

Journal of Chromatography A, 796 (1998) 157-164

JOURNAL OF CHROMATOGRAPHY A

# Frontal chromatography of proteins Effect of axial dispersion on column performance

G.A. Heeter<sup>a</sup>, A.I. Liapis<sup>a,b,\*</sup>

<sup>a</sup>Department of Chemical Engineering and Biochemical Processing Institute, University of Missouri-Rolla, Rolla, MO 65401-0249, USA

<sup>b</sup>Lehrstuhl B für Verfahrenstechnik, Technische Universität München, Boltzmannstrasse 15, D-85748 Garching, Germany

## Abstract

A mathematical model describing the dynamic adsorption of proteins in columns packed with spherical porous adsorbent particles is used to study the effect of axial dispersion on the performance of chromatographic systems. The values of the axial dispersion coefficient,  $D_{\rm L}$ , are estimated from a correlation based on a model describing axial dispersion in packed beds that provides satisfactory results when compared with experiment. Simulations of frontal chromatography in systems including axial dispersion and in systems without axial dispersion are made and compared to determine the effect of axial dispersion are examined. It is found that the reduction in the efficiency of the adsorption process; also, the system parameters that influence axial dispersion is small (<1%) for columns of length 10 cm or greater. However, for short columns, this efficiency reduction can be as large as 10%. Increasing the adsorbent particle diameter,  $d_p$ , is much more pronounced in a short column than in a long column. © 1998 Elsevier Science B.V.

Keywords: Axial dispersion; Frontal chromatography; Adsorption; Mathematical modelling; Proteins

# 1. Introduction

The adsorption of proteins from liquid streams into porous adsorbent particles in column systems can involve several mass transport mechanisms [1– 4]. Theoretical studies using dynamic models of the adsorption process have examined the effect on adsorption system performance of the intraparticle mass transfer mechanisms of pore diffusion [5–10] and intraparticle convection [7–10], the mechanism of external particle film mass transfer [5,6] and the mechanism of the interaction (adsorption) between the adsorbate molecules and the active sites on the surface of the pores of the chromatographic particles

\*Corresponding author.

[5,6,10]. All of these studies have considered that the mechanism of axial dispersion would have a negligible effect on the system performance. Heeter and Liapis [11] employed a theoretical model [5–10] that neglected the mechanism of axial dispersion and their theoretical results described fairly well the experimental data of the adsorption of bovine serum albumin (BSA) onto anion-exchange porous particles packed properly in a column of length 3 cm.

Arnold et al. [12,13] presented a method for evaluating the relative importance of the mass transfer mechanisms involved in the adsorption of proteins in a chromatographic system by analyzing the results of pulse experiments under non-retained solute conditions to determine the contribution of each mass transfer mechanism to the overall HETP

<sup>0021-9673/98/\$19.00 © 1998</sup> Elsevier Science B.V. All rights reserved. *PII* \$0021-9673(97)00951-5

(height equivalent to a theoretical plate). The results of applying their method to model systems [13] indicated that the contribution of axial dispersion to the overall HETP was much smaller than the contribution of pore diffusion within the adsorbent particle at higher flow-rates. The results of Arnold et al. [12,13] were obtained for systems of non-retained solutes, which means that an adsorption mechanism was not active. In the present work, retained solutes through a non-linear mechanism are considered.

In this work, a mathematical model describing the dynamic adsorption of proteins in columns packed with spherical porous adsorbent particles is used to study the effect of axial dispersion on the performance of chromatographic systems. Simulations of frontal chromatography in systems including axial dispersion and in systems without axial dispersion are made and compared to determine the effect of axial dispersion on the efficiency of the adsorption process; also, the system parameters that influence axial dispersion are examined.

## 2. Mathematical theory

The mathematical model used in this work considers that single component adsorption takes place from a flowing liquid stream in a fixed bed of spherical adsorbent particles under isothermal conditions. The superficial velocity of the liquid stream,  $V_{\rm f}$ , is taken to be independent of the column space variable x and the concentration gradients in the radial direction of the bed are considered to be not significant. The mass transfer mechanisms of axial dispersion in the flowing fluid stream of the column and pore diffusion within the adsorbent particles are considered to occur and the porous structure of the adsorbent particles is taken to be monodisperse. In addition, the interaction between the adsorbate molecules and the active sites on the surface of the pores of the adsorbent particles is taken to occur infinitely fast, and therefore, local equilibrium between the adsorbate in the pore fluid and in the adsorbed phase at each point in the pores is considered to exist.

