

Perfusion chromatography

Effect of micropore diffusion on column performance in systems utilizing perfusive adsorbent particles with a bidisperse porous structure

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ABSTRACT

A mathematical model describing single-component and multi-component adsorption in columns with bidisperse perfusive or bidisperse purely diffusive adsorbent particles is constructed and presented. The model is used to study the adsorption of lysozyme onto monoclonal anti-lysozyme in columns with bidisperse porous adsorbent particles. The influence of the effective pore diffusion coefficient of the adsorbate in the microparticles (microspheres) and the effects of particle size and intraparticle convective flow on column performance are examined. The results for the systems studied indicate that the systems with bidisperse perfusive particles provide a higher dynamic utilization of the adsorptive capacity of the column than the systems having bidisperse purely diffusive particles.

INTRODUCTION

The separation process that involves the flow of a mobile phase (*i.e.*, liquid phase) through the pores of porous chromatographic particles [1–6] has been called by Afeyan *et al.* [1] perfusion chromatography. In perfusive adsorbent particles the intraparticle convective fluid velocity, v_p , is non-zero [4], whereas in purely diffusive adsorbent particles the value of v_p is considered to be equal to zero.

Liapis and McCoy [4] constructed a theory of perfusion chromatography, and their mathematical models could describe the dynamic behavior of single- and multi-component adsorption in columns having perfusive ($v_p > 0$) adsorbent par-

ticles and also in columns having purely diffusive ($v_p = 0$) adsorbent particles. The results obtained by Liapis and McCoy [4], McCoy *et al.* [5] and McCoy [6] suggest that the dynamic behavior of columns with perfusive adsorbent particles could be more effective than that of columns with purely diffusive particles when both the intraparticle Peclet number [4–6] and the Porath parameter [4–11] are large. The intraparticle Peclet number is a general measure of the importance of intraparticle convection, as a means of mass transfer, compared with pore diffusion. The Porath parameter may be considered [4–11] to provide a measure of the speed of the adsorbate–active site (adsorbate–ligand) association step relative to the pore diffusion of the adsorbate in the pores of the adsorbent particle. It is important to note that the intraparticle Peclet number alone is inadequate to describe fully intraparticle mass transfer when adsorption

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occurs [4–6]. In adsorption systems, a second quantity, the Porath parameter [4–11], also comes into play. Also, the results obtained from the binary adsorption (competitive adsorption involving two components) system studied in the work of McCoy *et al.* [5] suggest that the times at which breakthrough begins for components 1 and 2, and the dynamic (unsteady state) relative separation between components 1 and 2 obtained from the column with perfusive particles, are higher than those obtained from the column having purely diffusive particles, especially as the particle size, z_0 , and the column fluid superficial velocity, V_f , increase. The improved separation efficiency obtained from the chromatographic columns with perfusive adsorbent particles is mainly due [4–6] to the intraparticle fluid flow which enhances intraparticle mass transport.

In porous adsorbent particles with a bidisperse [1,2,4,5,12,13] porous adsorbent structure, the microporous region of the particles has a large surface area, and hence a large proportion of the adsorptive capacity of such particles is within their micropores. In Eqns. 6–8 in ref. 4, the intraparticle fluid velocity and the effective pore diffusion coefficients characterize the overall intraparticle convective and pore diffusion mass transfer mechanisms, respectively, for a perfusive particle; of course, the value of the intraparticle fluid velocity and the values of the effective pore diffusion coefficients in perfusive particles with a monodisperse porous structure could be different than those obtained in perfusive particles with a bidisperse porous structure. In perfusive particles with a bidisperse porous structure, one could expect that intraparticle fluid flow occurs mainly within the macroporous [14] region (the region of the through-pores [1]) of the particle. Hence the degree of utilization of the adsorptive capacity of a perfusive particle with a bidisperse porous structure could depend on the relative magnitude of the time constants for pore diffusion and adsorption (the interaction mechanism between the adsorbate molecules and the active sites) in the microporous region, and for intraparticle fluid flow (convection), pore diffusion and adsorption in the macroporous region.

In this work, a mathematical model that could

describe single- and multi-component adsorption in columns having perfusive particles with a bidisperse porous structure is presented. The model is then solved and used to study the dynamic behavior of a column system involving the adsorption of lysozyme onto monoclonal anti-lysozyme immobilized in perfusive particles having a bidisperse porous structure.

MATHEMATICAL MODEL

Adsorption is considered to take place from a flowing liquid stream in a fixed bed of perfusive adsorbent particles of bidisperse porous structure under isothermal conditions. The differential mass balance for each adsorbate i ($i = 1, 2, \dots, n$) in the flowing fluid stream is given by eqn. 1 in ref. [4], and eqns. 2–4 in ref. 4 are considered to provide the initial and boundary conditions for the differential mass balance equation of each adsorbate; if the contribution of axial dispersion in the column can be neglected then eqn. 3 in ref. 4 is replaced with eqn. 5 in ref. 4.

