.8	8.42
2.198	2.34	0.1382	1.55	3.94	0.37	0.85	8.9	9.08
2.198	2.34	0.1382	1.55	3.94	0.37	0.85	10.0	11.05

$Q_s = C_s^*/(2.198 + 3.34C_i^*)$, $Q_r = C_r^*/(1.55 + 3.94C_i^*)$, $k_s = 0.1382$, $k_r = 0.37$, $D_{\text{ax}} = 0.85$, $T = 55°\text{C}$, $C_{0s} = 0.40$, $C_{0r} = 0.19$, $t_1 = 7.5$, $u = 2.21$, $\varepsilon = 0.31$, $d = 2.54$, $L = 50$, adsorbent: 734 Ca^{2+} resin.

of chromatographic separation. In this way, the root-mean-square errors $\beta_i\%$ of these parameters a_i, b_i, k_i and D_{ax} can be found out separately.

$$\beta_i\% = \left\{ \frac{\int_{\text{ts}}^{\text{te}} [C_i(t, L) - C_i(t, L)_{\text{expt.}}]^2\, dt}{\int_{\text{ts}}^{\text{te}} C_i^2(t, L)_{\text{expt.}}\, dt} \right\}^{0.5} \times 100\% \tag{11}$$

The data in Table 1 indicate that the root-mean-square error produced by the change of parameter a_i is the largest in all $\beta_i\%$. It means that the chromatographic elution curves are more sensitive to the changes of the parameters a_i in Langmuir isotherms than to the changes of other parameters. Therefore, the parameters a_i in Langmuir isotherms is a major factor affecting chromatographic separation in the studied system. The parameters in isotherm, the lumped mass transfer coefficients and the axial dispersion coefficients used in this paper are determined by means of transfer function method and plus-response experimental determining technique proposed by Li and Ye (1994) and Shu (1996). The resins used in our experiments are the commercial products of Nankai Chemicals Plant, China. The resin sizes in diameter are not uniform. The size distribution of the resins is ranged from 0.3 to 1.0 mm in diameter. The distilled water is used as solvent.

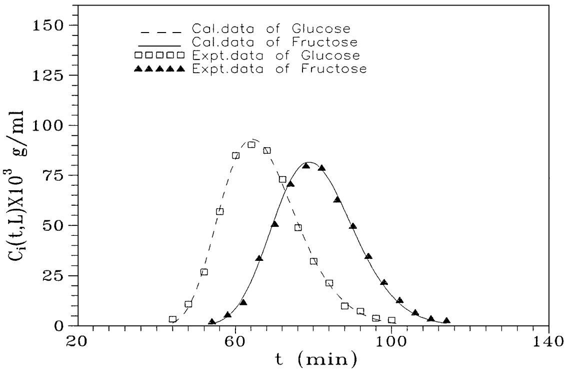

Figure 1. Comparison between experimental elution curve and the calculated elution curves using FAD-SMT model for the system of separating glucose and fructose. $Q_g = C_g^*/(5.154 + 0.436C_g^*)$, $Q_f = C_f^*/(2.967 + 0.285C_f^*)$, $k_g = 0.091$, $k_f = 0.273$, $T = 50°\text{C}$, $D_{\text{ax}} = 0.652$, $C_{0g} = 0.30$, $C_{0f} = 0.28$, $t_1 = 7.5$, $u = 2.57$, $d = 3.17$, $\varepsilon = 0.32$, $L = 116$, adsorbent: 032 resin.

Simulation of Liquid Adsorption Chromatography

The application of chromatography equations and FAD-SMT model proposed in this paper simulates the elution curves of large scale liquid adsorption chromatography in the systems of separating fructose and glucose, separating sucrose and reducing sugar and separating mannitol and sorbitol. Figures 1–3 show the comparison between the experimental elution curves and the elution curves calculated by means of the FAD-SMT model. It is evident from these figures that the agreement is excellent.

