ANALYTICAL SOLUTION OF THE IDEAL MODEL OF ELUTION CHROMATOGRAPHY IN THE CASE OF A BINARY MIXTURE WITH COMPETITIVE LANGMUIR ISOTHERMS

II. SOLUTION USING THE *h*-TRANSFORM

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SUMMARY

   Using the results published by Helfferich and Klein, an exact solution of the ideal model of chromatography (infinite column efficiency) is derived, giving the band profiles for the two-component elution problem in the case when the equilibrium isotherms are given by the classical competitive Langmuir equations. The variations of the band profile of each component during elution is analyzed and the interactions between the two profiles are investigated. Two concentration shocks appear, one at the front of each component elution profile. The chromatogram is separated into three zones. The first zone, between the two concentration shocks, contains only the first component. The second zone, immediately after the second shock, contains a mixture of the two components. The third zone, at the rear, contains only the second component. The profiles of the two components in the three zones and their concentrations on both sides of the second shock are given by simple analytical equations. If the sample is injected as a rectangular pulse, it takes some time to erode the corresponding concentration plateaux of each component. On both sides of the mixed zone, a second concentration plateau appears for each component. The heights of these plateaux remain constant as long as they are present. The first component plateau disappears rapidly, but the second component plateau, whose formation explains the "tag-along" effect, remains stable as long as the second zone has not vanished and decreases progressively after the two bands are resolved.
   Comparison between the profiles obtained as solutions of the ideal model and those calculated using the program of the semi-ideal model, which accounts for the finite efficiency of actual columns, shows very good agreement when the column efficiency exceeds a few hundreds to 1000 plates. The extent of the agreement depends on both the sample size and the column efficiency. The concentration shocks are replaced by shock layers whose thickness is proportional to the column plate height, but depends also on the shock height. The thickness of the second shock, which separates the first and second zones, seems to depend much more than the thickness of the first shock on the actual column efficiency.

INTRODUCTION

        In a previous paper[1], we discussed the derivation of an analytical solution of the ideal model of chromatography in the case of a two-component problem and for the injection of a rectangular pulse of mixture (elution). This solution further assumes that the equilibrium isotherms of the two components in the chromatographic phase system is Langmuirian. We used classical results of the theory of systems of non-linear, quasi-hyperbolic partial differential equations applied to the case of hyperbolic systems such as those encountered in the classical model of ideal chromatography[2,3]. The most important concepts used in this first derivation were the association of a velocity to each value of the concentration and the possibility for the system to propagate concentration shocks or discontinuities[4–6]. Accordingly, the analytical solution obtained is composed of two concentration discontinuities, the first affecting the first component only and the second one affecting both, and of four continuous concentrations profiles that have relatively simple equations[1].
        The purpose of this paper is to show that the same results can be derived using the general theory of the ideal model of chromatography constructed by Helfferich and Klein[7] and based on the use of the concept of coherence and of the h-transform. The advantage of this second solution is that it makes use of a theoretical tool specifically developed for handling problems of application of the ideal model of chromatography and, accordingly, the analytical solution of a two-component problem appears simpler to derive in that way. A first drawback, however, is that the approach derived by Helfferich and Klein[7] has received modest attention from chromatographers who are not familiar with its distance–time diagrams or with the concepts of coherence and of composition trajectories. A second drawback, which may in part explain that first, is that Helfferich and Klein essentially used their approach to investigate displacement chromatography[7]. This mode of chromatography is claimed by some[7,8] to be the most efficient one for preparative applications. Most users have not yet accepted this last point and, in practice, elution remains the mode of choice for most of the chromatographic purifications carried out in biotechnology laboratories. In addition to the experimental difficulties associated with the need to find a suitable displacer for each separation, this resistance appears to be due to the requirement of a close to total recovery yield by workers who have spent much time and energy in the preparation of minute amounts of rare and valuable biochemicals.
        More important, the approach of Helfferich and Klein is closely related to the ideal model and suffers from its unrealistic assumption of an infinitely efficient column. The shock theory suffered originally from the same difficulties, but is has been completed later by the concept of the shock layer, also derived from aeronautical research[9], which gives it a much deeper physical relevance and permits, in chromatography, the convenient handling of columns of finite efficiency. A shock layer propagates at the same velocity as the shock but has a thickness proportional to the column height equivalent to a theoretical plate[10]. In contrast, it has not been possible yet to correct the results derived using the approach of Helfferich and Klein for the finite column efficiency which is responsible, in both the displacement and elution modes, for a considerable decrease in the recovery yield[11].