The perfusive particles with a bidisperse porous structure are considered to have a microporous region made by spherical microparticles (microspheres [1]) [1,4] that are taken to be purely diffusive, and a macroporous region made by the through-pores [1,4] in which intraparticle convection and pore diffusion occur. Most of the adsorptive capacity of the perfusive particles is in the microporous region. The transport of the species in the macroporous region is considered to involve the following mass transfer mechanisms: (a) intraparticle convection, (b) diffusion in the pore fluid and (c) the mass transfer step involving the interaction of the adsorbates with the active sites on the surface of the pores (this step represents the adsorption mechanism). The transport of the species in the purely diffusive spherical microparticles of which the microporous region is composed involves the following mass transfer mechanisms: (i) diffusion in the pore fluid of the spherical microparticle and (ii) the mass transfer step involving the interaction (adsorption) of the adsorbates with the active sites on the surface of the pores of the spherical microparticle. In Fig. 1a a diagram of a perfusive

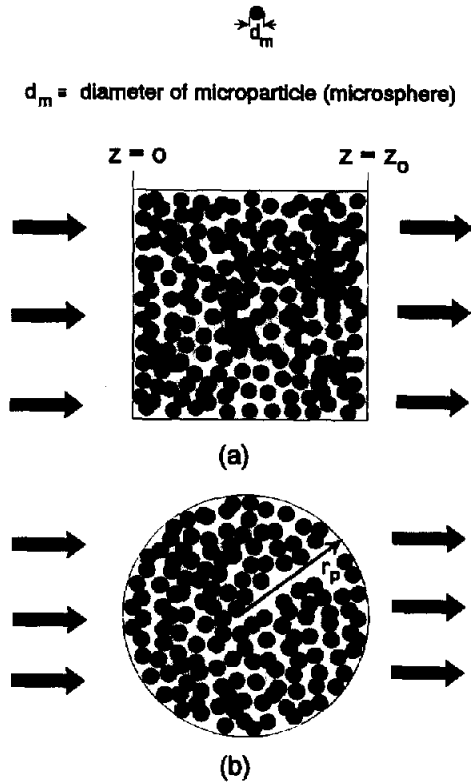


Fig. 1. Perfusive adsorbent particles with a bidisperse porous structure (the arrows indicate the direction of fluid flow): (a) perfusive particle of slab geometry; (b) perfusive particle of spherical geometry.

particle of slab geometry is shown and in Fig. 1b a diagram of a perfusive particle of spherical geometry is presented.

The differential mass balance for each adsorbate i in the macroporous region of a perfusive adsorbent particle of slab geometry is given by

$$\epsilon_p \left(\frac{\partial C_{pi}}{\partial t} \right) + \epsilon_p v_p \left(\frac{\partial C_{pi}}{\partial z} \right) + (1 - \epsilon_p) \frac{\partial \bar{C}_{si}}{\partial t} = \epsilon_p D_{pi} \left(\frac{\partial^2 C_{pi}}{\partial z^2} \right), \quad i = 1, 2, \dots, n \quad (1)$$

The mixtures of components to be separated by chromatographic systems are usually dilute and the form of eqn. 1 is appropriate for dilute mixtures [4]; for non-dilute mixtures, ref. 4 should be consulted. The value of the intraparticle velocity v_p in eqn. 1 could be estimated from

eqn. 20 in ref. 4. The initial and boundary conditions of eqn. 1 are as follows:

$$\text{at } t = 0 \quad C_{pi} = 0, \quad 0 \leq z \leq z_0, \quad i = 1, 2, \dots, n \quad (2)$$

$$\text{at } t = 0 \quad \bar{C}_{si} = 0, \quad 0 \leq z \leq z_0, \quad i = 1, 2, \dots, n \quad (3)$$

$$\text{at } z = 0 \quad C_{pi} = C_{di}, \quad t > 0, \quad i = 1, 2, \dots, n \quad (4)$$

$$\text{at } z = z_0 \quad C_{pi} = C_{di}, \quad t > 0, \quad i = 1, 2, \dots, n \quad (5)$$

The expressions in eqns. 4 and 5 were obtained by neglecting the external film mass transfer resistance. The external film mass transfer resistance is neglected because its contribution to the overall mass transfer resistance of porous particles has been found, for most systems of practical importance, to be negligible [4,6,11, 15,16].

The differential mass balance for each adsorbate i in a purely diffusive spherical microparticle is given by

$$\epsilon_{pm} \left(\frac{\partial C_{pmi}}{\partial t} \right) + \left(\frac{1}{1 - \epsilon_p} \right) \frac{\partial C_{smi}}{\partial t} = \epsilon_{pm} D_{pmi} \left(\frac{\partial^2 C_{pmi}}{\partial r^2} + \frac{2}{r} \cdot \frac{\partial C_{pmi}}{\partial r} \right), \quad i = 1, 2, \dots, n \quad (6)$$

Eqn. 6 is appropriate for dilute mixtures [4-11]; for non-dilute mixtures, ref. 11 should be consulted. The accumulation term, $\partial C_{smi} / \partial t$, of the adsorbed species i can be quantified if a thermodynamically consistent mathematical model could be constructed that could describe the mechanism of adsorption for component i . For isothermal adsorption systems, the term $\partial C_{smi} / \partial t$ could be of the form

$$\frac{\partial C_{smi}}{\partial t} = f_i(C_{pm}, C_{sm}, k), \quad i = 1, 2, \dots, n \quad (7)$$

where f_i represents the functional form of the dynamic adsorption mechanism for component i ; C_{pm} represents the concentration vector of the adsorbates in the pore fluid of the purely diffusive spherical microparticle, $C_{pm} = (C_{pm1}, C_{pm2}, \dots, C_{pmn})$; C_{sm} denotes the concentration

vector of the adsorbates in the adsorbed phase of the purely diffusive spherical microparticle, $C_{sm} = (C_{sm1}, C_{sm2}, \dots, C_{smn})$; and k represents the vector of the rate constants that characterize the interaction kinetics between the adsorbates and the active sites. For certain single- and multi-component adsorption systems, dynamic adsorption models of the form given in eqn. 7 have been constructed and presented in the literature. One well known form of eqn. 7 for single-component adsorption ($A + S \xrightleftharpoons[k_2]{k_1} AS$) is as follows (the subscript i is dropped as only one component is adsorbed) [4,7]:

$$\frac{\partial C_{sm}}{\partial t} = k_1 C_{pm} (C_T - C_{sm}) - k_2 C_{sm} \quad (8)$$

