

Some Considerations for Optimization of Desorption Chromatography



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The effect of isotherm parameters of a displacer on the efficiency of desorption chromatography has been investigated numerically. A general nonlinear multicomponent rate equation model with Langmuir isotherm was used in this study. It was found that the best displacer in this kind of operation is usually not the one that is more strongly adsorbed than the adsorbates when the operation is to displace and concentrate the adsorbates from a saturated or partially saturated column and to minimize the amount of displacer used. The desorption chromatography is different from the classical displacement development in both operational purpose and the requirement for the displacer. The desorption chromatography in industrial practice was also analyzed and discussed for the case in which the displacer is introduced in either the same or the reverse flow direction after an incomplete frontal adsorption operation.

INTRODUCTION

Desorption chromatography has received considerable attention recently in microbiological processes for in situ removal of toxic fermentation product(s).¹⁻⁵ This kind of in situ separation reduces product inhibition and thus enhances productivity. In such adsorption-combined fermentation processes, chromatographic columns are coupled with the fermentor to remove the product(s) simultaneously via preferential adsorption and the adsorbate(s) is (are) then recovered through a desorption column operation. Desorption chromatography is also widely used to recover biomolecules from a dilute solution after they are adsorbed onto a column. In both cases, frontal adsorption precedes the displacement process which often concentrates the adsorbate(s) using a suitable displacer. This kind of displacement operation is somewhat different from the classical displacement chromatography or displacement development first classified by Tiselius⁶ and extensively reviewed by Horvath and his co-workers.⁷⁻¹⁰

The classical displacement chromatography was described by many researchers as a process in which a

column packed with solid adsorbent is equilibrated with a mobile phase that has no or weak affinity to the adsorbent. A sample of mixtures is then introduced to the column. The sample usually takes up a fraction of the column volume in the inlet section. Subsequently, a development agent (called displacer) is pumped into the column. The displacer *must* have a higher affinity to the stationary phase than any of the components in the sample; i.e., its adsorption isotherm overlies those of the feed components.⁸⁻¹¹ Provided that the column is sufficiently long and isotherm curves are all favorably shaped (i.e., concave downward), sample components will eventually migrate inside the column with the same speeds to form individual product zones. The series of such zones is usually called displacement train.^{7-10,12-14} Figure 1 shows a displacement system with two sample solutes and one displacer. Compared with the elution chromatography, the displacement development has two distinct advantages: (1) the displacement

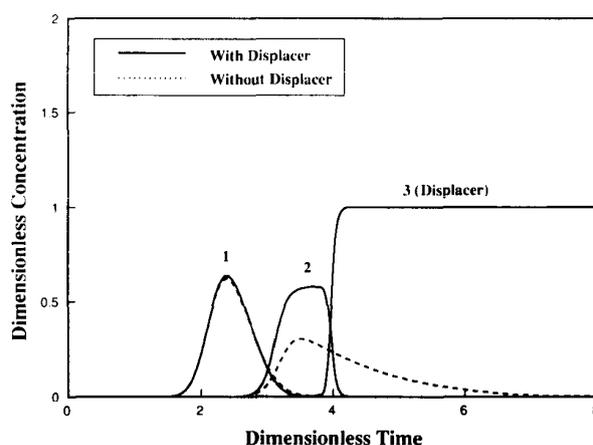


Figure 1. Displacement system with $Pe_{L1} = 100$, $Pe_{L2} = Pe_{L3} = 200$, $\eta_1 = 20$, $\eta_2 = 20$, $\eta_3 = 10$, $Bi_1 = 4$, $Bi_2 = 3$, $Bi_3 = 4$, $C_{f1} = C_{f2} = C_{f3} = 0.1$, $C_1^\infty = C_2^\infty = C_3^\infty = 0.25$, $b_1 = 4$, $b_2 = 20$, and $b_3 = 120$. Displacer is introduced after sample input time $\tau = 0.5$.