The differential mass balance for the adsorbate in the flowing fluid stream in the column is given by

$$\frac{\partial C_{\rm d}}{\partial t} - D_{\rm L} \frac{\partial^2 C_{\rm d}}{\partial x^2} + \frac{V_{\rm f}}{\epsilon} \frac{\partial C_{\rm d}}{\partial x} = -\frac{(1-\epsilon)}{\epsilon} \frac{\partial C_{\rm p}}{\partial t}$$
(1)

The initial and boundary conditions of Eq. (1) are as follows:

at 
$$t = 0$$
,  $C_{\rm d} = 0$ ,  $0 \le x \le L$  (2)

at 
$$x = 0$$
,  $\frac{V_{\rm f}}{\epsilon}C_{\rm d} - D_{\rm L}\frac{\partial C_{\rm d}}{\partial x}\Big|_{x=0} = \frac{V_{\rm f}}{\epsilon}C_{\rm d,in}, t > 0$  (3)

at 
$$x = L$$
,  $\frac{\partial C_d}{\partial x}\Big|_{x=L} = 0$ ,  $t > 0$  (4)

The average adsorbate concentration in the adsorbent particle,  $\overline{C}_{p}$ , is obtained from Eq. (5)

$$\overline{C}_{p} = \frac{3}{R_{p}^{3}} \left[ \int_{0}^{R_{p}} \epsilon_{p} C_{p} R^{2} dR + \int_{0}^{R_{p}} C_{s} R^{2} dR \right]$$
(5)

The differential mass balance for the adsorbate in the adsorbent particle is given by

$$\frac{\partial C_{\rm p}}{\partial t} + \left(\frac{1}{\epsilon_{\rm p}}\right)\frac{\partial C_{\rm s}}{\partial t} = D_{\rm p}\left(\frac{1}{R^2}\right)\frac{\partial}{\partial R}\left(R^2\frac{\partial C_{\rm p}}{\partial R}\right) \tag{6}$$

The initial and boundary conditions of Eq. (6) are

at 
$$t = 0$$
,  $C_{\rm p} = 0$ ,  $0 \le R \le R_{\rm p}$  (7)

at 
$$t = 0$$
,  $C_s = 0$ ,  $0 \le R \le R_p$  (8)

at 
$$R = R_{\rm p}, \ C_{\rm p} = C_{\rm d}(t,x), \ t > 0$$
 (9)

at 
$$R = 0$$
,  $\frac{\partial C_{\rm p}}{\partial R}\Big|_{R=0} = 0$ ,  $t > 0$  (10)

The value of the effective pore diffusion coefficient,  $D_p$ , in Eq. (6) is taken to be constant. Furthermore, the form of Eq. (9) indicates that the effect of the external mass transfer mechanism is not considered, since detailed calculations [5,6] have shown that for the flow-rates used in practical chromatographic systems the effect of the external film mass transfer mechanism is negligible. The equilibrium state of the adsorption system in this work is represented by the Langmuir equilibrium isotherm

$$C_{\rm s} = \frac{KC_{\rm T}C_{\rm p}}{1+KC_{\rm p}} \tag{11}$$

and, since local equilibrium between the adsorbate in the pore fluid and in the adsorbed phase at each point in the pores of the adsorbent particles is considered to exist, the accumulation term  $\partial C_s / \partial t$  in Eq. (6) is given by

$$\frac{\partial C_{\rm s}}{\partial t} = \frac{KC_{\rm T}}{(1+KC_{\rm p})^2} \frac{\partial C_{\rm p}}{\partial t}$$
(12)