In some adsorption systems, the rates of interaction between the adsorbates and the active sites may be much higher than the intraparticle convection and diffusional rates, and in such systems it may be possible to assume that equilibrium exists between the adsorbates in the pore fluid and in the adsorbed phase at each point in the pores. The term $\partial C_{smi} / \partial t$ in eqn. 6 is then given by

$$\frac{\partial C_{smi}}{\partial t} = \sum_{j=1}^n \left(\frac{\partial g_i}{\partial C_{pmj}} \right) \left(\frac{\partial C_{pmj}}{\partial t} \right), i = 1, 2, \dots, n \quad (9)$$

where

$$C_{smi} = g_i(C_{pm}, K), i = 1, 2, \dots, n \quad (10)$$

The functions g_i represent the equilibrium adsorption isotherms for the adsorbates, and K represents the vector of the equilibrium constants that characterize the equilibrium interactions between the adsorbates and the active sites. One well-known form of eqn. 10 for single-component adsorption [4,7] is as follows (the subscript i is dropped as only one component is adsorbed):

$$C_{sm} = \frac{C_T K C_{pm}}{1 + K C_{pm}} \quad (11)$$

Eqn. 11 represents the equilibrium Langmuir adsorption isotherm and is obtained from eqn. 8 by setting $\partial C_{sm} / \partial t$ equal to zero; the parameter K in eqn. 11 is the equilibrium adsorption constant ($K = k_1 / k_2$). When eqn. 11 is employed

in the right-hand side of eqn. 9, the following expression is obtained for $\partial C_{sm} / \partial t$:

$$\begin{aligned} \frac{\partial C_{sm}}{\partial t} &= \left(\frac{\partial C_{sm}}{\partial C_{pm}} \right) \left(\frac{\partial C_{pm}}{\partial t} \right) \\ &= \left[\frac{C_T K}{(1 + K C_{pm})^2} \right] \left(\frac{\partial C_{pm}}{\partial t} \right) \end{aligned} \quad (12)$$

The initial and boundary conditions of eqns. 6 and 7 are considered to be as follows:

$$\begin{aligned} \text{at } t = 0 \quad C_{pmi} &= 0, \quad 0 \leq r \leq r_m, \\ i &= 1, 2, \dots, n \end{aligned} \quad (13)$$

$$\begin{aligned} \text{at } t = 0 \quad C_{smi} &= 0, \quad 0 \leq r \leq r_m, \\ i &= 1, 2, \dots, n \end{aligned} \quad (14)$$

$$\begin{aligned} \text{at } r = 0 \quad \frac{\partial C_{pmi}}{\partial r} &= 0, \quad t > 0, \\ i &= 1, 2, \dots, n \end{aligned} \quad (15)$$

$$\begin{aligned} \text{at } r = r_m \quad C_{pmi} &= C_{pi}(z, t), \quad t > 0, \\ i &= 1, 2, \dots, n \end{aligned} \quad (16)$$

The variable \bar{C}_{si} in eqn. 1 could be calculated from the following expression:

$$\begin{aligned} \bar{C}_{si} &= \frac{3}{r_m^3} \left[\int_0^{r_m} \left(\frac{1}{1 - \epsilon_p} \right) C_{smi} r^2 dr \right. \\ &\quad \left. + \int_0^{r_m} \epsilon_{pm} C_{pmi} r^2 dr \right], \quad i = 1, 2, \dots, n \end{aligned} \quad (17)$$

The accumulation term $\partial \bar{C}_{si} / \partial t$ in eqn. 1 is obtained by differentiating eqn. 17 with respect to time, and hence

$$\begin{aligned} \frac{\partial \bar{C}_{si}}{\partial t} &= \frac{3}{r_m^3} \left\{ \frac{\partial}{\partial t} \left[\int_0^{r_m} \left(\frac{1}{1 - \epsilon_p} \right) C_{smi} r^2 dr \right] \right. \\ &\quad \left. + \frac{\partial}{\partial t} \left(\int_0^{r_m} \epsilon_{pm} C_{pmi} r^2 dr \right) \right\}, \quad i = 1, 2, \dots, n \end{aligned} \quad (18)$$

Finally, the term $\partial \bar{C}_{psi} / \partial t$ in eqn. 1 in ref. 4 is given by

$$\frac{\partial \bar{C}_{psi}}{\partial t} = \frac{1}{z_0} \left\{ \frac{\partial}{\partial t} \left[\int_0^{z_0} (1 - \varepsilon_p) \bar{C}_{si} dz \right] + \frac{\partial}{\partial t} \left(\int_0^{z_0} \varepsilon_p C_{pi} dz \right) \right\},$$

$$i = 1, 2, \dots, n \quad (19)$$

since

$$\bar{C}_{psi} = \frac{1}{z_0} \left[\int_0^{z_0} (1 - \varepsilon_p) \bar{C}_{si} dz + \int_0^{z_0} \varepsilon_p C_{pi} dz \right] \quad (20)$$