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effect reduces tailing (Fig. 1) and (2) sample loading can be higher.⁹ These features make the displacement development operation a very attractive alternative to elution in preparative scale column operation.⁸

The main difference between the displacement development and the desorption chromatography studied in this work is often the operation purpose itself. The former desires the products to be separated into a displacement train containing individual product zones in the effluent stream, while the latter requires the efficient displacement of the adsorbates. In other words, the desorption chromatography does not require a well-defined displacement train in the effluent; rather it requires the displacement of adsorbed component(s) with a minimum amount of displacer in a minimum length of time in order to obtain concentrated product(s). The product(s) in the effluent after displacement may be further purified if necessary after the desorption chromatography. A typical use of the desorption chromatography, as we have already mentioned, is the in situ separation during fermentation.¹⁻⁵ Another important difference is that the displacement development takes a sample which usually occupies only a fraction of the column inlet section while the desorption chromatography has no such limitation. The strong affinity of the displacer, which is required in the displacement development, should not be mistaken as a requirement for the desorption chromatography.

In this article, we will discuss the effects of adsorption characteristics of a displacer on the displacement efficiency of desorption chromatography. It will be shown that the selection of displacer in desorption chromatography will be somewhat different from that of the displacement development. As a matter of fact, a displacer with a stronger affinity is often not an ideal choice for the desorption chromatography. The analysis is based on computer simulation using a general nonlinear multicomponent rate equation model¹⁵ instead of the interference theory which has been widely used in the theoretical studies of the displacement development.^{9-11, 16-19} The use of the general model gives a more realistic picture of the displacement process since it accounts for diffusional and mass transfer effects which are often quite important in preparative and large scale chromatography. The displacer was treated as one of the components in the model equations and was included in the multicomponent isotherms.

MODEL

Consider a chromatographic column which is filled with spherical and uniform-sized porous solid adsorbents. Suppose that the process is isothermal, there is no concentration gradient in the radial direction of the column, and all the diffusional and mass transfer parameters are constants. Assuming that there exists a local equilibrium for each component between the pore surface and the stagnant liquid phase in the macropores

in the particle phase, the following governing equations for component i in the bulk fluid and particle phases can be obtained via differential mass balances:

$$-D_{bi} \frac{\partial^2 C_{bi}}{\partial Z^2} + v \frac{\partial C_{bi}}{\partial Z} + \frac{\partial C_{bi}}{\partial t} + \frac{3k_i(1 - \epsilon_b)}{\epsilon_b R_p} \times (C_{bi} - C_{pi, R=R_p}) = 0 \quad (1)$$

$$\frac{\partial}{\partial t} [(1 - \epsilon_p) C_{pi}^s + \epsilon_p C_{pi}] - \epsilon_p D_{pi} \left[\frac{1}{R^2} \frac{\partial}{\partial R} \left(R^2 \frac{\partial C_{pi}}{\partial R} \right) \right] = 0 \quad (2)$$

with the initial and boundary conditions:

$$t = 0$$

$$C_{bi} = C_{bi}(0, Z) \quad (3)$$

$$C_{pi} = C_{pi}(0, R, Z) \quad (4)$$

$$Z = 0: \quad \frac{\partial C_{bi}}{\partial Z} = \frac{v}{D_{bi}} (C_{bi} - C_{fi}(t)) \quad (5)$$

$$Z = L: \quad \frac{\partial C_{bi}}{\partial Z} = 0 \quad (6)$$

$$R = 0: \quad \frac{\partial C_{pi}}{\partial R} = 0 \quad (7)$$

$$R = R_p: \quad \frac{\partial C_{pi}}{\partial R} = \frac{k_i}{\epsilon_p D_{pi}} (C_{bi} - C_{pi, R=R_p}) \quad (8)$$

Equations for different components are coupled via C_{pi}^s , which is directly linked to the nonlinear multicomponent isotherms of the system. This partial differential equation (PDE) system can be transformed into the following dimensionless form:

$$-\frac{1}{Pe_{Li}} \frac{\partial^2 c_{bi}}{\partial z^2} + \frac{\partial c_{bi}}{\partial z} + \frac{\partial c_{bi}}{\partial \tau} + \xi_i (c_{bi} - c_{pi, r=1}) = 0 \quad (9)$$

$$\frac{\partial}{\partial \tau} [(1 - \epsilon_p) c_{pi}^s + \epsilon_p c_{pi}] - \eta_i \left[\frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial c_{pi}}{\partial r} \right) \right] = 0 \quad (10)$$

with the initial condition $\tau = 0$,

$$c_{bi} = c_{bi}(0, z) \quad (11)$$

$$c_{pi} = c_{pi}(0, r, z) \quad (12)$$

and with the boundary condition $z = 0$,

$$\partial c_{bi} / \partial z = Pe_{Li} (c_{bi} - C_{fi}(\tau) / C_{0i}) \quad (13)$$