The value of the axial dispersion coefficient,  $D_L$ , could be estimated from the expression developed by Gunn [14], who considered axial dispersion to be a stochastic process involving both convective and diffusive mechanisms. The expression developed by Gunn was shown to satisfactorily describe the available experimental results [14–16] and is reproduced here, in our notation, for convenience:

$$\frac{\epsilon D_{\rm L}}{V_{\rm f} d_{\rm p}} = \left\{ \frac{\text{ReSc}}{4\alpha_1^2 (1-\epsilon)} (1-p)^2 + \frac{(\text{ReSc})^2}{16\alpha_1^4 (1-\epsilon)^2} p (1-p)^3 \\ \times \left[ \exp\left(\frac{-4\alpha_1^2 (1-\epsilon)}{p (1-p) \text{ReSc}}\right) - 1 \right] \right\} \\ \times (1+\sigma_{\rm v}^2) + \frac{\sigma_{\rm v}^2}{2} + \frac{\epsilon}{\tau \text{ReSc}}$$
(13)

In Eq. (13),  $\alpha_1$  is the first root of the zero-order Bessel function,  $\tau$  is a tortuosity factor that accounts for dispersion paths which are longer than the length of the column [15], the Reynolds number, Re, is given by Eq. (14)

$$\operatorname{Re} = \frac{V_{\mathrm{f}} d_{\mathrm{p}} \rho}{\mu} \tag{14}$$

and the expression for the Schmidt number, Sc, is as follows:

$$Sc = \frac{\mu}{\rho D_{mf}}$$
(15)

The parameter  $\sigma_v^2$  is the dimensionless variance of the distribution of the fluid interstitial velocity over the column cross-section [14]. A value of  $\sigma_v^2=0$ indicates that the fluid velocity does not vary over the cross-section of the packed bed, while a non-zero value of  $\sigma_v^2$  indicates that the fluid velocity, and hence the packing arrangement of the particles, is non-uniform. By comparing the prediction of Eq. (13) to the available experimental results, Gunn concluded that the value of  $\sigma_v^2$  is likely in the range of 0.1–0.3 for well-packed beds, while in a maldistributed bed, the value of  $\sigma_v^2$  could be as large as 2.0 [14]. The results of recently published [17,18] experimental measurements of the radial distribution of the liquid velocity in chromatographic columns give values of  $\sigma_v^2$  of less than 0.002.

The parameter p represents the probability of a solute molecule being transported downstream by the fluid and is a function of the Reynolds number, Re, only [15,16]. Gunn [16] reports the following expression, based on experimental data, for the dependence of p upon Re for beds of spheres:

$$p = 0.17 + 0.33 \exp\left(-\frac{24}{\text{Re}}\right) \tag{16}$$

In Fig. 1, the axial dispersion coefficient,  $D_{\rm L}$ , is shown as a function of  $\sigma_{\rm v}^2$  for different values of  $d_{\rm p}$  and  $V_{\rm f}$ . The results in Fig. 1 were obtained from Eq. (13) using  $\epsilon = 0.35$ ,  $\tau = 1.4$ ,  $D_{\rm mf} = 5.90 \cdot 10^{-11} \text{ m}^2/\text{s}$ ,  $\rho = 1000 \text{ kg/m}^3$  and  $\mu = 0.001 \text{ Pa} \cdot \text{s}$ . The values of  $D_{\rm mf} = 5.90 \cdot 10^{-11} \text{ m}^2/\text{s}$ ,  $\rho = 1000 \text{ kg/m}^3$  and  $\mu = 0.001 \text{ Pa} \cdot \text{s}$ . The values of  $D_{\rm mf} = 5.90 \cdot 10^{-11} \text{ m}^2/\text{s}$ ,  $\rho = 1000 \text{ kg/m}^3$  and  $\mu = 0.001 \text{ Pa} \cdot \text{s}$  are those for aqueous solutions of BSA and the value of  $\tau$  is taken to be equal to 1.4 as indicated by Gunn [16]. The results in Fig. 1 show that the value of  $D_{\rm L}$  increases as  $\sigma_{\rm v}^2$  is increased, as  $d_{\rm p}$  is increased, and as  $V_{\rm f}$  is increased.