If the geometry of the perfusive adsorbent particle is spherical, then eqn. 1 should be replaced by eqn. 21 in ref. 4; in this case, the variable r in eqn. 21 in ref. 4 represents the radial distance in the perfusive particle and its physical meaning is different than that of the variable r in eqns. 6 and 13-18 in this work. In eqns. 6 and 13-18 in this work, the variable r represents the radial distance in the purely diffusive spherical microparticle. The values of the intraparticle velocity components v_{pr} and $v_{p\theta}$ in eqn. 21 in ref. 4 could be estimated from the expressions presented in ref. 14. Further, for spherical perfusive particles the term $\partial \bar{C}_{psi} / \partial t$ in eqn. 1 in ref. 4 is given by

$$\frac{\partial \bar{C}_{psi}}{\partial t} = \frac{1}{V_{pv}} \left\{ \frac{\partial}{\partial t} \left[\int_0^{V_{pv}} (1 - \varepsilon_p) \bar{C}_{si} dV \right] + \frac{\partial}{\partial t} \left(\int_0^{V_{pv}} \varepsilon_p C_{pi} dV \right) \right\},$$

$$i = 1, 2, \dots, n \quad (21)$$

The dynamic behavior of a column adsorption system involving perfusive adsorbent particles with a bidisperse porous structure could be obtained by solving eqns. 1-4 in ref. 4 simultaneously with eqns. 1-7, 13-16, 18 and 19 in this work, when the perfusive adsorbent particles have slab geometry. If the geometry of the perfusive adsorbent particles with a bidisperse porous structure is spherical, then eqns. 1-4 and 21 in ref. 4 should be solved simultaneously with eqns. 6, 7, 13-16, 18 and 21 in this work. The solution of the equations of the mathematical model presented in this work was obtained by

employing the method of orthogonal collocation [6,17,18] on the space variables of the continuity equations of the adsorbates in the macroporous and microporous regions of the perfusive particle, and the method of orthogonal collocation on finite elements [6] on the space variable along the axis of the column. The resulting ordinary non-linear differential equations were integrated by using Gear's method [18], which is employed in the LSODES component of the ODEPACK [19] software package. It should be mentioned that if the intraparticle velocity, v_p , is set equal to zero in eqn. 1, then the solution of the above-mentioned equations would provide the dynamic behavior of an adsorption system in a column having purely diffusive adsorbent particles with a bidisperse porous structure in which there is no intraparticle fluid flow [13,20-24].

RESULTS AND DISCUSSION

Frontal analysis results are presented for the system involving the adsorption of lysozyme onto monoclonal anti-lysozyme immobilized on the surface of adsorbent particles with a bidisperse porous structure. Purely diffusive ($v_p = 0$) and also perfusive ($v_p > 0$) adsorbent particles with a bidisperse porous structure are considered. The dynamics of the adsorption step are described by eqn. 8, and two different values for the particle size, z_0 , were considered: (i) $z_0 = 10^{-5}$ m and (ii) $z_0 = 2 \cdot 10^{-5}$ m. The diameter of the microparticle (microsphere), d_m , was taken to be equal to 10^{-6} m [1,12]. In Table I, the values of the parameters used in the model for the simulation of the adsorption system studied in this work are presented. The values of other parameters of the model are reported in the captions of the figures. The values of the parameters in Table I are from adsorption systems reported in the literature [4-6,11] and, for the purposes of the simulations of this work, are considered to have appropriate magnitudes; it should be mentioned that the value of C_T in Table I represents the largest (maximum) amount of adsorbate that could be adsorbed per unit volume of the particle.

The effect of micropore diffusion on column

TABLE I

VALUES OF THE PARAMETERS OF THE MODEL (ADSORPTION OF LYSOZYME ONTO MONOCLONAL ANTI-LYSOZYME)

$C_{d,in} = 0.1 \text{ kg/m}^3$	$C_T = 2.2 \text{ kg/m}^3$	$D_L = 0$
$d_m = 2r_m = 10^{-6} \text{ m}$	$D_p = 17.885 \cdot 10^{-12} \text{ m}^2/\text{s}$	$k_1 = 4.108 \text{ m}^3/\text{kg} \cdot \text{s}$
$k_2 = 0.2222 \text{ s}^{-1}$	$K = k_1/k_2 = 18.488 \text{ m}^3/\text{kg}$	$L = 0.1 \text{ m}$
$r_m = d_m/2 = 0.5 \cdot 10^{-6} \text{ m}$	$V_f = 2.778 \cdot 10^{-3} \text{ m}^3/\text{s}$	$T = 282.5 \text{ K}$
$\varepsilon = 0.35$	$\varepsilon_p = 0.50$	$\varepsilon_{pm} = 0.50$

performance may be examined by varying the value of the ratio of the diffusional time constants for the microparticle and the adsorbent particle, Φ . The expression for Φ is as follows:

$$\Phi = \frac{D_{pm}/r_m^2}{D_p/(z_0/2)^2} \quad (22)$$

From eqn. 22 the following expression is obtained for the ratio D_{pm}/D_p :

$$\frac{D_{pm}}{D_p} = \Phi \left[\frac{r_m^2}{(z_0/2)^2} \right] \quad (23)$$

For given values of r_m and z_0 , eqn. (23) indicates that the ratio D_{pm}/D_p increases as Φ increases. In adsorbent particles with a bidisperse porous structure, one could practically consider that the value of D_{pm} would be less than or equal to the value of D_p ($D_{pm} \leq D_p$), and hence the ratio D_{pm}/D_p would be less or equal to unity ($D_{pm}/D_p \leq 1$); this condition could then imply that the value of Φ could be less than or equal to $(z_0/2)^2/r_m^2$ [$\Phi \leq (z_0/2)^2/r_m^2$]. Hence, for the system with $z_0 = 10^{-5} \text{ m}$ and $r_m = 0.5 \cdot 10^{-6} \text{ m}$, the parameter Φ could be ≤ 100 ; for the system with $z_0 = 2 \cdot 10^{-5} \text{ m}$ and $r_m = 0.5 \cdot 10^{-6} \text{ m}$, the parameter Φ could be ≤ 400 . In this work, the values of D_p and r_m are kept fixed (see Table I) while the values of z_0 and Φ are varied; therefore, for a given value of z_0 , an increase in Φ would imply an increase in the effective pore diffusion coefficient of the lysozyme, D_{pm} , in the micropores (microparticle).