For frontal adsorption,

$$C_{fi}(\tau) / C_{0i} = 1$$

For elution,

$$C_{fi}(\tau) / C_{0i} = \begin{cases} 1 & 0 \leq \tau \leq \tau_{imp} \\ 0 & \text{else} \end{cases}$$

After the sample has been introduced (in the form of frontal adsorption), if component i is displaced,

$$C_{fi}(\tau) / C_{0i} = 0$$

and if component i is a displacer,

$$C_{fi}(\tau)/C_{0i} = 1$$

At $z = 1$,

$$\frac{\partial c_{bi}}{\partial z} = 0 \quad (14)$$

and

$$r = 0: \quad \frac{\partial c_{pi}}{\partial r} = 0 \quad (15)$$

$$r = 1: \quad \frac{\partial c_{pi}}{\partial r} = Bi_i(c_{bi} - c_{pi,r=1}) \quad (16)$$

NUMERICAL SOLUTION

This general nonlinear multicomponent rate equation model was solved using an efficient and robust numerical procedure.¹⁵ Finite element- and orthogonal collocation methods were used to discretize the bulk fluid- and particle phase PDE's, respectively. The resulting ordinary differential equation (ODE) system was solved by using Gear's stiff method.

In this work, a SUN 4/280 minicomputer was used for computation. The central processing unit (CPU) time for each simulated case was within 5 min except for the case shown in Figure 1 and the case of $b_2 = 60$ shown in Figure 7.

RESULTS AND DISCUSSION

To simplify the discussion, only the Langmuir type of isotherms will be used in this work. However, the results may be readily extended to systems with other types of competitive isotherms:

$$C_{pi}^s = \frac{a_i C_{pi}}{N_b + \sum_{j=1}^n b_j C_{pj}} \quad \text{i.e.}$$

$$c_{pi}^s = \frac{a_i c_{pi}}{N_b + \sum_{j=1}^n (b_j C_{oj}) c_{pj}} \quad (\text{dimensionless}) \quad (17)$$

in which a_i can also be expressed as $b_i C_i^\infty$. Although thermodynamic consistency requires that C_i^∞ for all components be the same, such an assumption is not realistic for physical adsorption of molecules of widely different sizes. If we consider Langmuir isotherms merely as analytical expressions, there is no reason to maintain the assumption that C_i^∞ for each component should be equal.¹¹ Figure 2 shows the Langmuir isotherm curves for single-component cases. Such isotherm curves can be used to obtain the isotachic conditions in the study of ideal displacement development.⁶⁻¹⁰ Figure 2 helps to illustrate the meaning for each physical parameter in the Langmuir isotherm. For simplicity, we only discuss the two-component displacement chromatographic processes in which component 1 is the component to be

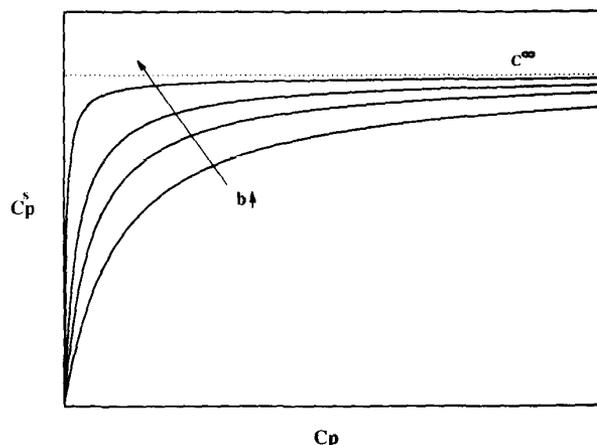


Figure 2. Single-component Langmuir isotherms.

displaced and component 2 is the displacer. Parameter values $\epsilon_p = 0.5$ and $\epsilon_b = 0.4$ were used in all cases. The error tolerance of the ODE solver used in the FORTRAN code was 10^{-5} . Other parameter values are listed in the figure legends.

