

Simulation of multicomponent elution with the mobile phase containing competing modifiers



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In elution chromatography, modifiers sometimes are added to the mobile phase to compete with sample solutes for binding sites in order to reduce the retention time and band spreading of sample solutes. In this work, the interrelationship between modifiers and sample solutes in preparative and large-scale chromatography is investigated using a nonlinear multicomponent rate model in which axial dispersion, film mass transfer, intraparticle diffusion, and multicomponent Langmuir isotherm are considered. The modifier with a constant concentration in the feed mobile phase is treated as one of the components in the governing equations of the model and is included in the multicomponent Langmuir isotherm. Peaks that are directly attributed to the modifier in the chromatogram are termed system peaks. It has been concluded that for an elution system with two sample solutes and one modifier, there exist three different patterns of system peaks if the sample contains the modifier, and six if the sample does not contain the modifier. It has been found that apart from the thermodynamic effects, the dispersion and mass transfer effects, in some cases, also play important roles in determining system peak patterns. Simulations for an elution system with two modifiers have also been investigated and discussed.

Keywords: chromatography; system peak; modifier; elution; model

Introduction

Mobile phase modifiers are widely used in analytical, preparative, and large-scale liquid chromatography. In elution mode, a modifier (or modifiers) is sometimes added to the mobile phase in order to reduce the retention time and band spreading of sample solutes.¹ Modifiers may interact with the adsorbent and sample solutes in several ways. In this article, only the case in which the modifiers compete with sample solutes for binding sites is presented.

Peaks attributed to the modifier in an elution chromatogram are called system peaks.²⁻⁴ They are divided into two types⁵⁻⁷: displacement and vacancy peaks. The displacement peaks are those system peaks that are above the baseline, whereas the vacancy peaks are those below the baseline.

Simulations of system peaks were first carried out by Solms et al.⁶, who used a plate model to simulate three cases of single component elution with mobile phase containing a competing modifier. Recently, simulations of binary elutions were carried out by another group of researchers^{8,9} using a semi-ideal model that considers axial dispersion and equilibrium effects with Langmuir isotherms. In preparative and large-scale chromatography, external film mass transfer and intraparticle diffusion resistances are often significant.¹⁰ Hence, a more sophisticated rate model, which accounts for axial dispersion, mass transfer, and equilibrium effects, is needed for the scale-up and process design of preparative and large-scale chromatography. It is worthwhile pointing out that the external film mass transfer and intraparticle diffusion resistances may not be lumped into a single artificial mass transfer resistance since such a lumped mass transfer mechanism is not supported by experimental correlations for parameter estimations, which are essential for scale-up and process design.

There are two different types of samples for elution chromatography with the mobile phase containing a

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modifier. The first type (type I) samples in this work, are prepared by dissolving sample solutes in a solution that has the same composition as the mobile phase. With this kind of sample, the elution system is strictly isocratic if the modifier concentration in the feed mobile phase is kept constant. The second type (type II) are samples prepared in an inert (blank) solution (e.g., the samples contain no modifier). In such cases, system peaks have different patterns from those with type I samples because of the deficit of modifier introduced during the sample injection.¹¹ Experiments with both types of samples were carried out by Levin and Grushka.⁵ They also investigated elution systems containing more than one modifier in the mobile phase. This kind of multimodifier system is quite complicated and no simulations have been reported.

Although not treated in this work, it is worthwhile pointing out that the concentration of modifier in the feed may be continuously changed during the elution process. This process is called gradient elution. Theoretical studies of gradient elution have been carried out by many researchers.^{1,12-21}

For the first time, the effect of the modifier on the performance of binary elution with type I or II sample was extensively studied in this work, and all possible system peak patterns were summarized for both cases. Binary elution with two modifiers in the mobile phase was also discussed to some extent. Computer simulations were carried out based on a general rate model that considers axial dispersion, external mass transfer, and intraparticle diffusion. The modifier(s) was treated

as one of the components in the governing equations of the model. The Langmuir isotherm in which the modifier was considered as one of the competing components was used.

Model

Consider a chromatographic column (Figure 1) that is packed with uniform spherical adsorbent particles. Suppose the process is isothermal, and the concentration gradient in the radial direction of the column is negligible. Assuming that local equilibrium is applicable to each component between the pore surface and the stagnant liquid phase in the macropores inside particles, then the following governing equations for component *i* in the bulk fluid and particle phases can be obtained via differential mass balances.

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

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

with the initial and boundary conditions

$$t = 0, \quad C_{bi} = C_{bi}(0, Z); \quad C_{pi} = C_{pi}(0, R, Z) \quad (3,4)$$

Notation	
a_i, b_i	constants in Langmuir isotherm for component <i>i</i>
Bi_i	Biot number of mass transfer for component <i>i</i> , $(k_i R_p / \epsilon_p D_{pi})$
C_{fi}	feed concentration of component <i>i</i>
C_{0i}	dimensional feed or sample concentration used for nondimensionalization $(\max \{C_{fi}(t)\})$
C_{pi}	concentration of component <i>i</i> in the fluid phase within particle
C_{pi}^s	concentration of component <i>i</i> in the solid phase within particle
C_{bi}	bulk phase concentration of component <i>i</i> (based on unit volume of particle solid, excluding pores)
C_i^∞	adsorption capacity for component <i>i</i>
c_{pi}^s	$= C_{pi}^s / C_{0i}$
c_{pi}	$= C_{pi} / C_{0i}$
c_{bi}	$= C_{bi} / C_{0i}$
D_{bi}	axial dispersion coefficient of component <i>i</i>
D_{pi}	effective diffusivity of component <i>i</i>
k_i	film mass transfer coefficient of component <i>i</i>
L	column length
N	number of interior collocation points
Ne	number of quadratic elements
Ns	number of components
Pe_{Li}	Peclet number in bulk fluid phase for component <i>i</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	$= Z/L$
<i>Greek letters</i>	
ϵ_b	bed void volume fraction
ϵ_p	particle porosity
η_i	dimensionless constant for component <i>i</i> $(\epsilon_p D_{pi} L / R_p^2 v)$
ζ_i	dimensionless constant for component <i>i</i> $(3Bi_i \eta_i (1 - \epsilon_b) / \epsilon_b)$
τ	dimensionless time $(t/(L/v))$
τ_{imp}	dimensionless time duration of a rectangular sample pulse