Fig. 1. The dependence of the axial dispersion coefficient,  $D_{\rm L}$ , upon the variance of the column liquid velocity over the column cross-section for different values of  $d_{\rm p}$  and  $V_{\rm f}$ . The solid lines are for  $V_{\rm f}$ =2000 cm/h and the dashed lines are for  $V_{\rm f}$ =1000 cm/h. The lines for  $d_{\rm p}$ =15  $\mu$ m,  $V_{\rm f}$ =2000 cm/h and  $d_{\rm p}$ =30  $\mu$ m,  $V_{\rm f}$ =1000 cm/h coincide. (A)  $d_{\rm p}$ =50  $\mu$ m,  $V_{\rm f}$ =2000 cm/h; (B)  $d_{\rm p}$ =30  $\mu$ m,  $V_{\rm f}$ =2000 cm/h; (C)  $d_{\rm p}$ =50  $\mu$ m,  $V_{\rm f}$ =1000 cm/h; (D)  $d_{\rm p}$ =15  $\mu$ m,  $V_{\rm f}$ =2000 cm/h and  $d_{\rm p}$ =30  $\mu$ m,  $V_{\rm f}$ =1000 cm/h; (E)  $d_{\rm p}$ =15  $\mu$ m,  $V_{\rm f}$ =1000 cm/h; (E)  $d_{\rm p}$ =15  $\mu$ m,  $V_{\rm f}$ =1000 cm/h.

The solution of the equations of the model (Eqs. (1)-(12)) was obtained by the numerical method of orthogonal collocation; details are reported elsewhere [19–21].

## 3. Results and discussion

The effect of axial dispersion on the efficiency with which the capacity of porous adsorbent particles is utilized by the adsorption of proteins in fixed bed column systems was studied in this work. Frontal chromatography was simulated (i) for systems involving non-linear adsorption in which the mass transfer mechanisms of axial dispersion and pore diffusion were included and (ii) for systems involving non-linear adsorption in which only the mass transfer mechanism of pore diffusion was considered [for systems of case (ii) the value of  $D_{\rm L} = 0$  was used in Eq. (1)]. Five system parameters that influence the importance of the effect of axial dispersion on adsorption system performance were varied in this study: the column length, L; the adsorbent particle diameter,  $d_{p}$ ; the column liquid superficial velocity,  $V_{\rm f}$ ; the column void fraction,  $\epsilon$ ; and the variance of the distribution of the liquid velocity over the column cross-section,  $\sigma_v^2$ . The values of other parameters, which were held constant for all simulations, are listed in Table 1. The value of  $\tau$  was taken to be equal to 1.4 in Table 1, as indicated by Gunn [16] for beds of spheres. The values of the other parameters in Table 1 are from an experimental system involving the adsorption of BSA from aqueous solution onto anion-exchange adsorbent particles packed in a column [11].

Table 1 Fixed values of the parameters of the adsorption system

Parameter	Value
$ \frac{C_{d,in}}{C_T} \\ D_{mf} \\ D_p \\ K \\ \epsilon $	0.03 kg/m <sup>3</sup> 50.82 kg/m <sup>3</sup> particle $5.90 \cdot 10^{-11} \text{ m}^2/\text{s}$ $2.93 \cdot 10^{-11} \text{ m}^2/\text{s}$ $472.1 \text{ m}^3/\text{kg}$ 0.48
$\overset{\scriptscriptstyle\mathrm{P}}{\mu}$ $ ho$ $ au$	0.001 Pa·s 1000 kg/m <sup>3</sup> 1.4

The criterion that was used to measure the effect of axial dispersion on adsorption system performance was the relative difference between the dynamic utilization of the adsorptive capacity of the column for a system including axial dispersion and the dynamic utilization of the adsorptive capacity of the column for an otherwise comparable system without axial dispersion. This relative utilization difference (denoted by  $\Delta \Phi_{ax}$ ) is given by

$$\Delta \Phi_{\rm ax} = \left(\frac{\Phi_{\rm ax} - \Phi_0}{\Phi_0}\right) (100) \tag{17}$$