Effect of Maximum Adsorption Capacity of the Displacer (C_2^∞)

Figure 3 shows the effect of maximum adsorption capacity of the displacer on the displacement efficiency. In these simulations, the column is assumed to be pre-saturated with component 1 before the displacer (component 2) was introduced at time 0. In cases of $C_2^\infty = 0.1, 0.35$, the concentration profiles of component 1 show the phenomenon of "roll-up," indicating the good displacement operation performed by the displacer when the purpose of the operation is to concentrate component 1 and/or to minimize the amount of displacer used. In the case of $C_2^\infty = 0.5$, the concentration profile of component 1 does not roll up, indicating that the displacement operation is not favored due to the lack of

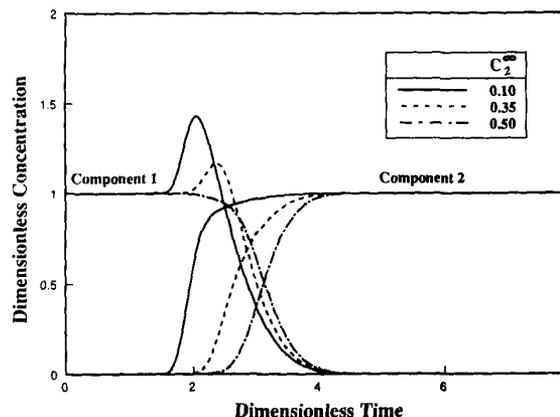


Figure 3. Effect of C_2^∞ on displacement performance with $Pe_{L1} = Pe_{L2} = 300$, $\eta_1 = 10$, $\eta_2 = 15$, $Bi_1 = 3$, $Bi_2 = 4$, $C_{f1} = C_{f2} = 0.1$, $b_1 = b_2 = 6$, and $C_1^\infty = 0.5$.

concentrating effect. Note that the area under the concentration profile of component 1 represents the amount of component 1 inside the column before displacement, and it should be the same in each case. Since the displacement process is often terminated when a major portion, e.g., 90%, of component 1 has been recovered, it can be easily seen from Figure 3 that the higher the roll-up peak, the higher the displacement efficiency.

Figure 3 shows that a smaller C_2^∞ gives a higher displacement efficiency. This is because one molecule of the displacer, which has a C_2^∞ smaller than C_1^∞ , may displace more adsorbate molecules. Also, the displacer with a smaller C_2^∞ retains less on the way of migration and allows the displacer concentration front to move faster in pushing out component 1. This argument can be explained by the following equations:

Dimensionless column hold-up capacity area of component 2 = $\{(1 - \epsilon_b)(1 - \epsilon_p)[b_2 C_2^\infty / (1 + b_2 C_{f2})]$

$$+ (1 - \epsilon_b)\epsilon_p + \epsilon_b\}/\epsilon_b \quad (18)$$

$$C_{p1}^s = \frac{b_1 C_1^\infty C_{p1}}{1 + b_1 C_{p1} + b_2 C_{p2}} \quad (19)$$

The column hold-up capacity area for a component in Eq. (18) refers to the area in the simulated chromatogram which corresponds to the amount of the component adsorbed in the equilibrium state. For example, in Figure 1, the area under concentration profile of component 1 is the column hold-up capacity area for component 1, and the area above the concentration profile of component 2 and below the feed concentration line is the hold-up capacity area for component 2. In both cases the hold-up capacity area is for the case in which the column is saturated with only one component due to the nature of the step-change operation. Equation (18) indicates that the position of the displacer concentration front is partially determined by the value of C_2^∞ and a smaller C_2^∞ gives a faster migration of displacer inside the column. Equation (19) shows that a large value of $b_2 C_{p2}$ decreases the concentration of adsorbed species (C_{p1}^s) and thus increases the displacement efficiency. Hence, a displacer with a smaller maximum adsorption capacity gives a faster movement of displacer inside the column so that the adsorbent inside the column can sense a high concentration of displacer earlier. This gives a larger $b_2 C_{p2}$ and so a smaller C_{p1}^s and a better displacement efficiency.