THEORY

The theory developed by Helfferich and Klein[7] is based on the use of the concept of coherence, on the determination of distance–time diagrams to represent the migration of band profiles and their progressive transformation and on the use of the h-transform to calculate the composition trajectories in these diagrams.

Helfferich and Klein called "coherent" those boundaries which migrate in a way such that "a given concentration of one species [then] remains accompanied by the same set of concentrations of all other species"[12]. This concept of coherent boundaries, first developed for breakthrough curves, has been extended to the migration of concentration pulses.

In principle, the theory of Helfferich and Klein, and especially the h-transform itself, should be valid only for stoichiometric retention mechanisms, such as ion exchange. Its extension to other retention mechanisms such as adsorption is straightforward, however, by assuming a fictitious component guaranteeing stoichiometric exchanges between the mobile and stationary phases.

Helfferich and Klein[13] published distance–time diagrams that describe the process of migration, dilution and progressive separation of the bands of the two components of a binary mixture injected as a rectangular pulse[13]. These diagrams have been calculated in the case when the equilibrium isotherm of the two components studied between the phases of the chromatographic system are given by the classical Langmuir isotherms. Hence these diagrams apply to the case we are investigating. However, they calculated only the trajectories of a given concentration, not the elution profiles of the two bands. This derivation is carried out here. We do not report the derivation of the trajectories, for which the interested reader is referred to the original work[7]. In the second part of this paper, the equations obtained for the different parts of the double band elution profile are compared with the results of the semi-ideal model[14].

Preliminary calculations

The principle of the h-transform is to replace the concentrations of the three compounds present in the band (the two components of the mixture and the fictitious compound required as explained above) by the two roots of an equation in h, where h is a dummy variable.

In the case of Langmuir competitive isotherms for the two components of a binary mixture eluted by a pure mobile phase, the h-transform is written as

$$\sum_{i=1,2} \left[\frac{b_i C_i}{(ha_i/a_1) - 1} - 1 \right] = 0 \tag{1}$$

where the coefficients a_i and b_i are those of the Langmuir isotherms (see Table I, eqn. I.1) and C_i is the local concentration of component i in the mobile phase.

This equation has two roots, h_1 and h_2. In contrast to the notation used by Helfferich and Klein, we interchange the subscripts 1 and 2, using the subscripts 1 for the first eluted component and the subscript 2 for the second one. The subscript

3 represents the dummy component, as in ref. 7. As chromatographers classically use $\alpha = a_2/a_1$ for the selectivity of the phase system, we use β where they use α, for

$$\beta = \alpha_{22}\ \alpha_{21}\ \alpha_{23} = \frac{a_2}{a_2} \cdot \frac{a_2}{a_1} \cdot \frac{a_2}{R} = \frac{a_2^2}{a_1 R} \tag{2}$$

since for the fictitious solute $\alpha_{23} = a_2/R$, with $R = \Sigma_i q_i/\Sigma_i C_i = $ constant. The value of that constant can be chosen arbitrarily in the interval $(0, a_1)$. q_i and C_i are the concentrations of the compound i in the stationary and the mobile phases, respectively, at equilibrium.

The solutions of eqn. 1 are:

$$h_1 = \frac{S + \sqrt{(S^2 - 4P)}}{2} \tag{3}$$

and

$$h_2 = \frac{S - \sqrt{(S^2 - 4P)}}{2} \tag{4}$$

where S and P are the sum and the product of the roots h_1 and h_2, respectively. S and P are derived by reducing eqn. 1 to its canonical form:

$$S = h_1 + h_2 = \alpha + 1 + b_2 C_2 + \alpha b_1 C_1 \tag{5}$$

and

$$P = h_1\ h_2 = \alpha(1 + b_2 C_2 + b_1 C_1) \tag{6}$$

Particular values of h_i used later are those corresponding to the pure eluent $(C_1 = C_2 = 0)$:

$$h_2' = 1; \qquad h_1' = a_2/a_1 = \alpha \tag{7}$$

and the values, h_1° and h_2°, which correspond to the injected sample, and which are obtained by inserting the initial concentrations C_1° and C_2° in eqns. 5 and 6.