where  $\Phi_{ax}$  is the dynamic utilization of the adsorptive capacity for the system including axial dispersion and  $\Phi_0$  is the dynamic utilization of the adsorptive capacity of the column for the system without axial dispersion. The dynamic utilization of the adsorptive capacity of a column is defined as the ratio of the total amount of adsorbate in the adsorbed phase of the column when the desired breakthrough (in this work, 1% breakthrough is taken to represent the desired breakthrough) occurs to the total adsorptive capacity of the column, which is the total amount of adsorbate in the adsorbed phase at equilibrium with respect to the column inlet concentration,  $C_{\rm d.in}$ . The value of  $\Delta \Phi_{\rm ax}$  obtained from Eq. (17) could be interpreted as the percentage by which the mechanism of axial dispersion changes the efficiency of the adsorption process.

The mechanism of axial dispersion causes the adsorption front (mass transfer zone) in the column to lengthen, reducing the amount of adsorbate in the adsorbed phase at breakthrough. The value of the relative utilization difference,  $\Delta \Phi_{ax}$ , is always less than zero, reflecting the reduction in efficiency due to axial dispersion. The dependence of  $\Delta \Phi_{ax}$ , upon the column length, L, is presented in Fig. 2 for three values of the adsorbent particle diameter,  $d_{p}$ , when  $V_{\rm f} = 1000 \text{ cm/h}, \epsilon = 0.35 \text{ and } \sigma_{\rm v}^2 = 0.$  The amount by which the mechanism of axial dispersion reduces the efficiency of the adsorption process is very small for long columns; there is less than 1% reduction for columns of length 10 cm or greater. However, when L is less than 5 cm, the reduction in efficiency is much larger. The effect of axial dispersion is more pronounced in short columns because the adsorption front takes up a larger portion of the column.



Fig. 2. The relative utilization difference,  $\Delta \Phi_{\rm ax}$ , as a function of the column length for different values of  $d_{\rm p}$  when  $V_{\rm f}$ =1000 cm/h,  $\epsilon$ =0.35 and  $\sigma_{\rm v}^2$ =0. (A)  $d_{\rm p}$ =15 µm; (B)  $d_{\rm p}$ =30 µm; (C)  $d_{\rm p}$ =50 µm.

Simulated breakthrough curves for adsorption systems with and without axial dispersion are compared in Fig. 3 for L=3 cm and L=10 cm when  $d_p = 50 \ \mu\text{m}$ ,  $V_f = 1000 \ \text{cm/h}$ ,  $\epsilon = 0.35$  and  $\sigma_v^2 = 0$ . For both column lengths, there is only a slight difference between the breakthrough curves with and without axial dispersion occurring at the earliest breakthrough times. This small difference corresponds to a value of  $\Delta \Phi_{ax} = -3.4\%$  for the 3 cm column and a value of  $\Delta \Phi_{ax} = -0.76\%$  for the 10 cm column.

In Fig. 4, the dependence of  $\Delta \Phi_{\rm ax}$  upon the



Fig. 3. Breakthrough curves for adsorption systems with and without axial dispersion for different column lengths when  $d_p = 50$   $\mu$ m,  $V_f = 1000$  cm/h,  $\epsilon = 0.35$  and  $\sigma_v^2 = 0$ . The solid curves are for systems without axial dispersion and the dashed curves are for systems including axial dispersion. (A) L=3 cm; (B) L=10 cm.



Fig. 4. The relative utilization difference,  $\Delta \Phi_{ax}$ , as a function of the adsorbent particle diameter for different values of the column length when  $V_{\rm f}$ =1000 cm/h,  $\epsilon$ =0.35 and  $\sigma_{\rm v}^2$ =0. (A) *L*=3 cm; (B) *L*=10 cm.

adsorbent particle diameter,  $d_p$ , is shown for two column lengths when  $V_f = 1000$  cm/h,  $\epsilon = 0.35$  and  $\sigma_v^2 = 0$ . The amount by which the efficiency is reduced by axial dispersion increases (the value of  $\Delta \Phi_{ax}$  becomes more negative) as  $d_p$  is increased, due to the increase in the value of  $D_L$  from Eq. (13) as  $d_p$ is increased. The change in  $\Delta \Phi_{ax}$  when  $d_p$  is changed is much less for the 10 cm column than for the 3 cm column; the effect of axial dispersion is subdued in the longer column.