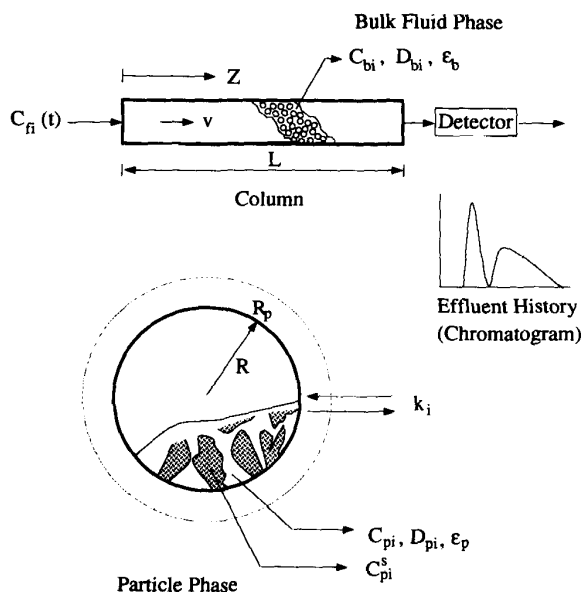


Figure 1 Anatomy of a chromatography column

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

$$Z = L, \quad \frac{\partial C_{bi}}{\partial Z} = 0 \quad (5,6)$$

$$R = 0, \quad \frac{\partial C_{pi}}{\partial R} = 0;$$

$$R = R_p, \quad \frac{\partial C_{pi}}{\partial R} = \frac{k_i}{\varepsilon_p D_{pi}} (C_{bi} - C_{pi, R=R_p}) \quad (7,8)$$

These equations can be transformed to the following dimensionless forms

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

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

Initial Conditions:

At $\tau = 0$, for sample solutes $c_{bi} = c_{pi} = 0$, and for the modifier(s) $c_{bi} = c_{pi} = 1$.

Boundary Conditions:

$$z = 0, \quad \frac{\partial c_{bi}}{\partial z} = Pe_{Li} \left(c_{bi} - \frac{C_{fi}(\tau)}{C_{0i}} \right) \quad (11)$$

For sample solutes injected in a rectangular pulse

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

For modifier(s) in systems with the type I sample

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

For modifier(s) in systems with the type II sample

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

$$z = 1, \quad \frac{\partial c_{bi}}{\partial z} = 0 \quad (12)$$

$$r = 0, \quad \frac{\partial c_{pi}}{\partial r} = 0;$$

$$r = 1, \quad \frac{\partial c_{pi}}{\partial r} = Bi_i (c_{bi} - c_{pi, r=1}) \quad (13,14)$$

The solution to the partial differential equation system shown previously provides the effluent history ($c_{bi, z=1}$ vs. τ) and concentration profiles inside the column at different column positions ($c_{bi}(\tau, z)$ vs. z). The concentration profiles inside each particle ($c_{pi}(\tau, r, z)$ vs. r) can also be obtained. In this article only effluent history plots are used for discussion.

Numerical solution

This general nonlinear multicomponent rate model was solved with an efficient and robust numerical procedure.^{22,23} Finite element and orthogonal collocation methods were used to discretize the bulk fluid phase and particle phase partial differential equations, respectively. The resulting ordinary differential equation system was solved using Gear's stiff method. Using this ordinary differential equation solver, very fine resolutions for the time grid of the simulated effluent histories can be achieved at almost no extra cost of central processing unit time. If a finite difference method is used to discretize the time axis instead of solving ordinary differential equations, a high resolution of time grid cannot be achieved without the cost of large memory space and central processing unit time. A sufficient resolution of the time grid for the simulated effluent histories is essential for checking mass balances of peak areas by numerical integration.

All the simulation computations in this work were carried out on a SUN 4/280 computer. Parameter values used for the simulation are listed in Table 1 or during discussions. In all simulated cases, axial dispersion and mass transfer effects represent situations in preparative and large-scale chromatography. In all runs, $\varepsilon_p = 0.4$ and $\varepsilon_b = 0.4$, with the sample size being $\tau_{imp} = 0.1$, unless otherwise specified. The error tolerance in the IVPAG subroutine²⁴ of the ordinary differential equation solver was set to 10^{-5} . Double precision was used in the Fortran code.

Table 1 Parameter values used for simulation*

Figures	Species	Physical parameters					Numerical parameters	
		Pe_{Li}	η_i	Bi_j	a_i	$b_j \times C_{0j}$	Ne	N
2 and 3	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	2	1×0.1		
4 and 5	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	7	3.5×0.1		
6 and 7	1	300	8	20	5	2.5×0.2	7	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	20	10×0.1		
8	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	40	20×0.1		
9	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	100	50×0.1		
12-14	1	300	8	20	5	5×0.4	9	2
	2	300	8	20	20	20×0.4		
	3	300	8	20	40	40×0.2		
16	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	6.6	3.3×0.2		
	3	350	9.5	9	2	1×0.1		
17	1	300	8	20	1	0.5×0.2	9	2
	2	400	9	12	10	5×0.2		
	3	350	9.5	9	100	50×0.1		
18	1	300	8	20	5	2.5×0.2	8	2
	2	400	9	12	6.6	3.3×0.2		
	3	350	9.5	9	7	3.5×0.48		
20 and 21	1	200	6	9	6	3×0.2	8	2
	2	200	6	9	20	10×0.2		
	3	200	6	9	2	1×0.2		
	4	200	6	9	20	10×0.2		
22	1	700	30	20	5	2.5×0.2	19	2
	2	700	30	12	10	5×0.2		
	3	700	30	9	100	50×0.1		

*Central processing unit times on SUN 4/280 computer for some cases (solid lines): Figure 2, 10.1 min; Figure 5, 10.8 min; Figure 6, 7.3 min; Figure 16, 9.4 min; and Figure 21, 18.6 min.