In order to compare the results derived in this paper with those calculated in our previous work, we need to derive a relationship between the roots of eqn. 1, h_1° and h_2°, and the roots, r_1 and r_2, of the Offord equation, $i.e.$, the equation which gives the characteristics of the Clairaut differential equation associated with the system of partial differential equations of the ideal model (eqn. 22 in ref. 1). This equation establishes a relationship between the concentrations of the two components which is valid as long as they coexist in the column. The Offord equation is written as

$$\alpha b_1 C_2^\circ r^2 - (\alpha - 1 + \alpha b_1 C_1^\circ - b_2 C_2^\circ)r - b_2 C_1^\circ = 0 \tag{8}$$

Comparison between the roots of eqn. 1, at $C_i = C_i^\circ$, and those of eqn. 8 gives

$$h_2^\circ = 1 + (b_2 + \alpha b_1 r_2)C_2^\circ = 1 + b_2(C_2^\circ - C_1^\circ/r_1) = 1 + b_2 C_2^B = \frac{\alpha}{\gamma} \tag{9}$$

where γ is defined in ref. 1 as $(\alpha b_1 r_1 + b_2)/(b_2 + b_1 r_1)$ and r_1 is the positive root of eqn. 8. C_2^B is the concentration of the plateau of the second component which appears immediately after the end of the second zone of the chromatogram[1] and is equal to $C_2^\circ - C_1^\circ/r_1$.

Finally, the adjustable time, τ, considered in the equations derived by Helfferich and Klein[7] is

$$\tau = \frac{u}{FR}\left(t - \frac{z}{u}\right) \tag{10}$$

and the pulse time $(\Delta\tau)$ is

$$\Delta\tau = \frac{u t_p}{FR} \tag{11}$$

where F is the phase ratio, t_p the width of the rectangular pulse of sample injected in the column and R is defined in eqn. 2.

TABLE I

DEFINITIONS

(1) *Equilibrium isotherms:*

$$q_i = a_i C_i/(1 + b_1 C_1 + b_2 C_2) \tag{I.1}$$

where q_i and C_i are the concentration of component i at equilibrium in the stationary and mobile phases, respectively

(2) *Relative retention:*

$$\alpha = a_2/a_1 \tag{I.2}$$

(3) *Constant γ:*

$$\gamma = \frac{\alpha b_1 r_1 + b_2}{b_1 r_1 + b_2} \tag{I.3}$$

(4) *Roots of the Clairaut differential equation:*
    They are the roots $(r_1 > 0, r_2 < 0)$, of the following equation:

$$\alpha b_1 C_2^\circ r^2 - (\alpha - 1 + \alpha b_1 C_1^\circ - b_2 C_2^\circ)r - b_2 C_1^\circ = 0 \tag{I.4}$$

(5) *Loading factor:*

$$L_f = \left(1 + \frac{b_1 r_1}{b_2}\right)L_{f,2} \tag{I.5}$$

$$L_{f,2} = \frac{b_2 C_2^\circ t_p}{t_{R,2}^\circ - t_0} = \frac{b_2 N_2}{F_v(t_{R,2}^\circ - t_0)} = \frac{b_2 N_2}{\varepsilon S L k_{o,2}'} \tag{I.6}$$

Table I gives some useful definitions and equations used in the following sections.

Trajectory of the second component shock and time of certain events

When a rectangular pulse of the binary mixture is injected, and the two components have competitive Langmuir isotherms, the front of each concentration profile is sharp (discontinuity) and the rear is diffuse, or continuous[10]. Consider the plateau at the top of this rectangular injected pulse. The front part moves as the shock, *i.e.*, more slowly than the rear which migrates as a continuous profile[1], so the width of this plateau narrows progressively.

In a distance–time diagram, the coordinates of the intersection between the trajectory of the sharp front (shock) of the second component and the beginning of the continuous part of the first component profile (point I in ref. 1) is given by eqn. A.77 in ref. 7:

$$z_0 = \frac{h_2' h_2^\circ h_1^{\circ 2}}{(h_1^\circ - h_2')\beta} \cdot \Delta\tau \tag{12}$$

and

$$\tau_0 = \frac{h_1^\circ}{h_1^\circ - h_2'} \cdot \Delta\tau \tag{13}$$

Inserting eqns. 2, 6, 7, 10, 11 in eqns. 12 and 13 gives

$$z_0 = ut_p \cdot \frac{(1 + b_1 C_1^\circ + b_2 C_2^\circ)^2}{Fa_2(1 + b_1 C_1^\circ + b_2 C_2^\circ - h_2^\circ/\alpha)} \tag{14}$$

and

$$t_0 = \frac{z_0}{u}\left(1 + \frac{Fa_2}{1 + b_1 C_1^\circ + b_2 C_2^\circ}\right) \tag{15}$$

Eqns. 14 and 15 are identical with eqns. 33 and 34 in ref. 1 if h_2° is replaced by its value given by eqn. 9.