The relationship between  $\Delta \Phi_{ax}$  and the column liquid superficial velocity,  $V_f$ , is shown in Fig. 5, for two values of  $d_p$  and two values of L, when  $\epsilon = 0.35$ and  $\sigma_v^2 = 0$ . Although there is a small increase in the efficiency reduction due to axial dispersion as  $V_f$  is increased when the value of  $V_f$  is small, there is little change in the value of  $\Delta \Phi_{ax}$  when  $V_f$  is changed above about 1000 cm/h. The reason that the value of  $\Delta \Phi_{ax}$  is relatively insensitive to changes in the value of  $D_L$  from Eq. (13), there is an increase in convective transport down the column when  $V_f$  is increased and the relative importance of these two mechanisms are kept approximately in balance.

Fig. 6 shows the relationship between  $\Delta \Phi_{ax}$  and the column void fraction,  $\epsilon$ , for two values of  $d_p$  and two values of *L* when  $V_f = 1000$  cm/h and  $\sigma_v^2 = 0$ . Changes in the value of  $\epsilon$  within the range 0.3–0.4 have nearly no effect on the value of  $\Delta \Phi_{ax}$  for the



Fig. 5. The relative utilization difference,  $\Delta \Phi_{ax}$ , as a function of the column liquid superficial velocity for different values of  $d_p$  and L when  $\epsilon = 0.35$  and  $\sigma_v^2 = 0$ . The solid curves are for  $d_p = 30$   $\mu$ m and the dashed curves are for  $d_p = 50$   $\mu$ m. (A) L = 10 cm,  $d_p = 30$   $\mu$ m; (B) L = 10 cm,  $d_p = 50$   $\mu$ m; (C) L = 3 cm,  $d_p = 30$   $\mu$ m; (D) L = 3 cm,  $d_p = 50$   $\mu$ m.

same reason that changes in  $V_{\rm f}$  have little effect (note that changing  $\epsilon$  changes the interstitial fluid velocity).

The dependence of  $\Delta \Phi_{ax}$  upon the variance of the column liquid velocity over the column cross-section,  $\sigma_v^2$ , is presented in Fig. 7 for two values of  $d_p$  and two values of L when  $V_f = 1000$  cm/h and



Fig. 6. The relative utilization difference,  $\Delta \Phi_{ax}$ , as a function of the column void fraction for different values of  $d_p$  and L when  $V_t = 1000$  cm/h and  $\sigma_v^2 = 0$ . The solid curves are for  $d_p = 30 \ \mu\text{m}$  and the dashed curves are for  $d_p = 50 \ \mu\text{m}$ . (A)  $L = 10 \ \text{cm}$ ,  $d_p = 30 \ \mu\text{m}$ ; (B)  $L = 10 \ \text{cm}$ ,  $d_p = 50 \ \mu\text{m}$ ; (C)  $L = 3 \ \text{cm}$ ,  $d_p = 30 \ \mu\text{m}$ ; (D)  $L = 3 \ \text{cm}$ ,  $d_p = 50 \ \mu\text{m}$ .



Fig. 7. The relative utilization difference,  $\Delta \Phi_{ax}$ , as a function of the variance of the column liquid velocity over the column cross-section for different values of  $d_p$  and L when  $V_r = 1000$  cm/h and  $\epsilon = 0.35$ . The solid curves are for  $d_p = 30$  µm and the dashed curves are for  $d_p = 50$  µm. (A) L = 10 cm,  $d_p = 30$  µm; (B) L = 10 cm,  $d_p = 50$  µm; (C) L = 3 cm,  $d_p = 30$  µm; (D) L = 3 cm,  $d_p = 50$  µm.

 $\epsilon = 0.35$ . The magnitude of the efficiency reduction increases as  $\sigma_v^2$  is increased, due to the increase in the value of  $D_L$  from Eq. (13) as  $\sigma_v^2$  is increased. The effect of increasing  $\sigma_v^2$  is much less for the 10 cm column than for the 3 cm column.