In Figs. 2 and 3, the breakthrough curves of lysozyme are presented for different values of v_p , z_0 and Φ . The results clearly indicate that, for a given value of Φ , the performance of the systems

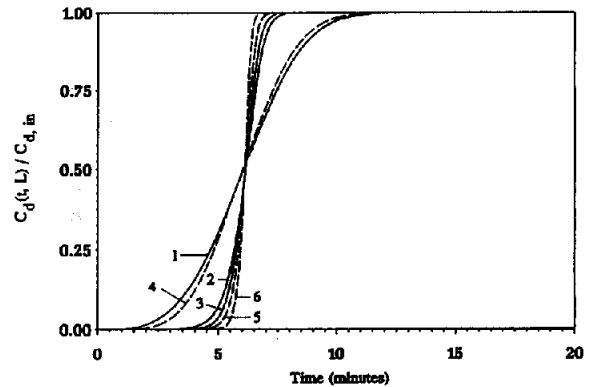


Fig. 2. Breakthrough curves of lysozyme for different values of v_p and Φ (the solid curves are for $v_p = 0.00$ and the broken curves are for $v_p = 0.01V_f$); the particle size is $z_0 = 10^{-5} \text{ m}$. (1) $v_p = 0.00$, $\Phi = 0.10$; (2) $v_p = 0.00$, $\Phi = 1.00$; (3) $v_p = 0.00$, $\Phi = 10.00$; (4) $v_p = 0.01V_f$, $\Phi = 0.10$; (5) $v_p = 0.01V_f$, $\Phi = 1.00$; (6) $v_p = 0.01V_f$, $\Phi = 10.00$.

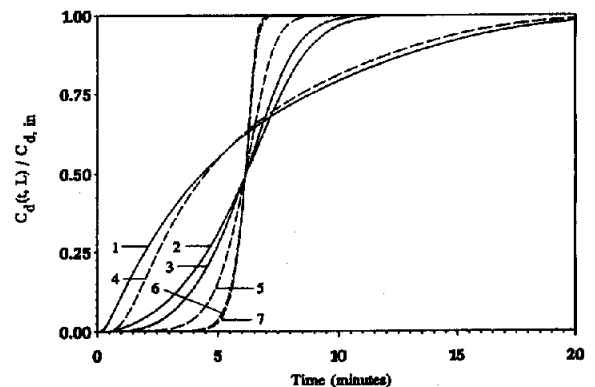


Fig. 3. Breakthrough curves of lysozyme for different values of v_p and Φ (the solid curves are for $v_p = 0.00$ and the broken curves are for $v_p = 0.01V_f$); the particle size is $z_0 = 2 \cdot 10^{-5} \text{ m}$. (1) $v_p = 0.00$, $\Phi = 0.10$; (2) $v_p = 0.00$, $\Phi = 1.00$; (3) $v_p = 0.00$, $\Phi = 10.00$; (4) $v_p = 0.01V_f$, $\Phi = 0.10$; (5) $v_p = 0.01V_f$, $\Phi = 1.00$; (6) $v_p = 0.01V_f$, $\Phi = 10.00$; (7) $v_p = 0.01V_f$, $\Phi = 50.00$.

employing perfusive particles is higher than the performance obtained from the systems having purely diffusive particles, and the difference in the performance increases as the particle size, z_0 , increases. In Figs. 2 and 3, the results also indicate that, for a given value of z_0 , the performance of the column improves as Φ increases. Further, for a given value of Φ , the performance of the column with smaller size, z_0 , adsorbent particles is higher than that obtained from the column having larger size, z_0 , adsorbent particles (compare the results in Figs. 2 and 3); this behavior is clearly shown, for the column systems with perfusive ($v_p = 0.01V_f$) adsorbent particles, by the results presented in Fig. 4.

In Fig. 2, results are presented for $\Phi = 0.10$, 1.00 and 10.00. For $\Phi > 10.00$ and $\Phi \leq 100.00$, the breakthrough curves obtained from the columns with purely diffusive ($v_p = 0$) or perfusive ($v_p = 0.01V_f$) adsorbent particles almost coincide [for the scales selected for the variables $C_d(t, L)/C_{d,in}$ and t in Fig. 2] with their corresponding breakthrough curves obtained when $\Phi = 10.00$; this result suggests that for the systems examined and presented in Fig. 2, an increase in the value of D_{pm} above $0.1D_p$ ($D_{pm} > 0.1D_p$) might not provide a significant improvement in the breakthrough behavior of the column.