Simulation of Cycling Adsorption Chromatography ***B.C.***

$$C_i(t, 0) = h(t) \tag{12}$$

When $n = 1$,

$$h(t) = C_{0i}, \tag{13}$$

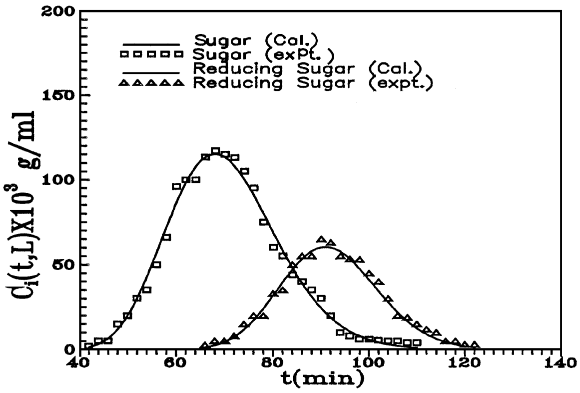

Figure 2. Comparison between experimental elution curve and the calculated elution curves using FAD-SMT model for the system of separating sugar and reducing sugar. $Q_s = C_s^*/(3.372 + 4.1C_s^*)$, $Q_r = C_r^*/(1.961 + 2.341C_r^*)$, $k_s = 0.152$, $k_r = 1.105$, $D_{\text{ax}} = 1.411$, $T = 50°\text{C}$, $C_{0s} = 0.40$, $C_{0r} = 0.19$, $t_1 = 8$, $u = 2.81$, $\varepsilon = 0.287$, $d = 3.17$, $L = 116$, adsorbent: D70 resin.

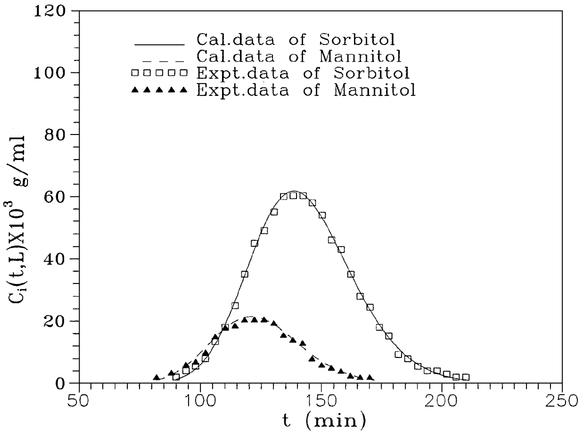

Figure 3. Comparison between experimental elution curve and the calculated elution curves using FAD-SMT model for the system of separating mannitol and sorbitol. $Q_s = C_s^*/(0.92 + 0.33C_s^*)$, $Q_m = C_m^*/(1.16 + 0.27C_m^*)$; $k_s = 0.796$, $k_m = 0.692$, $D_{\text{ax}} = 1.672$, $T = 50°\text{C}$, $C_{0s} = 0.417$, $C_{0m} = 0.126$, $t_1 = 8$, $u = 3$, $\varepsilon = 0.2$, $d = 3.17$, $L = 116$, adsorbent: D80 resin.

and when $n > 1$,

$$h(t) = \begin{cases} C_i^{n-1}(t, L) & t_1^{n-1} \le t \le t_2^{n-1} \\ 0 & t > t_2^{n-1} \end{cases} \quad n > 1 \tag{14}$$

Cycling chromatography is a novel chromatographic process (Andreas and Guiochon, 1993; Li and Shu, 1997). The model of cycling chromatography is different from the model of conventional chromatography in boundary condition. An important character of cycling chromatography is its unsteady boundary condition, as shown in Eqs. (12)–(14). The functions $C_i(t, 0)$ are usually rectangular profiles for the first cycling, $n = 1$, just like in the case of a conventional chromatography, and when $n \ge 2$, the functions $C_i(t, 0)$ become the overlap of two component elution curves of last cycling separation. Without increasing column length and column inlet pressure, continuous recycling offers an easy way to simulate a longer column. Guiochon (Andreas and Guiochon, 1993) and Li (Li and Shu, 1997) have theoretically proved that recycling separation could not only improve the recovery yield but also significantly increase production rate by using equilibrium-dispersive theory and non-equilibrium theory separately. In this paper, the FAD-SMT model is used to simulate the elution curves of cycling chromatography in the systems of separating sucrose and reducing sugar (see Figs. 4 and 5). It can be seen from Fig. 6 that the cycling chromatographic elution curves calculated by using the FAD-SMT model are good agreement with the experimental elution curves of the