#### 4. Conclusions and remarks

Simulation results from a model of single component liquid adsorption in columns packed with spherical porous adsorbent particles were used to study the effect of axial dispersion on the performance of chromatographic systems, as measured by the relative difference between the dynamic utilization of the adsorptive capacity of the column for systems including axial dispersion and for otherwise comparable systems without axial dispersion. The effect of the system parameters that influence axial dispersion on the amount by which axial dispersion reduces the efficiency of the adsorption process was examined. The parameters that were varied are: the column length, L; the adsorbent particle diameter,  $d_{p}$ ; the column liquid superficial velocity,  $V_{\rm f}$ ; the column void fraction,  $\epsilon$ ; and the variance of the distribution of the liquid velocity over the column cross-section,  $\sigma_v^2$ .

The reduction in the efficiency of the adsorption process due to axial dispersion is small (<1%) for columns of length 10 cm or greater. However, for short columns, this efficiency reduction can be as large as 10%. Increasing the adsorbent particle diameter increases the magnitude of the reduction in efficiency due to axial dispersion; the effect of increasing  $d_{p}$  is much more pronounced in a short column than in a long column. Changes in the values of  $V_{\epsilon}$  and  $\epsilon$  have little effect on the amount by which axial dispersion reduces adsorption system efficiency. Increases in the variance of the liquid velocity over the column cross-section, such as would be caused by non-uniformity in the column packing, cause increases in the magnitude of the efficiency reduction due to axial dispersion. However, the effect of the variance in velocity is subdued in longer columns and it is likely that the variance in velocity is small in well-packed columns.

The results presented in this work have several practical implications for the design and operation of chromatographic systems involving the adsorption of proteins. The column in a chromatographic system must be packed properly and the feed stream must be evenly distributed over the column cross-section to avoid large values of the variance of the liquid velocity over the column cross-section; minimizing the velocity variance is particularly important in systems with short columns. If the chromatographic column is reasonably well packed and the feed stream is properly distributed, the most important mass transfer resistances will occur within the adsorbent particles and axial dispersion will play only a minor role in determining the overall adsorption efficiency of the system. The results presented in this work suggest that it is appropriate to model most chromatographic systems involving the adsorption of proteins, except those with short columns, using mathematical models that neglect the mass transfer mechanism of axial dispersion.

# Symbols

 $C_{\rm d}$  Concentration of adsorbate in the flowing fluid stream of the column, kg/m<sup>3</sup> of bulk fluid

- $C_{d,in}$  concentration of adsorbate at the column inlet, kg/m<sup>3</sup> of bulk fluid
- $C_{d,out}$  concentration of adsorbate at the column outlet, kg/m<sup>3</sup> of bulk fluid
- $C_p$  concentration of adsorbate in the fluid of the pores of the adsorbent particle, kg/m<sup>3</sup> of pore fluid
- $C_{\rm p}$  average concentration of adsorbate in the adsorbent particle given by Eq. (5), kg/m<sup>3</sup> of adsorbent particle
- $C_{\rm s}$  concentration of adsorbate in the adsorbed phase of the adsorbent particle, kg/m<sup>3</sup> of adsorbent particle
- $C_{\rm T}$  maximum equilibrium concentration of adsorbate in the adsorbed phase of the adsorbent particle, kg/m<sup>3</sup> of adsorbent particle
- $d_{p}$  diameter of adsorbent particle, m
- $\dot{D}_{\rm L}$  axial dispersion coefficient of adsorbate, m<sup>2</sup>/s
- $D_{\rm mf}$  free molecular diffusivity of adsorbate, m<sup>2</sup>/s
- $D_{\rm p}$  effective pore diffusion coefficient of adsorbate, m<sup>2</sup>/s
- *K* equilibrium adsorption constant for the Langmuir isotherm model, m<sup>3</sup> of pore fluid/kg
- *L* column length, m
- *p* probability of a solute molecule being transported downstream by the fluid given by Eq. (16), dimensionless
- *R* radial distance in adsorbent particle, m
- $R_{\rm p}$  radius of adsorbent particle, m
- Re Reynolds number defined by Eq. (14), dimensionless
- Sc Schmidt number defined by Eq. (15), dimensionless
- t time, s
- $V_{\rm f}$  column fluid superficial velocity, m/s
- x axial distance in column, m