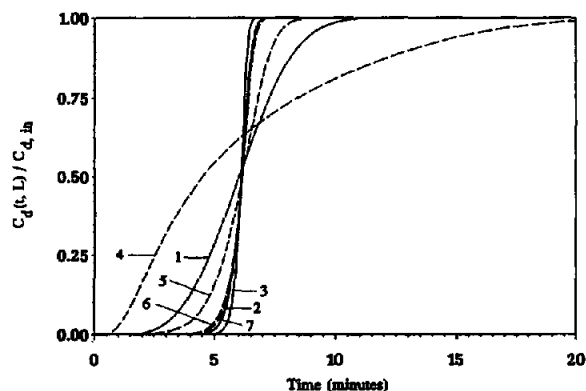


Fig. 4. Breakthrough curves of lysozyme for different values of z_0 and Φ (the solid curves are for $z_0 = 10^{-5}$ m and the broken curves are for $z_0 = 2 \cdot 10^{-5}$ m); the intraparticle convective velocity is $v_p = 0.01V_f$. (1) $z_0 = 10^{-5}$ m, $\Phi = 0.10$; (2) $z_0 = 10^{-5}$ m, $\Phi = 1.00$; (3) $z_0 = 10^{-5}$ m, $\Phi = 10.00$; (4) $z_0 = 2 \cdot 10^{-5}$ m, $\Phi = 0.10$; (5) $z_0 = 2 \cdot 10^{-5}$ m, $\Phi = 1.00$; (6) $z_0 = 2 \cdot 10^{-5}$ m, $\Phi = 10.00$; (7) $z_0 = 2 \cdot 10^{-5}$ m, $\Phi = 50.00$.

For the systems presented in Fig. 3, the breakthrough curves obtained from the columns with purely diffusive or perfusive adsorbent particles for $\Phi > 50.00$ and $\Phi \leq 400.00$ almost coincide [for the scales selected for the variables $C_d(t, L)/C_{d,in}$ and t in Fig. 3] with their corresponding breakthrough curves obtained when $\Phi = 50.00$; this result suggests that for the systems examined and presented in Fig. 3, an increase in D_{pm} above $0.125D_p$ ($D_{pm} > 0.125D_p$) might not provide a significant improvement in the breakthrough behavior of the column.

In Tables II and III, the percentage utilization of the adsorptive capacity of the column at 1% and 10% breakthrough, respectively, are presented. The total adsorptive capacity of the column is defined as the total amount of adsorbate in the adsorbed phase (in the column) at equilibrium (evaluated with respect to the value of $C_{d,in}$). The dynamic utilization of the adsorptive capacity of the column is defined as the ratio of the total amount of the adsorbate in the adsorbed phase of the column when the desired breakthrough occurs to the total adsorptive capacity of the column. The percentage utilization of the adsorptive capacity of the column is obtained by multiplying the dynamic utilization of the adsorptive capacity of the column (defined above) by 100. The results in Tables II and III clearly show that the dynamic adsorptive capacity of the systems with perfusive particles is higher than that of the systems with purely diffusive particles, and the difference becomes significantly larger as the particle size, z_0 , increases; also, the difference is larger, for given values of z_0 and Φ , at 1% breakthrough when compared with the difference obtained at 10% breakthrough. Further, it can be observed that the increase in the percentage utilization of the adsorptive capacity at 10% breakthrough compared with that obtained at 1% breakthrough is larger for the column systems with purely diffusive particles; this result also indicates that the columns with perfusive particles are more effective than the columns with purely diffusive particles in the dynamic utilization of the adsorptive capacity of the column. Hence the use of perfusive particles could allow one to make a column switch at a percentage breakthrough

TABLE II

PERCENTAGE UTILIZATION OF THE ADSORPTIVE CAPACITY OF THE COLUMN AT 1% BREAKTHROUGH $\{[C_d(t, L)/C_{d,m}] \cdot 100 = 1\%$

z_0 (m)	Φ	$\frac{D_{pm}}{D_p}$	Utilization of the adsorptive capacity of the column (%)		
			$v_p = 0.00$	$v_p = 0.01V_f$	$v_p = 0.02V_f$
10^{-5}	0.10	10^{-3}	29.1	38.3	41.0
10^{-5}	1.00	10^{-2}	66.9	80.5	84.5
10^{-5}	10.00	10^{-1}	75.0	87.3	91.3
10^{-5}	50.00	0.50	75.8	88.0	92.0
10^{-5}	100.00	1.00	75.9	88.1	92.0
$2 \cdot 10^{-5}$	0.10	$0.25 \cdot 10^{-3}$	3.7	11.3	13.3
$2 \cdot 10^{-5}$	1.00	$0.25 \cdot 10^{-2}$	15.7	51.8	60.2
$2 \cdot 10^{-5}$	10.00	$0.25 \cdot 10^{-1}$	30.6	73.9	83.4
$2 \cdot 10^{-5}$	50.00	0.125	33.0	76.2	85.8
$2 \cdot 10^{-5}$	100.00	0.25	33.3	76.5	86.2
$2 \cdot 10^{-5}$	200.00	0.50	33.5	76.7	86.3
$2 \cdot 10^{-5}$	400.00	1.00	33.5	76.8	86.4

lower than that which would be desirable if the column were using purely diffusive particles, as the system with the perfusive particles has a higher dynamic utilization of the adsorptive capacity of the column for a given percentage breakthrough; this result suggests that for a given overall time of operation more adsorption cycles could be obtained when columns with perfusive adsorbent particles are used, and less

amount of adsorbate could have left the column by the time that column switching occurs.