Results and discussion

The multicomponent Langmuir isotherm used in this work is shown below.

$$C_{pi}^s = \frac{a_i C_{pi}}{1 + \sum_{j=1}^{N_s} b_j C_{pj}}$$

$$\text{i.e., } c_{pi}^s = \frac{a_i c_{pi}}{1 + \sum_{j=1}^{N_s} (b_j C_{0j}) c_{pj}} \quad (\text{dimensionless})$$

where $a_i = C_i^\infty b_i$. In this work a_i/b_i values are selected as the same for all components so the relative affinity of a component is solely reflected by its adsorption equilibrium constant b_i .

Since the competing modifier is treated as one of the components in the governing equations of the model, it is also considered as a competing component in the

isotherm shown previously. Hence, a binary elution with a competing modifier in the mobile phase constitutes a three-component system.

Note that $b_j C_{0j}$ can be treated as a dimensionless group for each component. In other words, two systems would give the same dimensionless concentration profiles if their dimensionless groups, including $b_j C_{0j}$, are all the same. For example, a single-component system with $a = 10$, $b = 5$, $C_0 = 0.2$, and $C^\infty = a/b = 2$ will be the same as the single-component system with $a = 10$, $b = 10$, $C_0 = 0.1$, and $C^\infty = a/b = 1$, provided all other parameter values are the same for both systems. This shows that the concentration increase in Langmuir isotherm is equivalent to the increase of adsorption equilibrium constant, b , and the proportional decrease of the saturation capacity, C^∞ . The same argument applies to multicomponent systems.

Based on theoretical simulation, the discussion of the system peaks and the interrelationship between the

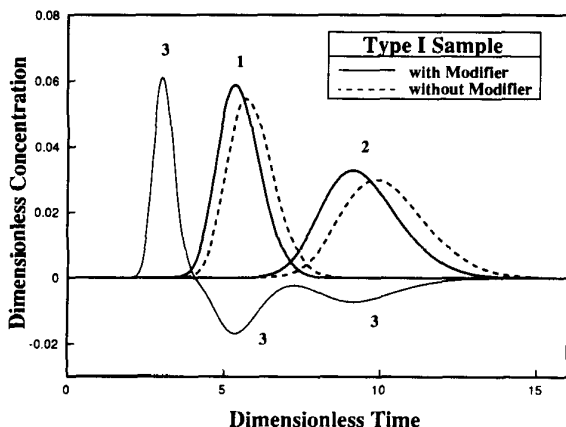


Figure 2 Binary elution with a weak modifier (type I sample)

modifier(s) and the sample solutes was divided into the following parts. Binary elutions with a single competing modifier are discussed first.

Modifier affinity is weaker than those of sample solutes

Figure 2 (solid lines) shows a simulated effluent history (chromatogram) of a binary elution with a type I sample and a competing modifier (component 3) in the mobile phase. Components 1 and 2 are the two sample solutes. The affinity of the modifier is smaller than those of the sample components. Parameter values used for simulation are listed in Table 1. Note that the scale for the modifier concentration shown in Figure 2 (as well as in all other figures) is $c_{b3} - 1$. The actual baseline value for the modifier concentration is $c_{b3} = 1$. By transforming the baseline value to zero (i.e., $c_{b3} - 1 = 0$), the effluent history becomes more presentable. It is obvious that a negative system peak does not mean that the modifier concentration is negative, rather, it means that the modifier concentration is below its baseline value.

The case shown in Figure 2 gives one positive system peak and two negative system peaks that are due to the displacement effect of the two sample solutes on the modifier.⁹ The mass balance of each species was checked to evaluate the accuracy of the numerical solution. For the modifier, the numerical integration (using the subroutine QDAGS from IMSL²⁴ of the concentration profile of the modifier ($c_{b3} - 1.0$) in Figure 2, which consists of 400 data points, from $\tau = 1$ to $\tau = 15$ gives a value of 0.0000, which is in agreement with its theoretical value zero. For sample solutes, mass balances are also held. The excellent mass balance is a partial indication that the numerical approach used in this work is quite accurate.

Figure 2 (dashed lines) also shows the binary elution case in the absence of the modifier. It is evident that the use of the modifier results in the decrease of the

retention time and band spreading, and an increase of the peak height for each sample solute.

Figure 3 shows the chromatogram with a type II sample. Other conditions for Figure 3 are the same as for Figure 2. It can be seen in Figure 3 that there are three negative system peaks and no positive system peak. The numerical integration of the concentration profile for the modifier (component 3) of the three system peaks was found to be -0.1000 . This negative value indicates the deficit of the modifier introduced during sample injection. It is in agreement with the sample size, $\tau_{imp} = 0.1$. Figure 3 shows that the first system peak is negative, instead of positive as shown in Figure 2. This is due to the large negative system peak resulting from the deficit of the modifier in the sample overcoming the positive peak from the displacement effect of the sample solutes. It can be easily verified by checking the concentration profile of the modifier with a blank sample that contains only this inert carrier liquid. This case is also shown in Figure 3 (dashed line). It gives only a single large negative peak, and the peak area was found to be equal to the injection pulse size, $\tau_{imp} = 0.1$.

