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ANALYSIS OF A NONLINEAR, COUPLED CHROMATOGRAPHIC SYSTEM

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Abstract—A relatively simple mathematical derivation is employed to obtain the relationship between the solute concentrations and their velocities along the column. These equations are used to calculate numerically the breakthrough curves and delineate the elution behaviors of competing solutes in the chromatographic column. A hodograph constructed from the derived equations using published data for the coupled adsorption isotherms is adopted to visualize the concepts of the shock and the diffusive waves. The resulting elution curves at different column lengths show a successful application of the scaling relationship between the column length and feed period to the nonlinear coupled system.

INTRODUCTION

Chromatography has become a method of choice where a high resolution is required in the purification process of biochemical products. Despite its efficiency in separating hard-to-separate mixtures, the scale-up of column chromatographic processes has not been successful because of its inherent complexity of the separation dynamics. However, there have been several attempts to relate the separation behavior in columns of different sizes. Wankat and Koo [1] examined the rules for scaling column diameter, length and operating conditions in an uncoupled chromatographic system. Elution chromatography has mostly been used to separate two or more solutes of similar physicochemical properties. Consequently, the solutes compete for the limiting binding sites of adsorbent, and the adsorption becomes coupled. In other words, the isotherms are the functions of all solutes present in the fluid phase. Industrial processes often deal with large amounts of solutes, which belong to the range of nonlinearity. Rhee, Aris and Amundson [2] and Helfferich and Klein [3] described mathematically the chromatographic dynamics, but their analysis was confined to the Langmuir isotherms and a constant separation factor, respectively. In this study, a relatively simple mathematical derivation is employed to obtain the relationship between the solute concentrations and their velocities along the column. These equations are used to calculate numerically the breakthrough curves and delineate the elution behaviors of competing solutes in the chromatographic column. Finally, the elution curves at different column lengths show that the scaling relationship between the column length and feed period applies to the nonlinear coupled system successfully.

THEORY AND PROCEDURES

Dynamic analysis of column elution chromatography is based on the mass balance of solute in a finite volume in a column.

$$\frac{\partial}{\partial t}[\alpha+(1-\alpha)\varepsilon]c_1+\frac{\partial}{\partial t}(1-\alpha)q_1+\alpha v\frac{\partial c_1}{\partial z}=0 \qquad (1)$$

Here, q, c, z, v, α and ε stand for adsorbed concentration, fluid concentration, axial distance along the column, interstitial velocity, interstitial porosity and intrastitial porosity, respectively. The first term of Eq. (1) represents the accumulation of solutes in fluid phase, the second term, the accumulation of solutes in solid phase and the third, the convection in a column. The subscript denotes the solute species. Eq. (1) is rearranged to Eq. (2).

$$\frac{\partial}{\partial t}(Ac_1+q_1)+Bv\frac{\partial c_1}{\partial z}=0 \qquad (2)$$

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Here, $A=[\alpha+(1-\alpha)\varepsilon]/(1-\alpha)$, $B=\alpha/(1-\alpha)$. The total differential of c_1 is zero as the solute concentration does not change along the characteristic line. It is rearranged to give an expression for the reciprocal of solute movement velocity, dz/dt.

$$\frac{\partial c_1}{\partial z}=-\frac{\partial c_1}{\partial t}\frac{dt}{dz} \tag{3}$$

This also applies to solute 2.

$$\left(A+\frac{\partial q_1}{\partial c_1}-Bv\frac{dt}{dz}\right)\frac{\partial c_1}{\partial t}+\frac{\partial q_1}{\partial c_2}\frac{\partial c_2}{\partial t}=0 \tag{4}$$

$$\frac{\partial q_2}{\partial c_1}\frac{\partial c_1}{\partial t}+\left(A+\frac{\partial q_2}{\partial c_2}-Bv\frac{dt}{dz}\right)\frac{\partial c_2}{\partial t}=0 \tag{5}$$

The determinant of the coefficient matrix of Eqs. (4) and (5) should be zero to satisfy the equality. If we let $\lambda=-A+Bv(dt/dz)$, the determinant becomes Eq. (6).

$$\begin{vmatrix} \frac{\partial q_1}{\partial c_1}-\lambda & \frac{\partial q_1}{\partial c_2} \\ \frac{\partial q_2}{\partial c_1} & \frac{\partial q_2}{\partial c_2}-\lambda \end{vmatrix}=0 \tag{6}$$

In Eq. (6), λ is the eigenvalue of Jacobian, $[\partial(q_1, q_2)/\partial(c_1, c_2)]$ from definition.