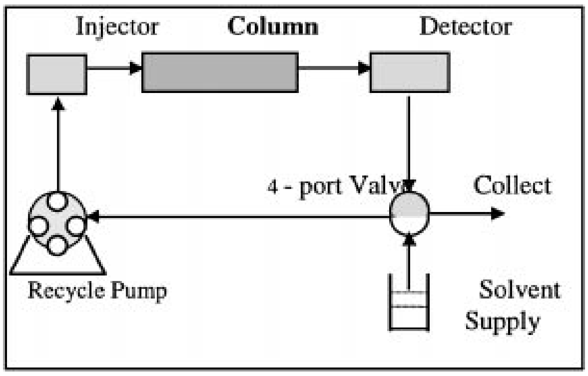

Figure 4. Apparatus of recycling chromatography.

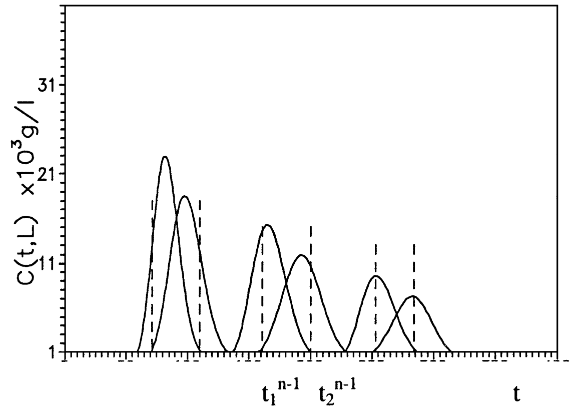

Figure 5. Cutting points of elution curves for collecting and recycling during each of the first three cycles.

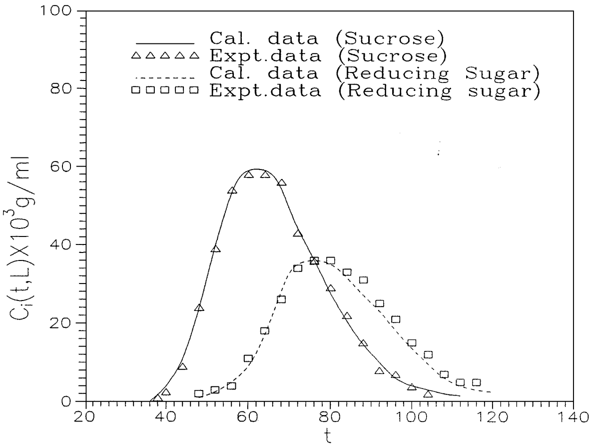

Figure 6. Comparison between the experimental elution curves and calculated elution curves by using FAD-SMT model for the second cycle of cycling chromatography. $Q_s = C_s^*/(1.92 + 2.8C_s^*)$, $Q_r = C_r^*/(1.43 + 4.6C_r^*)$, $k_s = 0.31$, $k_r = 0.45$, $D_{\mathrm{ax}} = 1.25$, $C_{0s} = 0.35$, $C_{0r} = 0.17$, $T = 50°\mathrm{C}$, $u = 2.91$, $\varepsilon = 0.31$, $d = 2.54$, $L = 50$, adsorbent: D601 Ca^{2+} resin.

cycling chromatography separating sucrose and reducing sugar.