It should be pointed out that a positive system peak(s) also occurs in some cases involving the type II sample, if the positive system peak overcomes the negative one due to sample introduction, as we will discuss. The number and direction (positive/negative, i.e., upward/downward) of system peaks are determined primarily by the sample type and their relative affinity to those sample solutes, and of course, the number of sample solutes.

Modifier affinity is between those of sample solutes

Figure 4 gives the chromatogram for the case shown in Figure 2 except that the affinity of the modifier is between those of the two sample solutes (Table 1). Figure 4 shows one positive system peak and two negative system peaks, which is similar to Figure 2. However,

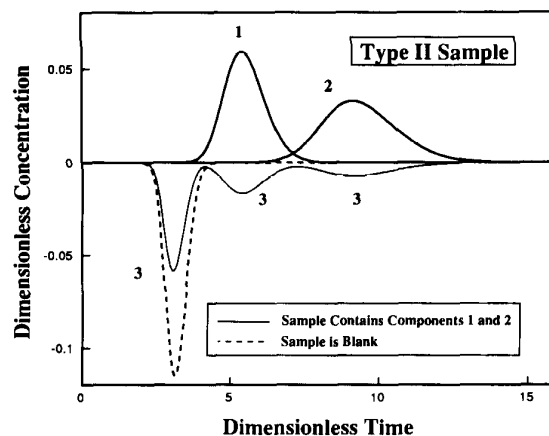


Figure 3 Binary elution with a weak modifier (type II sample)

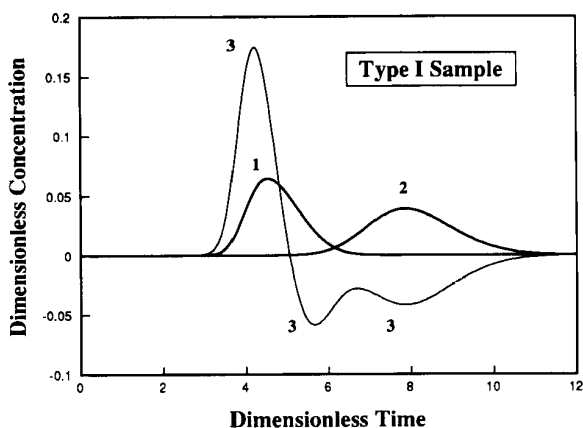


Figure 4 Modifier affinity is between those of sample solutes (type I sample)

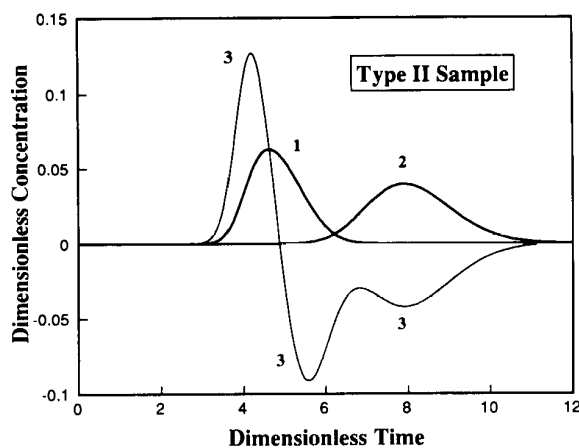


Figure 5 Modifier affinity is between those of sample solutes (type II sample)

the retention time of the positive system peak is prolonged and the peak height is increased. Both changes are due to the increase of modifier affinity, which results in more modifier molecules adsorbed onto the stationary phase than can be dislodged by the sample solutes. It should not be surprising, if one considers the case in which the modifier has no affinity to the column packing, that this results in a flat concentration profile for the modifier. On the other hand, if the affinity of the modifier further increases when its affinity is already not far from the leveling off range of the Langmuir isotherm, the increase of modifier's loading in the stationary phase can be overshadowed by the affinity increase that could make it too difficult to be dislodged by the sample solutes. In such cases, the increase of modifier affinity may result in a reduced positive system peak at the front.

Figure 5 shows a chromatogram that has the same conditions as shown in Figure 4, except that a type II sample was used. In this case, the chromatogram shows one positive and two negative system peaks.

The result is quite different from Figure 3 which has the same conditions as Figure 5, except that the affinity of the modifier in Figure 5 is stronger. This is due to the fact that the displacement effect from components 1 and 2 causes a larger positive system peak, which overcomes the negative one caused by the lack of modifier in the sample. The fact that the positive system peak in Figure 5 is smaller than that in Figure 4 is in agreement with the argument.

Modifier affinity is stronger than those of sample solutes

Figure 6 shows a case in which the affinity of the modifier is stronger than both sample solutes. In this case, the system peaks include two positive and one negative peaks. The first positive system peak partially overlaps with the component 1 peak, and it departs from the component 1 peak when the component 2 peak starts to take off. The corresponding case with the type II sample is shown in Figure 7, which gives a similar system peak pattern.