The solute movement velocity, v_s, can be expressed as a function of λ.

$$v_s=\frac{dz}{dt}=\frac{Bv}{A+\lambda} \tag{7}$$

This is the apparent speed at which a solute migrates along the column. The total differential of q_1 is written with respect to c_1, c_2 in Eq. (8).

$$dq_1=\frac{\partial q_1}{\partial c_1}dc_1+\frac{\partial q_1}{\partial c_2}dc_2 \tag{8}$$

The same derivation can be done for q_2. If we let $dq_1=\lambda\ dc_1$, $dq_2=\lambda\ dc_2$ and substitute into Eq. (8), the resulting determinant of the coefficient matrix of these equations becomes the same as Eq. (6). Then Eq. (9) holds true.

$$\frac{dq_1}{dc_1}=\frac{dq_2}{dc_2}=\lambda \tag{9}$$

We obtain the relationship between the concentration changes of the two solutes by substituting Eq. (9) into Eq. (8).

$$\frac{dc_2}{dc_1}=\frac{\lambda-(\partial q_1/\partial c_1)}{\partial q_1/\partial c_2} \tag{10}$$

When there arises a discontinuity in c_1 and c_2, a shock wave occurs. The shock wave velocity can be calculated from the mass balance just before and after that discontinuity. When two solutes exist in both sides of the shock wave, the following relations hold.

$$\frac{\Delta q_1}{\Delta c_1}=\frac{q_1^b-q_1^a}{c_1^b-c_1^a} \tag{11}$$

$$\frac{\Delta q_2}{\Delta c_2}=\frac{q_2^b-q_2^a}{c_2^b-c_2^a} \tag{12}$$

Here supercripts a and b stand for after and before the shock wave, respectively. And as only one shock wave exists for two solutes at that point, shock wave velocities of the two solutes are equal.

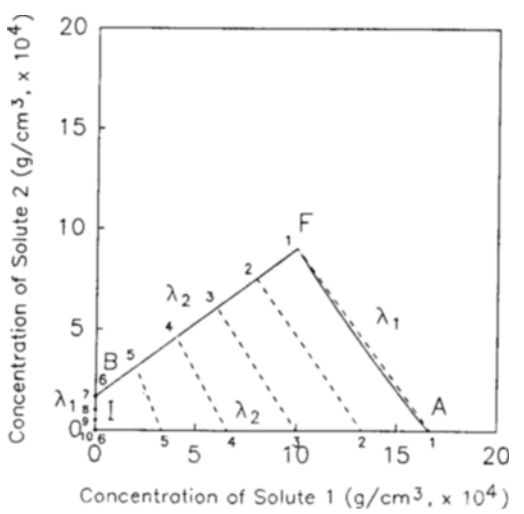
$$\frac{\Delta q_1}{\Delta c_1}=\frac{\Delta q_2}{\Delta c_2} \tag{13}$$

Substitution of Eqs. (11) and (12) into Eq. (13) gives the relations between the concentrations of two solutes before and after the shock wave. As the concentration of solutes of one side are known, the concentration of the other side can be calculated from Eqs. (11), (12) and (13). Then we can calculate the shock wave velocity at the intersecting point of diffusive and shock waves by substituting $\Delta q_1/\Delta c_1$ or $\Delta q_2/\Delta c_2$ into λ in Eq. (7). The diffusive wave velocity after the intersection point also changes because the concentration of the wave changes to meet the mass balance around the point. With Eqs. (6), (7), (10) and (13), we can quantify any breakthrough curves of two nonlinear competing solutes and consequently analyze the column dynamics, providing the adsorption isotherms have continuous first derivatives. Multicomponent system with more than two solutes can also be described by the same principles. The numerical calculation procedure to obtain the breakthrough curves of solutes is outlined below.