The trajectory of the front of the slower band beyond *I* is given by eqn A.85 in ref. 7:

$$z_{A_2(\tau)} = \frac{h_2' h_2^\circ}{\beta}[\sqrt{h_2'(t - \Delta\tau)} + \sqrt{(h_1^\circ - h_2')\Delta\tau}]^2 \tag{16}$$

Combining eqns. 2, 6, 7 and 9–11 with eqn. 16 and solving for *t* gives

$$t = t_p + \frac{z}{u} + \gamma\left[\sqrt{Fa_2 \cdot \frac{z}{u}} - \sqrt{\left(b_1 C_1^\circ + b_2 C_2^\circ + 1 - \frac{1}{\gamma}\right)t_p}\right]^2 \tag{17}$$

which is identical with eqn. 38 in ref. 1. Replacing *z* by *L* and *z/u* by t_0 (dead time) in this equation gives the retention time of the second component, *i.e.*, the elution time of the

second discontinuity of the chromatogram (eqn. 40 of ref. 1). Eqn. 17 remains to represent the trajectory of the second component shock as long as there is a mixed band, *i.e.*, until the separation is complete. The separation between the two bands is just complete at the "crossover point", the coordinates of which are given by eqns. A.88 in ref. 7:

$$z_{1/2} = \frac{h_2^{\circ} h_2' h_1'^2 (h_1^{\circ} - h_2') \Delta\tau}{(h_1' - h_2')^2 \beta}$$ (18)

and

$$\tau_{1/2} = \left[1 + \frac{h_2'(h_1^{\circ} - h_2')}{(h_1' - h_2')^2} \right] \Delta\tau$$ (19)

Combining eqns. 2, 6, 7 and 9–11 with eqns. 18 and 19 gives

$$z_{1/2} = u \left(\frac{\alpha}{\alpha - 1} \right)^2 \cdot \frac{t_p(b_1 C_1^{\circ} + b_2 C_2^{\circ} + 1 - 1/\gamma)}{F a_2}$$ (20)

and

$$t_{1/2} = t_p + \frac{z_{1/2}}{u} \left(1 + \frac{\gamma F a_2}{\alpha^2} \right)$$ (21)

which are identical with eqns. 69 and 70 in ref. 1, giving the trajectory of the point where the resolution between the two bands is just complete. Beyond that point, the slow component band begins to migrate alone but, first, the plateau which has appeared during the progressive separation between the bands of the two components shrinks and disappears. During that time, the trajectory of the front shock of its band is given by the relationship A.93 in ref. 7:

$$z_{\Delta_2(\tau)} = \frac{h_2' h_1' h_2^{\circ}}{\beta} \left(\tau + \frac{h_1^{\circ} - h_2'}{h_1' - h_2'} \cdot \Delta\tau \right)$$ (22)

Combining this equation with eqns. 2–11 gives

$$t = t_p + \frac{z}{u} + \gamma \left[F a_1 \cdot \frac{z}{u} - \frac{t_p(1 + b_1 C_1^{\circ} + b_2 C_2^{\circ} - 1/\gamma)}{\alpha - 1} \right]$$ (23)

This equation is equivalent to eqn. 72 in ref. 1. While the second band front migrates on this trajectory, the concentration plateau of component 2 shrinks. It disappears at point *L* (see ref. 1) of coordinates given by eqn. A.56 in ref. 7:

$$z_2 = \frac{h_2^{\circ 2} h_2' h_1' (h_1^{\circ} - h_2') \Delta\tau}{(h_1' - h_2')(h_2^{\circ} - h_2')\beta}$$ (24)

and

$$\tau_2 = \left[1 + \frac{h_2'(h_1^\circ - h_2')}{(h_1' - h_2')(h_2^\circ - h_2')}\right]\Delta\tau \tag{25}$$

These equations may be rearranged as the previous ones into

$$z_2 = \frac{\alpha - 1}{\alpha - \gamma} \cdot z_{1/2} \tag{26}$$

and

$$t_2 = t_p + \frac{z_2}{u}\left(1 + \frac{Fa_2\gamma^2}{\alpha^2}\right) \tag{27}$$

which are identical with eqns. 73 and 74 in ref. 1.