Conclusion

The use of the FAD-SMT model can decompose the complex partial differential equations describing adsorption chromatographic process into a simple convection diffusion partial differential equation and a set of ordinary differential equations. These equations can be easily solved by numerical methods. The good agreements between the experimental elution curves and the elution curves calculated by means of the FAD-SMT model are obtained in the systems of separating fructose and glucose, separating sucrose and reducing sugar and separating mannitol and sorbitol. Therefore, the FAD-SMT model can be used to simulate the elution curves of large scale liquid adsorption chromatography and cycling chromatography. The chromatographic elution curves are more sensitive to the changes of the parameters a_i in Langmuir isotherms than to the change of other parameters in the studied system.

Acknowledgment

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Nomenclature

a_i	parameter in Langmuir isotherm for component *i*	g/ml
b_i	parameter in Langmuir isotherm for component *i*	—
C_i	adsorbate concentration for component *i* in mobile phase	g/ml
C_{0i}	injection sample concentration for component *i*	g/ml
d	the diameter of chromatographic column	cm
D_{ax}	axial dispersion coefficient	cm^2/min
k_i	lumped mass transfer coefficient of component *i*	$cm^3/(g \cdot min)$
L	length of chromatographic column	cm
Q_i	amount adsorbed by adsorbent particle for component *i*	g/g
T	temperature	°C
t	time	min
t_1	time at which injection ends	min
u	interstitial flow velocity	cm/min
x	column axial direction position	cm
ε	porosity of the packed column	—
ρ	adsorbent density	g/cm^3

Subscripts

f	fructose
g	glucose
m	mannitol
r	reducing sugar
s	sucrose in Fig. 2, Fig. 6 and Table 1
s	sorbitol in Fig. 3.

References

Andreas, Seidel-Morgrenstem and G. Guiochon, “Theoretical Study of Recycling in Preparative Chromatography,” *AIChE J.*, **39**(5), 809 (1993).

Chen, T.L. and J.T. Hsu, “Prediction of Breakthrough Curves by the Application of Fast Fourier Transform,” *AIChE J.*, **33**(8), 1387–1390 (1987).

Cho, B.K. and L.L. Hegedus, “Discrete Cell Model of Pore-Mouth Poisoning of Fixed Bed Reactors,” *AIChE J.*, **29**(2), 289 (1983).

Gu, T., Gow-Jen Tsai, and George T. Tsao, “New Approach to a General Nonlinear Multicomponent Chromatography Model,” *AIChE J.*, **36**, 5784 (1990).

Li, Zhong and Wenli Shu, “Non-Linear and Non-Equilibrium Cycling Chromatography,” *Advances in Adsorption Separation Science and Technology*, Z. Li (Ed.), pp. 214–219, SCUT Press, Guangzhou, China, 1997.

Li, Zhong and Z.H. Ye, “A New Method of Thermodynamic and Dynamic Parameter Identification of Large Scale Chromatography,” *Journal of Chinese Chemical Engineering (Hua Gong Xue Bao)*, (5), 601–609 (1994).

Liapis, A.I. and R.J. Litchfield, “Ternary Adsorption in Columns,” *Chem. Eng. Sci.*, **35**, 2366 (1980).

Liapis, A.I. and D.W.T. Rippin, “The Simulation of Binary Adsorption in Activated Carbon Columns Using Estimates of Diffusion Resistance within the Carbon Particles Derived from Batch Experiments,” *Chem. Eng. Sci.*, **33**, 539 (1978).

Mansour, A.R., “The Simulation of Multicomponent Sorption Processes with Axial Diffusion,” *Sep. Sci. Technol.*, **24**(12), 1047 (1989).

Poulain, C.A. and B.A. Finlaysonn, “A Comparison of Numerical Methods Applied to Non-Linear Adsorption Columns,” *International Journal of Numerical Methods in Fluids.*, **17**, 839–859 (1993).

Shu, Wenli, “Study of Non-Linear and Non-Equilibrium Cycling Chromatographic Separation,” Thesis of Master Degree, South China University of Technology, Guangzhou, China, 1996.

Yu, Q. and N.H.L. Wang, “Computer Simulation of the Dynamics of Multicomponent Ion Exchange in Fixed-Bed-Gradient-Direction Moving Finite Element Method,” *Comp. Chem. Eng.*, **13**(8), 915 (1989).