1. Obtain the derivatives of q_i with respective to c_i.
2. Evaluate the eigenvalues of Jacobian [Eq. (6)].
3. Start calculations of solute velocities [Eq. (7)] in conjunction with the incremental changes of solid concentration [Eq. (10)].
4. Calculate the shock wave velocities [Eq. (13)].
5. Adjust the shock and diffusive wave velocities after the intersection point to meet the mass balances of each solute around the point.

RESULTS AND DISCUSSION

A nonideal Langmuir isotherm [4] was chosen to



Liapis and Rippin:

$$q_1 = \frac{171\, c_1}{1 + 1400\, c_1 + 2835\, c_2} \qquad c_{bed} = (\,0.,\ 0.\,)$$

$$q_2 = \frac{373\, c_2}{1 + 1573\, c_1 + 2565\, c_2} \qquad c_{feed} = (\,0.001\ ,\ 0.0009\,)$$

Fig. 1. Hodograph and adsorption isotherms [4] for solutes 1 and 2; F: feed condition, A: first plateau for solute 1, B: second plateau for solute 2, I: initial bed condition.

represent the nonlinear competing solute system. The adsorption parameters are shown in Fig. 1. The interstitial velocity chosen for the computer calculation was 2 cm/sec, and the values for the interstial and intrastitial porosities were 0.5 and 0.7, respectively. A general perspectives for the elution behavior of solutes in a column can be obtained from the relation between solute concentrations, as shown in Fig. 1. This hodograph was calculated from Eqs. (6) and (10), starting from point I (initial bed condition of $c_1=0$ g/cm^3 and $c_2=0$ g/cm^3), and F (feed condition of $c_1=0.001$ g/cm^3 and $c_2=0.0009$ g/cm^3). The concentration increment of solute 1 was 10^{-6} g/cm^3. The higher eigenvalues (λ_1) constitute the line IB and FA, while the smaller eigenvalues (λ_2) constitute the line IA and FB. The λ value increases along the line FBI and decreases along IAF.

The resulting breakthrough curves are drawn in Fig. 2, where the numbered lines represent the constant concentration (concentration units are omitted for convenience); 1 [$c_1=0.001$, $c_2=0.0009$ (F), then after passing shock wave, $c_1=0.00167$, $c_2=0$ (A)], 2 ($c_1=0.0008$, $c_2=0.00075$, then $c_1=0.00133$, $c_2=0$), 3 ($c_1=0.0006$, $c_2=0.00061$, then $c_1=0.00100$, $c_2=0$), 4 ($c_1=0.0004$, $c_2=0.00046$, then $c_1=0.00066$, $c_2=0$), 5 ($c_1=0.0002$, $c_2=0.00031$, then $c_1=0.00033$, $c_2=0$), 6 [$c_1=0$, $c_2=0.00017$ (B), then $c_1=0$, $c_2=0$ (I_2)], 7 [$c_1=0$, $c_2=0.00017$ (B)], 8 ($c_1=0$, $c_2=0.0001$), 9 ($c_1=0$, $c_2=0.00005$), 10 [$c_1=0$, $c_2=0(I_3)$]. The dashed lines in the hodograph are simply to show that the numbered points at the ends of the lines denote the lines of the same concentration numbered same in Fig. 2.