Effect of Feed Concentration of Displacer (C_{f2})

Figure 4 shows that the higher the displacer concentration in the mobile phase, the higher the roll-up peak on the concentration profile of component 1. This is due to the fact that a higher displacer concentration in the feed gives a faster migration rate for the concentration front of the displacer inside the column [Eq. (18)], a larger $b_2 C_{p2}$ value [Eq. (19)], and hence a better displacement efficiency. Figure 5 shows a case in which the

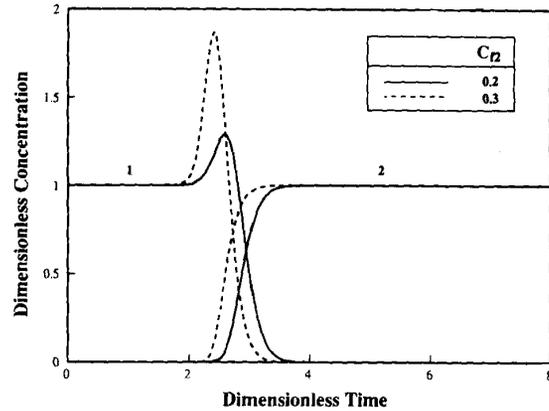


Figure 4. Effect of displacer concentration on displacement with $Pe_{L1} = Pe_{L2} = 300$, $\eta_1 = 10$, $\eta_2 = 15$, $Bi_1 = 3$, $Bi_2 = 4$, $C_{f1} = 0.1$, $C_1^\infty = C_2^\infty = 0.5$, $b_1 = 6$, and $b_2 = 8$.

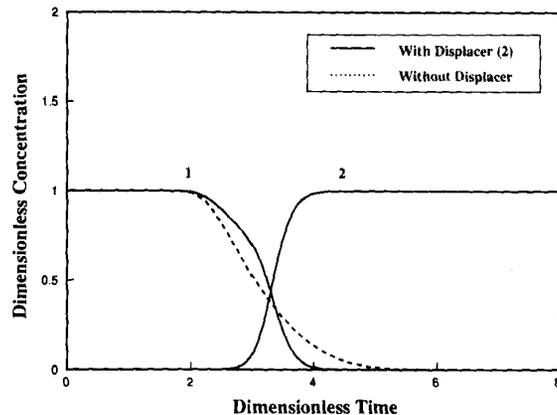


Figure 5. Same conditions as Figure 4 except that the concentration of the displacer is lower ($C_{f2} = 0.11$).

displacer does not give much help in the desorption of component 1 from the column because the concentration of the displacer is too low. This kind of situation was mentioned by some researchers.^{18,20} In Figure 6, the affinity of the displacer is lower than that of the adsorbate. It shows that if the concentration of the displacer is high enough, a desirable displacement of the adsorbate can also be achieved.

Effect of Adsorption Equilibrium Constant of Displacer (b_2)

The effect of b_2 on displacement performance is shown in Figure 7. It can be seen that an increase in b_2 delays the appearance of the roll-up peak, gives a sharper displacer front, and reduces the tailing of the displaced component. The maximum roll-up peak occurs somewhere in the middle range of the b_2 value. If the primary goal of displacement is to obtain a large fraction of pure component 1, a larger b_2 is obviously favorable. However, if the mixing of displacer in the product is not a setback, such as in the case when the displacer is a

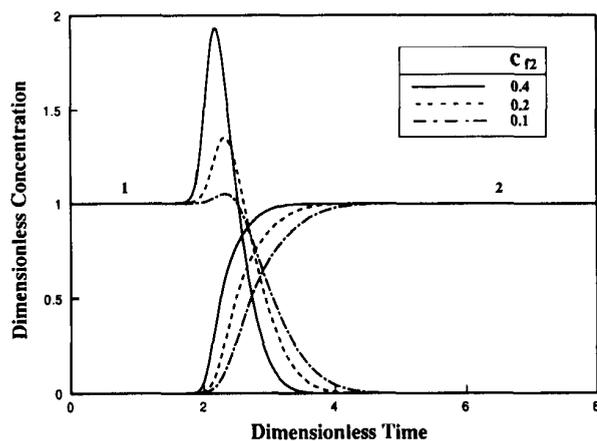


Figure 6. Effect of displacer concentration on displacement for a case in which $b_2 < b_1$: $Pe_{L1} = Pe_{L2} = 300$, $\eta_1 = 10$, $\eta_2 = 15$, $Bi_1 = 3$, $Bi_2 = 4$, $C_{f1} = 0.1$, $C_1^{\infty} = C_2^{\infty} = 0.5$, $b_1 = 6$, and $b_2 = 4$.