## **Greek letters**

 $\epsilon$ 

- $\alpha_1$  first root of the zero-order Bessel function ( $\alpha_1 \cong 2.4048$ )
  - void fraction of column, dimensionless
- $\epsilon_{p}$  void fraction of adsorbent particles, dimensionless

- $\mu$  viscosity of solvent, Pa·s
- $\rho_{2}$  density of solvent, kg/m<sup>3</sup>
- $\sigma_v^2$  variance of the distribution of the liquid velocity over the column cross-section, dimensionless
- au tortuosity factor for the packed column, dimensionless
- $\Phi_0$  dynamic utilization of the adsorptive capacity of the column for the system without axial dispersion, dimensionless
- $\Phi_{ax}$  dynamic utilization of the adsorptive capacity of the column for the system including axial dispersion, dimensionless
- $\Delta \Phi_{\rm ax}$  relative utilization difference given by Eq. (17), %

## Acknowledgements

The authors gratefully acknowledge partial support of this work by Monsanto. Professor A.I. Liapis gratefully acknowledges the support provided through the Humboldt Research Prize awarded to him in 1996 by the Alexander von Humboldt Foundation in Bonn, Germany.

# References

[1] A.I. Liapis, J. Biotechnol. 11 (1989) 143.

- [2] A.I. Liapis, Sep. Purif. Methods 19 (1990) 133.
- [3] A.I. Liapis, in A.B. Mersmann and S.E. Scholl (Editors), Fundamentals of Adsorption (Proceedings of the Third International Conference on Fundamentals of Adsorption, Sonthofen, May 7–12, 1989), Engineering Foundation, New York, 1990, pp. 25–61.
- [4] A.I. Liapis and K.K. Unger, in G. Street (Editor), Highly Selective Separations in Biotechnology, Blackie, Glasgow, 1994, pp. 121–162.
- [5] B.H. Arve, A.I. Liapis, Biotechnol. Bioeng. 32 (1988) 616.
- [6] M.A. McCoy, A.I. Liapis, J. Chromatogr. 548 (1991) 25.
- [7] A.I. Liapis, M.A. McCoy, J. Chromatogr. 599 (1992) 87.
- [8] A.I. Liapis, M.A. McCoy, J. Chromatogr. A 660 (1994) 85.
- [9] A.I. Liapis, Y. Xu, O.K. Crosser, A. Tongta, J. Chromatogr. A 702 (1995) 45.
- [10] G.A. Heeter, A.I. Liapis, J. Chromatogr. A 743 (1996) 3.
- [11] G.A. Heeter, A.I. Liapis, J. Chromatogr. A 776 (1997) 3.
- [12] F.H. Arnold, H.W. Blanch, C.R. Wilke, Chem. Eng. J. 30 (1985) B9.
- [13] F.H. Arnold, H.W. Blanch, C.R. Wilke, Chem. Eng. J. 30 (1985) B25.
- [14] D.J. Gunn, Trans. Inst. Chem. Eng. (London) 49 (1971) 109.
- [15] D.J. Gunn, Trans. Inst. Chem. Eng. (London) 47 (1969) T351.
- [16] D.J. Gunn, Chem. Eng. Sci. 42 (1987) 363.
- [17] T. Farkas, J.Q. Chambers, G. Guiochon, J. Chromatogr. A 679 (1994) 231.
- [18] T. Farkas, M.J. Sepaniak, G. Guiochon, J. Chromatogr. A 740 (1996) 169.
- [19] M.A. McCoy, Ph.D. Dissertation, Department of Chemical Engineering, University of Missouri-Rolla, Rolla, MO, 1992.
- [20] Y. Xu, Ph.D. Dissertation, Department of Chemical Engineering, University of Missouri-Rolla, Rolla, MO, 1995.
- [21] G.A. Heeter, Ph.D. Dissertation, Department of Chemical Engineering, University of Missouri-Rolla, Rolla, MO, 1997.