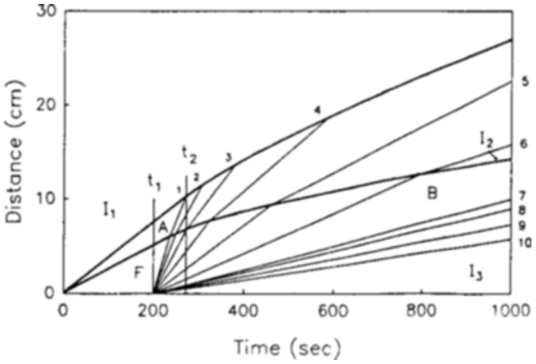


Fig. 2. Breakthrough curves of solutes 1 and 2; F: feed condition, A: first plateau for solute 1, B: second plateau for solute 2, I_1: initial bed condition, I_2: region between the elution curves of solutes 1 and 2, I_3: region after the elution curves of solute 2.

Note that the point numbered 6 (upper) and 7 at the same time, and B for the same concentration ($c_1=0$, $c_2=0.00017$) in the hodograph correspond to the plateau B, surrounded by the lines 6 and 7 in Fig. 2. The points numbered 8, 9 and 10 are only for solute 2 as solute 1 already passed through. The λ value decreases and the velocity increases at the same time by Eq. (7) along the line IA in the hodograph.

A shock wave develops between I_1 and A, because at a fixed point in the column, the fast moving plateau A (high concentration) catches up the slow moving baseline I_1 (low concentration). Along the line AF, the λ value decreases and the velocity increases. For solute 1, the fast moving plateau F (low concentration) pushes the slow moving plateau A (high concentration), resulting in a shock wave between A and F. For solute 2, the fast moving plateau F (high concentration) catches up the slow moving baseline (low concentration), resulting in a shock wave between A and F.

The λ value increases and the velocity decreases along the line FB. As the concentrations of the solutes at point F are higher than those at point B, diffusive waves of solute 1 and 2 develop between F and B. Along the line BI, the λ value increases and the veloc-

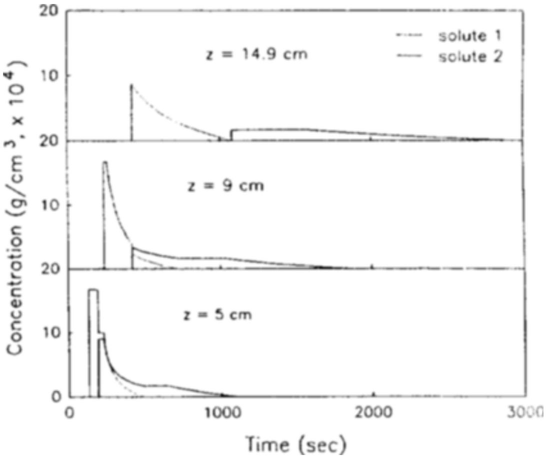


Fig. 3. Elution curves of solutes 1 and 2 at different column lengths.

ity decreases. As the concentration of solute 2 is higher at point B than at point I, a diffusive wave of solute 2 develops between B and I_3. Along the line AI, the λ value increases and the velocity decreases. As the concentration of solute 1 is higher at point A than at point B, a diffusive wave of solute 1 develops between A and I_2. We can judge from these that a shock wave develops in the front end and a diffusive wave in the rear end. The thick lines including those between I_1 and A, A and F, and I_2 and B are the shock wave paths. The thin lines between A through I_2, F through B, and B through I_3 are diffusive wave paths. Solute 2, the more strongly adsorbed species, displaces solute 1, resulting in region A where the concentration of solute 1 is higher than the feed concentration.

Elution curves of solutes at different column lengths are shown in Fig. 3. At a column length of 5 cm, we can observe solute 1 being displaced by the more strongly adsorbed solute 2 and forming a plateau (A), the concentration of which is 0.00167, higher than that of the feed. Both solutes show shocks at 193 sec. The second plateau of solute 1 disappears at a column length of 9 cm, while the first plateau (A) holds, though the length of which is shortened. At the same length of the column, the first plateau of solute 2 disappears, while the length of the second plateau (B) is lengthened. The elution curves verify the fact that a discontinuity in one solute concentration must accompany that of the other solute. Finally, the two solutes are separated completely from each other at a column length of 14.9 cm. The second plateau of solute 2 is to disappear as it continues to migrate along the column.