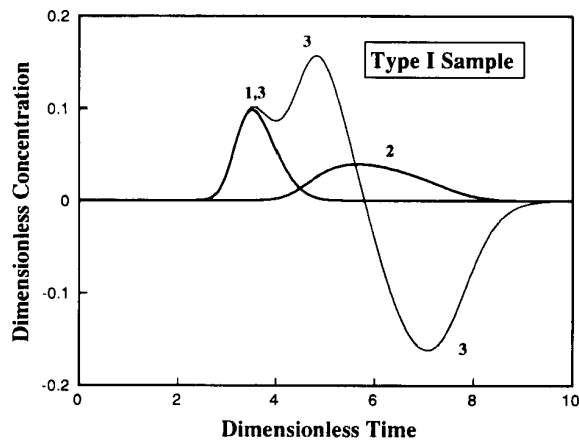


Figure 6 Binary elution with a strong modifier (type I sample)

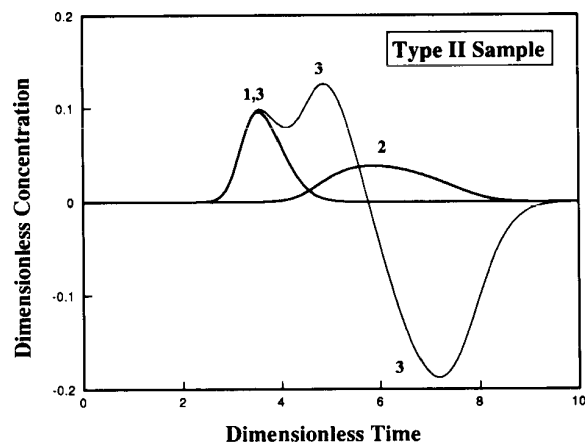


Figure 7 Binary elution with a strong modifier (type II sample)

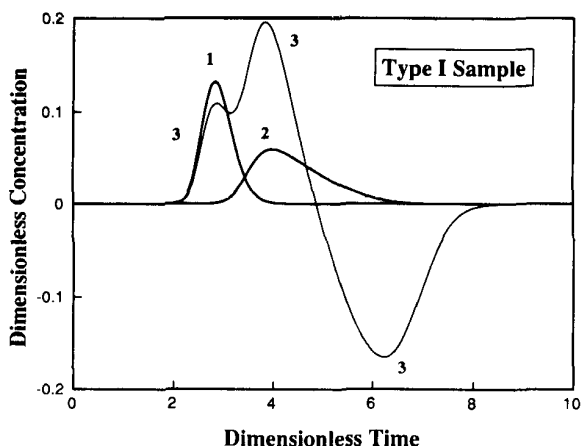


Figure 8 Same conditions as Figure 6, except that modifier affinity is stronger

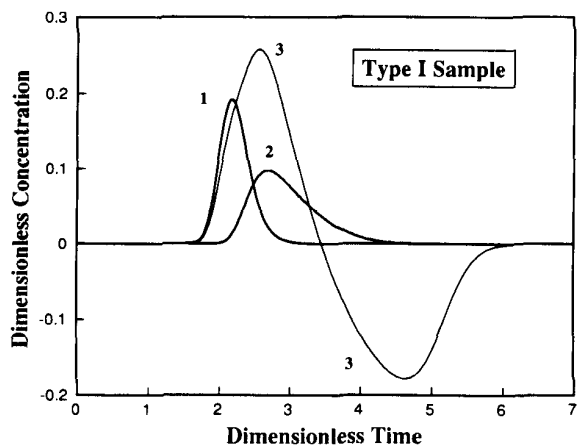


Figure 9 Same conditions as Figure 8, except that modifier affinity is stronger

In Figure 6, if the affinity of the modifier is further increased, the first positive system peak will no longer overlap with the component 1 peak, as is clearly shown in Figure 8. Figure 9 shows the degenerated case that was obtained by simply increasing the affinity of the modifier shown in Figure 8. It is obvious that the merging of two positive system peaks in Figure 9 is due to the partial overlapping of the component 1 peak with the component 2 peak.

Effect of modifier concentration on system peak patterns

The increase of modifier concentration obviously will reduce the retention times of the sample solutes because of the added ability of the modifier to compete with sample solutes for adsorption sites. This effect has been reported by previous researchers,⁹ and thus is not discussed in this work.

Figure 10 shows a case in which the modifier concentration is 10 times higher than that in Figure 4. Comparing Figure 4 with Figure 10 (both with type I samples), it can be seen that the system peaks in Figure 10 are much smaller than those in Figure 4. This means that the disturbance caused by the sample solutes to the concentration profile of the modifier becomes smaller if the concentration of the modifier increases. Note that in all figures the concentration scale is dimensionless concentration. Thus, a smaller peak does not necessarily mean a smaller dimensional concentration.

Figure 11 shows the case of the type II sample, in which the concentration of the modifier is 10 times higher than in Figure 5. The increase of the modifier concentration changes the first system peak from a positive one (shown in Figure 5) to a negative one (shown in Figure 11). When the modifier concentration is increased, the peak direction is reversed. The negative system resulting from the deficit of the modifier during sample injection overcame the positive system

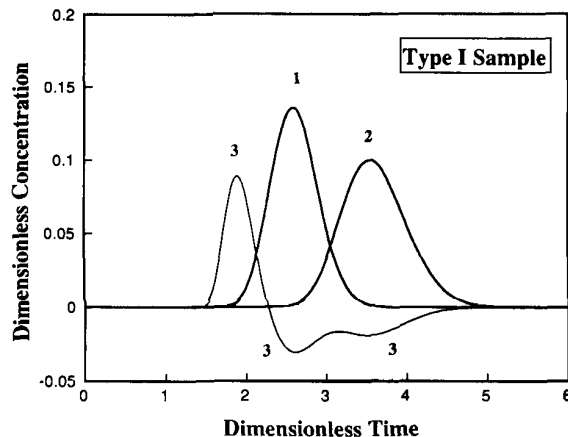


Figure 10 Same conditions as Figure 4, except modifier concentration is higher ($C_{03} = 1.0$)