The results in Tables II and III also show that, for given values of z_0 and Φ , the highest percentage utilization of the adsorptive capacity of the column is obtained from the systems having perfusive particles with intraparticle velocity $v_p = 0.02V_f$, which corresponds to the largest intraparticle velocity studied in this work. Fur-

TABLE III

PERCENTAGE UTILIZATION OF THE ADSORPTIVE CAPACITY OF THE COLUMN AT 10% BREAKTHROUGH $\{[C_d(t, L)/C_{d,m}] \cdot 100 = 10\%$

z_0 (m)	Φ	$\frac{D_{pm}}{D_p}$	Utilization of the adsorptive capacity of the column (%)		
			$v_p = 0.00$	$v_p = 0.01V_f$	$v_p = 0.02V_f$
10^{-5}	0.10	10^{-3}	55.9	61.7	63.2
10^{-5}	1.00	10^{-2}	84.5	91.0	92.8
10^{-5}	10.00	10^{-1}	88.0	94.3	96.1
10^{-5}	50.00	0.50	88.3	94.6	96.4
10^{-5}	100.00	1.00	88.4	94.7	96.4
$2 \cdot 10^{-5}$	0.10	$0.25 \cdot 10^{-3}$	13.5	24.4	26.0
$2 \cdot 10^{-5}$	1.00	$0.25 \cdot 10^{-2}$	48.3	76.1	79.9
$2 \cdot 10^{-5}$	10.00	$0.25 \cdot 10^{-1}$	59.5	88.7	92.7
$2 \cdot 10^{-5}$	50.00	0.125	60.4	89.8	93.9
$2 \cdot 10^{-5}$	100.00	0.25	60.6	89.9	94.0
$2 \cdot 10^{-5}$	200.00	0.50	60.6	90.0	94.1
$2 \cdot 10^{-5}$	400.00	1.00	60.7	90.0	94.1

ther, the results indicate that, for given values of z_0 and Φ , the largest increase in the percentage utilization of the adsorptive capacity of the column is obtained when the value of the intraparticle velocity, v_p , is changed from 0.00 to $0.01V_f$ (this increase is significantly larger than that obtained when v_p is changed from $0.01V_f$ to $0.02V_f$). These results suggest that a high dynamic utilization of the adsorptive capacity of a column with perfusive particles could be obtained by employing intraparticle fluid velocities of moderate magnitude. Perfusive particles with high permeabilities (see eqn. 20 in ref. 4) could permit high intraparticle fluid velocities that could lead to a high dynamic utilization of the adsorptive capacity of the column having these perfusive particles; however, perfusive particles with high permeabilities might not have the appropriate structural strength for a particular use of practical interest. Again, the results in Tables II and III suggest that a high dynamic utilization of the adsorptive capacity may be obtained by employing perfusive particles with permeabilities that could provide appropriate structural strength and permit intraparticle fluid velocities of moderate magnitude.

For the results presented in Tables II and III, it can be observed that as the value of D_{pm} increases from $10^{-3}D_p$ (highly restricted pore diffusion in the microparticle) to $10^{-1}D_p$ for the particles with $z_0 = 10^{-5}$ m, or as the value of D_{pm} increases from $0.25 \cdot 10^{-3}D_p$ (highly restricted pore diffusion in the microparticle) to $0.125D_p$ for the particles with $z_0 = 2 \cdot 10^{-5}$ m, the dynamic utilization of the adsorptive capacity of the column increases; further, as the value of D_{pm} increases, the relative increases in the dynamic utilization of the adsorptive capacity of the column become smaller as the value of v_p increases from 0.00 to $0.02V_f$. Also, a careful examination of the data presented in Tables II and III indicates that for values of D_{pm} between $10^{-2}D_p$ and $1.0D_p$ for the particles with $z_0 = 10^{-5}$ m, or for values of D_{pm} between $0.25 \cdot 10^{-2}D_p$ and $1.0D_p$ for the particles with $z_0 = 2 \cdot 10^{-5}$ m, the dynamic utilization of the adsorptive capacity of the column obtained from the systems with perfusive particles is higher than that obtained from the systems with purely diffusive

particles, even when the value of D_{pm} in the microparticles of the perfusive particles is lower than the value of D_{pm} in the microparticles of the purely diffusive particles. The results in Tables II and III suggest that while the value of D_{pm} plays an important role in determining the dynamic performance of the systems with perfusive particles, the effect of the value of D_{pm} on the dynamic performance of systems using purely diffusive particles is higher than the effect of the value of D_{pm} on the dynamic performance of systems using perfusive particles. Also, the results in Tables II and III indicate that for values of D_{pm} greater than $0.1D_p$ for particles with $z_0 = 10^{-5}$ m, or for values of D_{pm} greater than $0.125D_p$ for the particles with $z_0 = 2 \cdot 10^{-5}$ m, the effect of the value of D_{pm} on the dynamic performance of the columns with perfusive or purely diffusive adsorbent particles, is rather small.

CONCLUSIONS AND REMARKS

A mathematical model that could be used to describe single- and multi-component adsorption in columns with bidisperse perfusive or bidisperse purely diffusive adsorbent particles was constructed and presented.

The model was used to study the adsorption of lysozyme on to monoclonal anti-lysozyme in columns with bidisperse perfusive or bidisperse purely diffusive adsorbent particles, for (i) different values of the effective pore diffusion coefficient of the adsorbate in the micropores (microparticles), D_{pm} , (ii) different values of the intraparticle convective velocity, v_p , in the macroporous region of the perfusive particles, and (iii) different values of the adsorbent particle size, z_0 . The results indicate that the systems with bidisperse perfusive particles provide a higher dynamic utilization of the adsorptive capacity of the column than that obtained from the systems with bidisperse purely diffusive particles. The dynamic utilization of the adsorptive capacity of the column was found to increase when the particle size, z_0 , decreases, or when the intraparticle convective velocity, v_p , increases. The results also indicate that a high dynamic utilization of the adsorptive capacity of a column with perfusive particles could be ob-

tained by employing intraparticle fluid velocities of moderate magnitude. Further, the results show that the dynamic utilization of the adsorptive capacity of the column increases as the effective pore diffusion coefficient of the adsorbate in the microparticles, D_{pm} , increases. However, while the value of D_{pm} is important in determining the dynamic performance of the systems with perfusive particles, the results for the systems studied in this work suggest that the effect of the value of D_{pm} on the dynamic performance of systems using purely diffusive particles is greater than that of the value of D_{pm} on the dynamic performance of systems using perfusive particles.