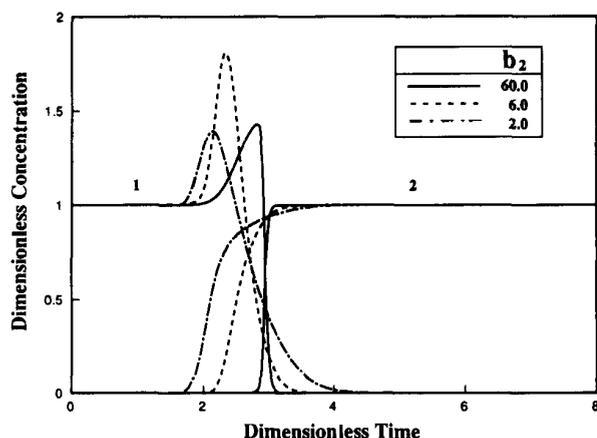


Figure 7. Effect of b_2 on displacement performance with $Pe_{L1} = Pe_{L2} = 300$, $\eta_1 = 10$, $\eta_2 = 15$, $Bi_1 = 3$, $Bi_2 = 4$, $C_{f1} = 0.1$, $C_{f2} = 0.3$, $C_1^{\infty} = C_2^{\infty} = 0.5$, and $b_1 = 6$.

volatile organic solvent and the product is readily recovered by evaporation after the displacement, a larger b_2 is not always favorable. As a matter of fact, if the displacement is terminated when the major portion of the product has been recovered, then a small b_2 may be a better choice because the roll-up peak appears earlier.

Compared with the displacement development, we have a somewhat different conclusion here. The displacement development requires a displacer which has an affinity higher than any other component in the sample. However, this is hardly true for the desorption chromatography, as we have already discussed in the cases of Figures 6 and 7.

Industrial Practice

In industrial application, column operations often include both adsorption and desorption. The adsorption stage uses the frontal operation until the concentration of the key adsorbed species in the effluent reaches a certain fraction, say, 10%, of its influent value. Then the

process switches to the desorption operation in the second stage. Switching before the complete frontal adsorption operation is due to the concern of loss of valuable products or release of environmentally hazardous adsorbates in the column exit or overall process efficiency during the operation. Also, the displacement operation can be carried out in either flow direction, forward or reverse. The reverse flow displacement operation may reduce the fouling of the column due to clogging of irregular or fractured adsorbent particles. In some cases, especially when the frontal adsorption period is brief, reverse flow displacement may give better displacement efficiency. Reverse flow regeneration in gas adsorption is a standard practice, and forward flow is used only in special situations which preclude the use of reverse flow.¹¹ Reverse flow was also reported by some researchers in the chromatographic separation of biomolecules.^{21,22}

Figures 8 and 9 show chromatograms for forward and reverse flow operations, respectively. In both cases, the frontal adsorption operation is switched to the displacement operation at $\tau = 2.0$. The reverse flow case, as shown in Figure 9, gives two peaks for the displaced component. The first peak is due to the sudden change in flow direction when the displacer is introduced, and the second peak is due to the displacement effect from the displacer. Compared with Figure 8, Figure 9 shows that the reverse flow displacement gives a better displacement efficiency as far as the minimization of displacer amount is concerned. Note that in the reverse flow displacement mode, a fast moving displacer is usually desired because of the high adsorbate concentration on the other end of the column at the beginning of desorption.

Simulations shown in Figures 8 and 9 reveal some interesting features in the practical application of adsorption and desorption processes. However, optimization of such combined adsorption/desorption processes requires more detailed information.