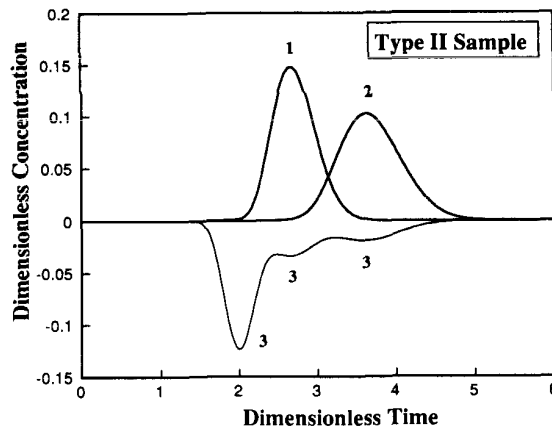


Figure 11 Same conditions as Figure 5, except modifier concentration is higher ($C_{03} = 1.0$)

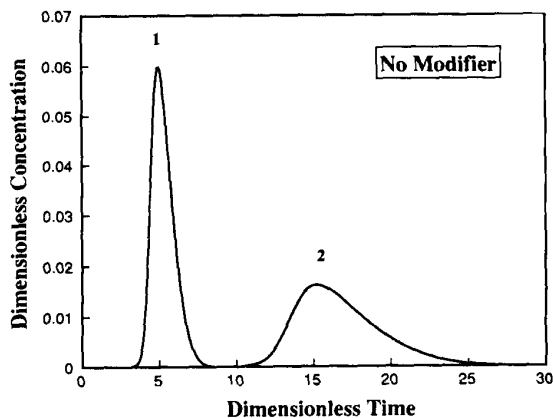


Figure 12 Binary elution without modifier

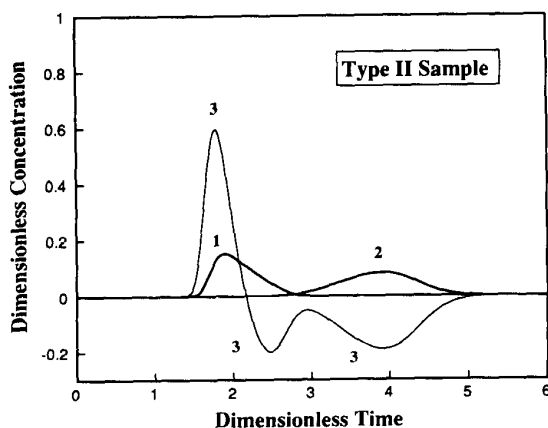


Figure 13 Effect of added modifier (type I sample)

peak that resulted from the displacement effect of the sample solutes to the modifier.

Effect of modifier on sample solutes

Figure 12 shows a binary elution without any modifier. The retention time and the resolution of the two solute peaks are both unnecessarily high for the complete separation of the two components. In such an elution system, adding a proper modifier may reduce the process duration while still achieving a baseline separation. Figure 13 shows the effect of the added modifier in the binary elution system shown in Figure 12. It is clear that the retention times and the resolution of the two sample solutes are drastically reduced. The baseline separation of the two sample solutes is achieved even though the elution duration is cut to one-fifth of that in Figure 12. The peak heights are increased, and the band spreadings of these peaks are reduced when the modifier is used. This is because of the displacement effect of the modifier. Figure 14 has the same conditions as shown in Figure 13, except that the type

I sample was employed in Figure 14. It is clear that the result shown in Figure 14 is also desirable.

It has been reported⁹ that when the modifier concentration is high the common Langmuir shape elution peaks might reverse their asymmetry and become anti-Langmuir, i.e., the tailing of a peak became smaller than the diffused front flank of the peak. In Figures 13 and 14, we have shown that at low modifier concentration levels, the phenomenon of peak shape reversal also occurs if the adsorption equilibrium constant of the modifier (b_3) is high enough and the adsorption capacity is low (see Table 1 for parameter values). It is very interesting to note that in Figures 13 and 14, the component 1 peak still retains its Langmuir-type shape whereas the peak shape of component 2 becomes anti-Langmuir.

Effect of the type of sample

The sample type affects the direction, size, and location of system peaks, as clearly shown previously. On the other hand, the sample type also affects the elution pattern of sample solutes. In general, the larger the

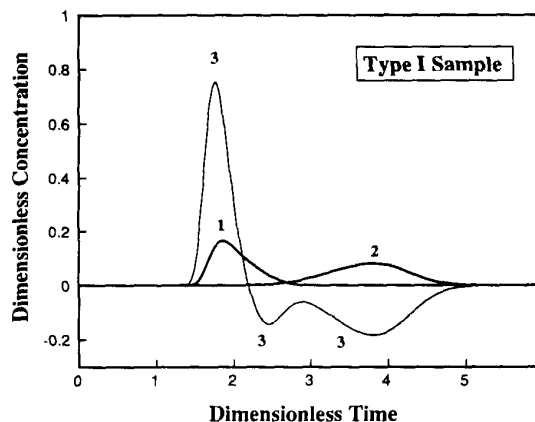


Figure 14 Effect of added modifier (type II sample)