Further studies could be directed at determining the bounds of perfusive behavior. This includes, but is not limited to, studying the bounds of the effects of model parameters on the dynamic performance of columns with bidisperse perfusive adsorbent particles.

SYMBOLS

A	molecule of adsorbate		
A_0	external surface area of adsorbent particle, m^2		
AS	adsorbate-active site complex		
C_d	concentration of adsorbate (single-component system) in the flowing fluid stream of the column, kg/m^3 of bulk fluid		
C_{di}	concentration of component i (multi-component system; see eqn. 1 in ref. 4) in the flowing fluid stream of the column, kg/m^3 of bulk fluid		
$C_{d,in}$	concentration of adsorbate (single-component system) at $x < 0$ when $D_L \neq 0$, or at $x = 0$ when $D_L = 0$, kg/m^3 of bulk fluid		
$C_{di,in}$	concentration of component i (multi-component system; see eqn. 3 in ref. 4) at $x < 0$ when $D_{Li} \neq 0$, or at $x = 0$ when $D_{Li} = 0$, kg/m^3 of bulk fluid		
C_p	concentration of adsorbate (single-component system) in the fluid of the macropores (through-		pores), kg/m^3 of macropore volume
		C_{pi}	concentration of component i (multi-component system) in the fluid of the macropores (through-pores), kg/m^3 of macropore volume
		C_{pm}	concentration of adsorbate (single-component system) in the fluid of the micropores, kg/m^3 of micropore volume
		C_{pm}	vector of concentration variables defined after eqn. 7
		C_{pmi}	concentration of component i (multi-component system) in the fluid of the micropores, kg/m^3 of micropore volume
		\bar{C}_{psi}	average concentration of component i defined in eqn. 20, kg/m^3 of perfusive particle
		\bar{C}_s	average concentration of adsorbate (single-component system) defined in eqn. 17 (the subscript i is dropped for a single-component system), kg/m^3 of microparticle
		\bar{C}_{si}	average concentration of component i (multi-component system) defined in eqn. 17, kg/m^3 of microparticle
		C_{sm}	concentration of adsorbate (single-component system) in the adsorbed phase of the microparticle, kg/m^3 of perfusive particle
		C_{sm}	vector of concentration variables defined after eqn. 7
		C_{smi}	concentration of component i (multi-component system) in the adsorbed phase of the microparticle, kg/m^3 of perfusive particle
		C_T	maximum equilibrium concentration of adsorbate (single-component system) in the adsorbed phase of the microparticle, kg/m^3 of perfusive particle
		D_L	axial dispersion coefficient of adsorbate (single-component system), m^2/s

D_{L_i}	axial dispersion coefficient of component i (multi-component system), m^2/s	r	radial distance in microparticle, m
d_m	diameter of microparticle (microsphere), m	r_m	radius of microparticle (microsphere), m
D_p	effective pore diffusion coefficient of adsorbate (single-component system) in the macropores (through-pores), m^2/s	r_p	radius of spherical perfusive particle, m
D_{p_i}	effective pore diffusion coefficient of component i (multi-component system) in the macropores (through-pores), m^2/s	S	active site
D_{p_m}	effective pore diffusion coefficient of adsorbate (single-component system) in the micropores, m^2/s	T	temperature, K
$D_{p_{mi}}$	effective pore diffusion coefficient of component i (multi-component system) in the micropores, m^2/s	t	time, s
dV	volume differential in eqn. 21	V_f	column fluid superficial velocity, m/s
$f_i(C_{pm}, C_{sm}, k)$	functional form defined after eqn. 7	v_p	intraparticle (interstitial) fluid velocity (intraparticle convective velocity), m/s
$g_i(C_{pm}, K)$	functional form defined after eqn. 10	V_{pv}	volume of perfusive particle, m^3
K	equilibrium adsorption constant of adsorbate (single-component system), $K = k_1/k_2$, m^3/kg	x	axial distance in column, m
\mathbf{K}	vector of equilibrium adsorption constants defined after eqn. 10	z	space coordinate of perfusive particle of slab geometry, m
\mathbf{k}	vector of adsorption rate constants defined after eqn. 7	z_0	length (size) of perfusive particle of slab geometry, m
k_1	adsorption rate constant in $A + S \xrightleftharpoons[k_2]{k_1} AS$, m^3 of micropore volume/kg \cdot s	<i>Greek letters</i>	
k_2	adsorption rate constant in $A + S \xrightleftharpoons[k_2]{k_1} AS$, s^{-1}	ϵ	void fraction in column
L	column length, m	ϵ_p	macropore (throughpore) void fraction
n	total number of components	ϵ_{pm}	micropore void fraction
Pe_{in}	intraparticle Peclet number [$Pe_{in} = (v_p z_0)/D_p$], dimensionless	Φ	ratio of diffusional time constants for the microparticle and the adsorbent particle $\{\Phi = (D_{pm}/r_m^2)/[D_p/(z_0/2)^2]\}$, dimensionless
Po	Porath parameter in macropores [$Po = (k_1 A_0)/(\epsilon_p D_p)$], m^3/kg	ACKNOWLEDGEMENTS	
Po_m	Porath parameter in micropores [$Po_m = (k_1 A_0)/(\epsilon_{pm} D_{pm})$], m^3/kg	The authors gratefully acknowledge support of this work by Monsanto and the NATO Scientific Affairs Division under Grant No. 880770.	

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