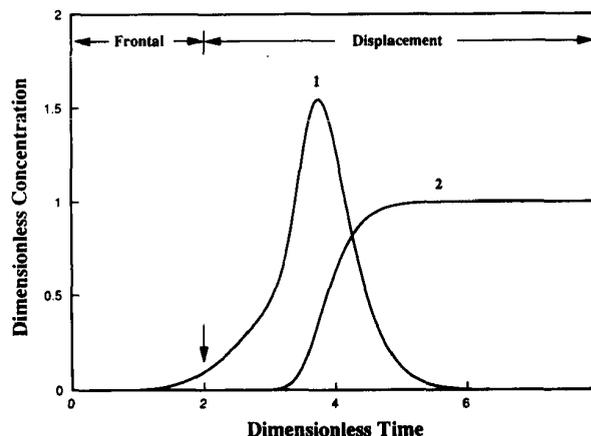


Figure 8. Frontal operation switched to forward flow displacement operation with $Pe_{L1} = Pe_{L2} = 100$, $\eta_1 = \eta_2 = 1$, $Bi_1 = 3$, $Bi_2 = 4$, $C_1^{\infty} = C_2^{\infty} = 0.5$, $b_1 = b_2 = 6$, $C_{f1} = 0.1$, and $C_{f2} = 2.0$.

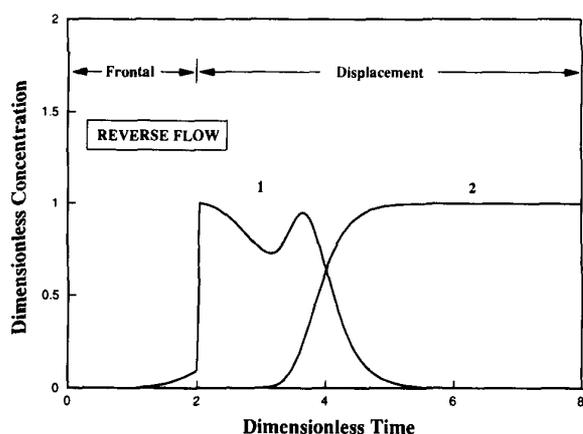


Figure 9. Same conditions as Figure 6 except that flow direction was reversed for the displacement process.

CONCLUSIONS

This article presents some interesting effects of isotherm characteristics of the displacer on the optimization of desorption chromatography and some considerations in the industrial practice of such operations. It is concluded that a displacer with a low maximum adsorption capacity (if possible), a high feed concentration, and a suitable adsorption equilibrium constant is often a desirable choice when the purpose of the displacement operation is to displace and to concentrate the adsorbed species and to minimize the amount of displacer employed.

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NOMENCLATURE

a_i, b_i	constants in Langmuir isotherm for component i
Bi_i	Biot number of mass transfer for component i ($k_i R_p / \epsilon_p D_{pi}$)
C_{bi}	bulk phase concentration of component i
C_{fi}	feed concentration of component i
C_{0i}	feed or sample concentration of component i used for nondimensionalization [$\max\{C_{fi}(t)\}$]
c_{bi}	$= C_{bi}/C_{0i}$
C_{pi}	concentration of component i in the fluid phase within particle
c_{pi}	$= C_{pi}/C_{0i}$
C_{pi}^s	concentration of component i in the solid phase of particle (based on unit volume of particle solid, excluding pores)
c_{pi}^s	$= C_{pi}^s/C_{0i}$
C_i^∞	adsorption capacity (saturation limit) for component i
D_{bi}	axial dispersion coefficient of component i
D_{pi}	effective diffusivity of component i
k_i	film mass transfer coefficient of component i
L	column length
N_s	number of components
Pe_{Li}	Peclet number in bulk fluid phase for component i (vL/D_{bi})
R	radial coordinate for particle

R_p	particle radius
r	$= R/R_p$
t	time
v	interstitial velocity
Z	axial coordinate variable
z	$= Z/L$

Greek letters

ϵ_b	bed void volume fraction
ϵ_p	particle porosity
η_i	dimensionless constant for component i ($\epsilon_p D_{pi} L / R_p^2 v$)
ξ_i	dimensionless constant for Component i ($3Bi_i \eta_i (1 - \epsilon_b) / \epsilon_b$)
τ	dimensionless time [vt/L]
τ_{imp}	dimensionless time duration for the rectangular pulse of the sample

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