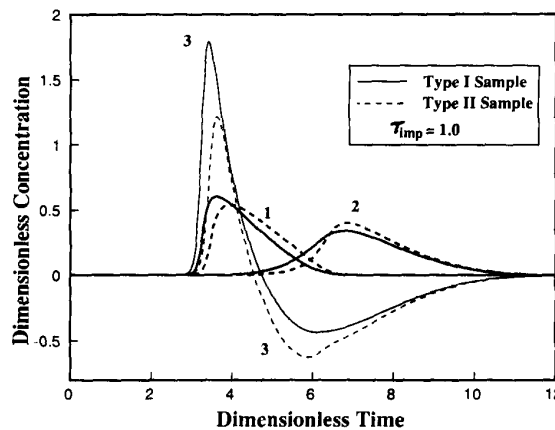


Figure 15 Effect of type of sample at large sample size

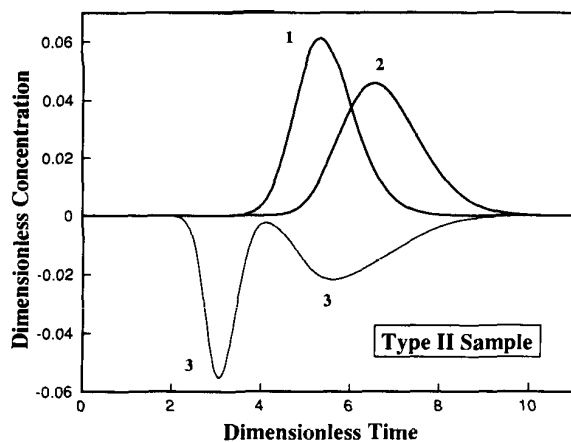


Figure 16 Same conditions as *Figure 3*, except that component 2 has a weaker affinity

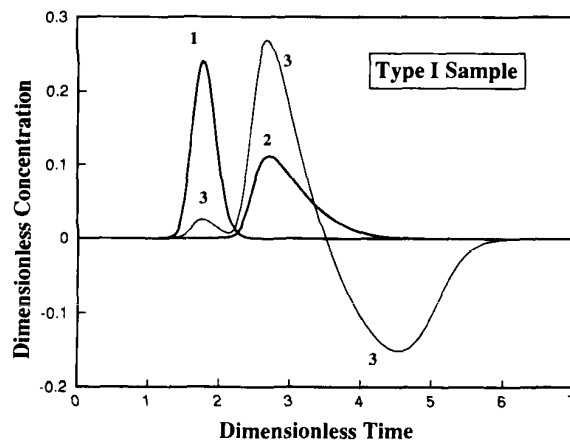


Figure 17 Same conditions as *Figure 9*, except that component 1 has a weaker affinity

sample size, the larger the discrepancy. *Figure 15* supports such a conclusion as compared with *Figures 4* and *5*. Notice that *Figure 15* has the same conditions as *Figures 4* and *5* except that the sample size is $\tau_{imp} = 1.0$, which is 10 times larger than those used in *Figures 4* and *5*.

Effect of sample solutes on the modifier

The relative affinities of the sample solutes also affect the system peaks as shown in *Figure 16*. *Figure 16* has the same conditions as *Figure 3*, except that in *Figure 16* the affinity of component 2 is smaller and thus closer to that of component 1 (*Table 1*). *Figure 16* (with type II sample) shows that when component 1 and component 2 peaks overlap to some degree, the two corresponding negative system peaks will degenerate into a single one. Similar system peak patterns in the case of the type I sample were observed by Golshan-Shirazi and Guiochon⁹ using a semi-ideal model. The comparison of *Figure 9* with *Figure 17* proves that the partial overlapping of the peaks for sample solutes may also cause the merging of positive system peaks.

Summary of system peak patterns

Table 2 summarizes all possible combinations of system peak patterns for binary elution with one compet-

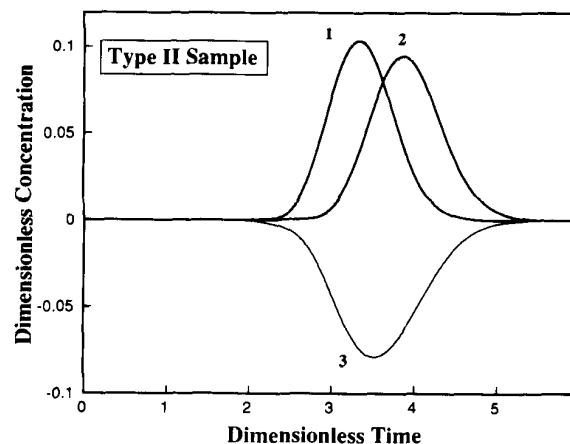


Figure 18 Binary elution showing only one system peak (type II sample)

ing modifier. There are twice as many combinations for cases with type II sample than for those with type I. It is interesting to point out that *Figure 18* shows a severely degenerated case, giving only one negative system peak. In this case, the first system peak is degenerated, leaving only a slightly negative trace preceding the only negative system peak, which degenerates due to the

Table 2 Possible system peak combinations in a binary elution with a competing modifier in the mobile phase

Sample	System peak combinations (positive peak(s)/negative peak(s))					
	I	II	III	IV	V	VI
Type I	1/2 (<i>Figure 2</i>)	1/1 (<i>Figure 9</i>)	2/1 (<i>Figure 6</i>)			
Type II	0/3 (<i>Figure 3</i>)	0/2 (<i>Figure 16</i>)	0/1 (<i>Figure 18</i>)	1/1 (<i>Figure 19</i>)	2/1 (<i>Figure 7</i>)	1/2 (<i>Figure 5</i>)

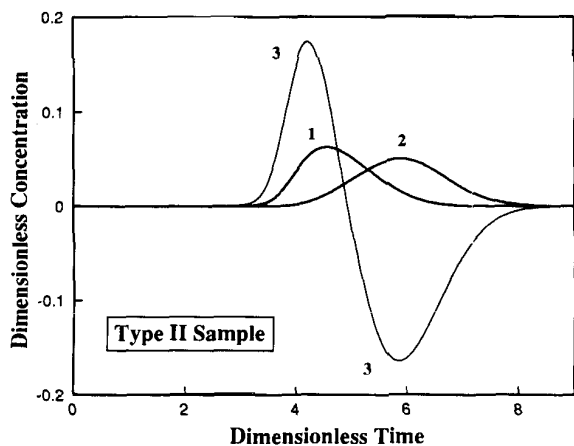


Figure 19 Binary elution showing one positive and one negative peak, respectively (type II sample)