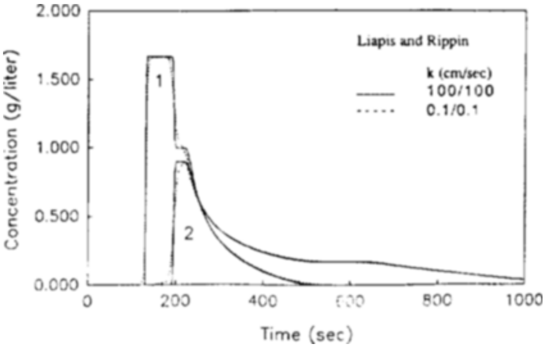


Fig. 4. Elution curves of solutes 1 and 2 calculated from the mass transfer model with different values of mass transfer coefficients at z=5 cm.

The total mass of each solute in the column at time t_1 was numerically calculated to be exactly same as in the feed. The mass balance was exact for solute 1 and was less than 3% off for solute 2 at time t_2. The deviation in the mass balance of solute 2 is ascribed to the inherent error originated from the numerical addition.

The elution behaviors of nonlinear, coupled system predicted in this study was partly confirmed by comparing them with the elution curves predicted by the mass transfer model. In the mass transfer model, we assume that the rate of variation of the concentration of each component in the stationary phase is proportional to the difference between the actual concentration in this phase and the equilibrium value with respect to the corresponding mobile phase concentration. The mass transfer coefficient (k) works as the proportionality constant in that relation. For the same nonlinear adsorption isotherms [4], the elution curves of the two solutes, calculated numerically from the mass transfer model, are shown in Fig. 4. Finite difference method was used for the numerical integration. The elution curves look closer to the ones at $z=5$ cm in Fig. 3 as the k values (cm/sec) for each solute become larger from 0.1/0.1 to 100/100, confirming the propriety of this method. Note that in the local equilibrium model upon which the theory of this study is based, the mass transfer resistance is neglected (i.e., the k value is infinite).

A simple scaling relation between column length and feed period were examined by calculating the breakthrough curves with different feed periods. As shown in Table 1, the time and distance of the complete separation of two solutes vary exactly in proportion to the feed periods. For example, the solutes of

Table 1. Scaling behaviors of nonlinear coupled chromatographic system

Feed period (sec)	Complete separation	
	Time (sec)	Distance (cm)
50	269.9	3.73
100	539.8	7.46
200	1079.5	14.92

same concentration can be found at doubled distance and at doubled elution time for the doubled feed period. Therefore, a same separation can be achieved with the column length and elution time which are proportional to the previous ones implying a successful scaling.

In summary, we developed simple mathematical manipulations based on the mass balance in a column to describe the separation behaviors in a nonlinear, coupled chromatographic system. Compared with the previous attempts, this study is relatively easy to understand the physical meanings underlying each equation derived. Also, many nonlinear adsorption isotherms differentiable with respect to the constituting fluid concentration, such as polynomial or bi-Langmuir type, are considered to be analyzed by this method. The calculated elution curves with different feed periods illustrate that the scaling rules successfully applied to the nonlinear, coupled chormatographic systems, often occurring in bioseparation processes. The applications of this analysis to the nonisocratic elution chromatography and related separation processes such as chromatofocussing and isotachophoresis remain as future works.

NOMENCLATURE

c_i : concentration of solute i in fluid phase [g/cm^3]
c_i^a : concentration of solute i in fluid phase after the shock wave [g/cm^3]
c_i^b : concentration of solute i in fluid phase before the shock wave [g/cm^3]
q_i : concentration of solute i in solid phase [g/cm^3]
q_i^a : concentration of solute i in solid phase after the shock wave [g/cm^3]
q_i^b : concentration of solute i in solid phase before the shock wave [g/cm^3]
t : time [sec]
v : interstitial velocity [cm/sec]
v_s : solute movement velocity [cm/sec]

Greek Letters

α : interstitial porosity
ε : intrastitial porosity
λ : eigenvalue of Jacobian in Eq. (6)

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