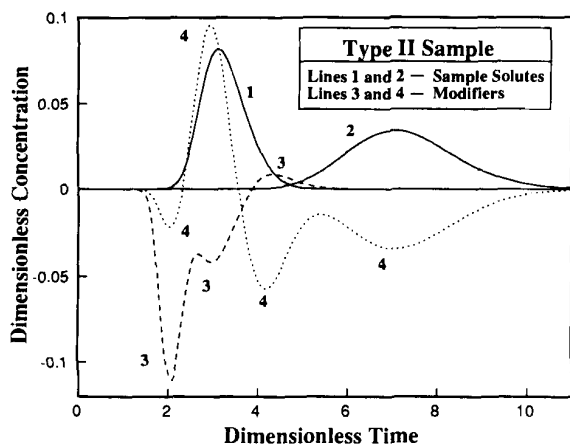


Figure 20 Binary elution with two modifiers (type II sample)

overlapping of the component 1 and 2 peaks. Figure 19 has the same conditions as Figure 18, except that the modifier concentration, 0.1, is lower than that in Figure 18. Because of the decrease of the modifier concentration, the previously degenerated peak (in Figure 18) becomes very prominent in Figure 19.

In general, both sample types (I and II) could only have a maximum of three system peaks for binary elution with one competing modifier. For binary elutions with type I sample, the minimum number of system peaks should be two because the existence of a positive system peak necessitates the existence of a negative system peak in order to meet the mass balance, which requires that the sum of peak areas of positive system peaks be equal to the sum of peak areas of negative system peaks. On the other hand, this requirement does not apply to cases with type II samples. In these cases, the minimum number of system peaks is one (Figure 18).

Binary elution with two different modifiers in the mobile phase

As we have already discussed, system peak behavior can be very complex and elusive. This fact was also realized by previous researchers.^{5,8,9} The situation can be further complicated if there is more than one modifier in the mobile phase. In practice, the multiple modifier cases are not rare. Experiments by Levin and Grushka⁵ showed that different modifiers gave different sets of system peaks.

Figure 20 shows a case involving two sample solutes (components 1 and 2) and two different modifiers (components 3 and 4). The first modifier (component 3) has a weaker affinity than the second modifier (component 4). Figure 21 has the same conditions as Figure 20, except that a type I sample is used. There is a positive system peak at the tail of the concentration profile of the first modifier (component 3) in both figures. We have never observed this kind of tail during simulations for single modifier systems. Its presence is likely due to the involvement of the second modifier in the system.

Dispersion and mass transfer effects

Apart from thermodynamic effects (isotherm characteristics), dispersion and mass transfer effects are also important factors in determining system peak patterns, especially when the effects are affecting the overlapping of the two solute peaks. Figure 22 has the same conditions as Figure 9, except that the Peclet numbers and η_i values are higher in Figure 22. In Figure 22 the axial dispersions are weaker and the mass transfer rates are faster, thus the overlapping of peaks 1 and 2 is reduced compared with that in Figure 9. The degenerated positive system peak in Figure 9 splits in Figure 22 becoming two positive system peaks. This causes a change in the system peak pattern.

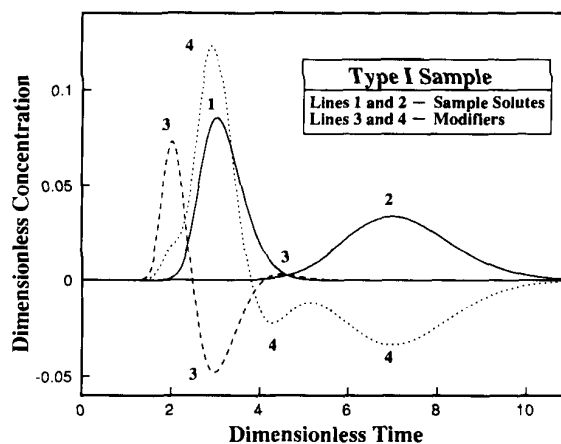


Figure 21 Binary elution with two modifiers (type I sample)

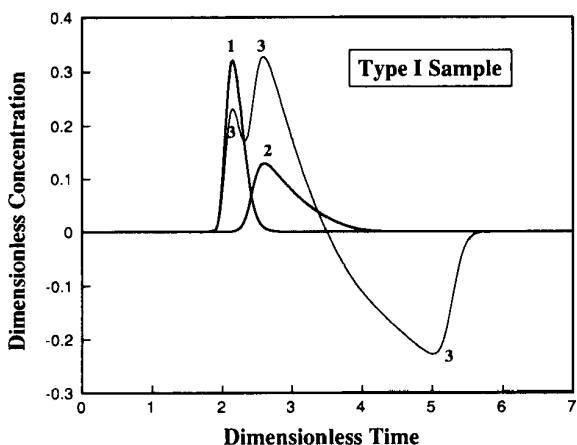


Figure 22 Dispersion and mass transfer effects

Conclusions

The interrelationship between sample solutes and the modifier(s) in binary elution was investigated using extensive computer simulations based on a general rate model. It was concluded that for binary elution with one competing modifier in the mobile phase, there are three system peak patterns if type I samples are used, and six if type II samples are used. In addition, the binary elution system with two competing modifiers was also briefly discussed. This study showed that system peaks in many cases can be explained by using the concept of displacement effect due to the competitive nature of the isotherms involving all the components in the system, including the modifier. The deficit of the modifier(s) in the sample also plays an important role in determining the system peak patterns if type II samples are used. It was observed that interaction between the modifiers in an elution system with two competing modifiers affects the shapes of the system peak considerably. It was also found that in some cases, dispersion and mass transfer can also affect the system peak pattern.

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