Finally, eqn. A.93 in ref. 7 gives the trajectory of the second component front after the separation has been completed. After rearrangement, this equation becomes

$$t = t_p + \frac{z}{u} + \left(\sqrt{Fa_2 \cdot \frac{z}{u}} - \sqrt{b_2 C_2^\circ t_p}\right)^2 \tag{28}$$

which is equivalent to eqn. 75 in ref. 1, with $z = L$.

The main equations in this section, which give the position of the most important events on the chromatogram, are summarized in Table II. The corresponding points are shown in Fig. 1.

Equations for the continuous parts of the profiles

As the continuous parts of the concentration profiles of the first and second components were given by Helfferich and Klein[7] as the H-function roots, we have to transform the h roots into concentrations. This can be done using the general equation

$$C_j = \frac{\pi_{i=1}^n(h_i a_j/a_1 - 1)}{b_j \pi_{i=1, i \neq j}^n(a_j/a_i - 1)} \tag{29}$$

In the case of two solutes we have

$$C_1 = \frac{(h_1/\alpha - 1)(h_2/\alpha - 1)}{b_1(1 - \alpha)/\alpha} \tag{30}$$

$$C_2 = \frac{(h_1 - 1)(h_2 - 1)}{b_2(\alpha - 1)} \tag{31}$$

In order to obtain the equations for the continuous parts of the profiles in the different zones of the chromatogram, we need to find first the roots h_1 and h_2 of the H-function in these zones.

TABLE II

RETENTION TIMES OF THE CHARACTERISTIC FEATURES OF THE CHROMATOGRAM IN FIG. 1

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(1) *Second shock:*

$$t_{R,2} = t_p + t_0 + \gamma(t^\circ_{R,2} - t_0)(1 - \sqrt{L_f})^2 \tag{II.1}$$

(2) *End of the first component band:*

$$t_B = t_p + t_0 + \frac{\gamma}{\alpha}(t^\circ_{R,1} - t_0) \tag{II.2}$$

(3) *End of the second component concentration plateau:*

$$t_{B'} = t_B + \frac{\gamma(\gamma - 1)}{\alpha^2}(t_{R,0,2} - t_0) \tag{II.3}$$

(4) *End of the second component band:*

$$t_e = t_p + t^\circ_{R,2} \tag{II.4}$$

(5) *First shock:*
The retention time of the first shock cannot be calculated analytically. It is derived by calculating the lower boundary of the finite integral of the profiles of the first component (eqns. III.1 and III.2, Table III). This integral is the mass of first component injected[1].

For the diffuse rear part of the slower band profile, the trajectory in a distance–time diagram associated with a certain concentration can be derived from eqns. A.80 and A.81 in ref. 7:

$$z''_2(\tau) = h^{\circ 2}_2 h'_1 \cdot \frac{\tau - \Delta\tau}{\beta} \qquad \text{for } z \leqslant z_2 \tag{32}$$

and

$$z(h_2, \tau) = h^2_2 h'_1 \cdot \frac{\tau - \Delta\tau}{\beta} \qquad \text{for } z \leqslant z_{\Delta_2(\tau)} \tag{33}$$

Accordingly, at the column exit ($z = L$), where we have $h'_1 = \alpha$ and $a_2 = (t^\circ_{R,2} - t_0)/Ft_0$, the h_2 root of the H-function in the different zones of the chromatogram is obtained by combining eqns. 2, 10, 11, 32 and 33:

$$h_2 = \sqrt{\frac{t^\circ_{R,2} - t_0}{t - t_p - t_0}} \qquad \text{for } t'_B < t \tag{34}$$
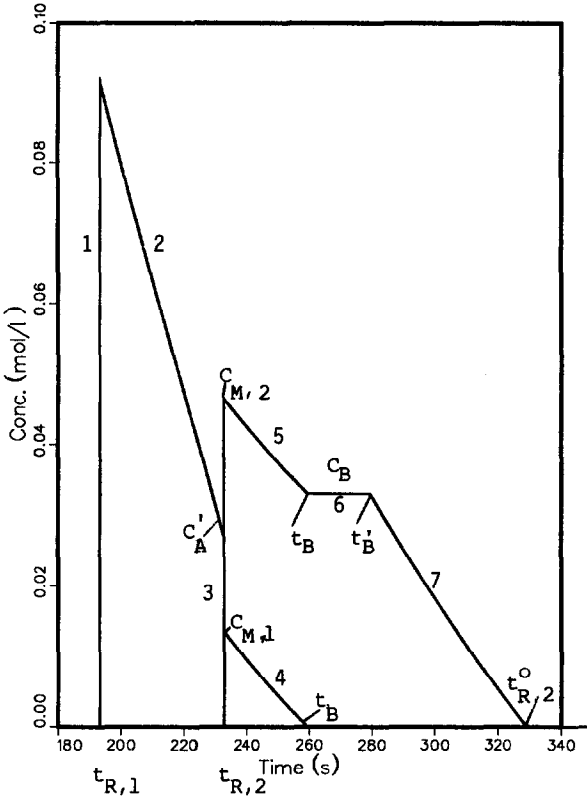
Fig. 1. Example of the solution of the ideal model for a two-component mixture when the two bands are not completely resolved at the end of the column. 1 = Front shock of the first component; 2 = first arc of the first component band; 3 = rear shock of the first component and front shock of the second component; 4 = second arc of the first component band; 5 = first arc of the second component band; 6 = concentration plateau of the second component band; 7 = second arc of the second component band. The retention times of the second concentration shock (3), the end of the first component band and of the mixed zone, the end of the concentration plateau (6) of the second component and the end of the second component zone are given in Table II. The equations for the continuous parts of the concentration profiles of the first component [between the two shocks (2) and after the second shock (4)] and of the second component (between the second concentration shock (5) and the beginning of the plateau and after the end of the plateau (7)] are given in Table III. Experimental conditions: relative retention, α = 1.20; relative composition, 1:1; feed concentrations, $C_1^\circ = C_2^\circ$ = 2.5 M; column length, 25 cm; phase ratio, F = 0.25; $k'_{0,1}$ = 6.0; injection duration, 1 s. Retention times of the fronts: 193.3 and 232.7 s. Retention times of the rear plateau of the second component profile: 259.4 and 279.3 s. Retention time of the second component at infinite dilution: 328 s. Concentrations of the first component: at the top of the first shock, 0.091 M; at the front of the second shock, 0.0027 M; at the rear of the second shock, 0.014 M. Concentration of the second component: at the top of the second shock, 0.046 M; at the rear plateau, 0.033 M.

$$h_2 = h_2^\circ = \alpha/\gamma \qquad \text{for } t_{R,2} \leqslant t \leqslant t'_B \qquad (35)$$

$$h_2 = h'_2 = 1 \qquad \text{for } t \leqslant t_{R,2} \qquad (36)$$

(see Tables II and III and Fig. 1 for the definition of t'_B and similar parameters).

TABLE III

EQUATIONS FOR THE CONTINUOUS PARTS OF THE CHROMATOGRAM SHOWN IN FIG. 1

(1) *First arc of the first component band:*

$$t = t_p + t_0 + (t_{R,1,0} - t_0) \left\{ \frac{1}{(1 + b_1 C_1)^2} - L_{f,2} \cdot \frac{\alpha - 1}{\alpha} \cdot \frac{1}{[(\alpha - 1)/\alpha + b_1 C_1]^2} \right\} \qquad \text{(III.1)}$$

(2) *Second arc of the first component band:*

$$C_1 = \frac{1}{b_1 + b_2/\alpha r_1} \left[\sqrt{\left(\frac{\gamma}{\alpha} \cdot \frac{t_{R,1}^\circ - t_0}{t - t_p - t_0} \right)} - 1 \right] \qquad \text{(III.2)}$$

(3) *First arc of the second component band:*

$$C_2 = \frac{1}{b_2 + \alpha b_1 r_1} \left[\sqrt{\left(\gamma \cdot \frac{t_{R,2}^\circ - t_0}{t - t_p - t_0} \right)} - 1 \right] \qquad \text{(III.3)}$$

(4) *Second arc of the second component band:*

$$C_2 = \frac{1}{b_2} \left[\sqrt{\left(\frac{t_{R,2}^\circ - t_0}{t - t_p - t_0} \right)} - 1 \right] \qquad \text{(III.4)}$$

Similarly, for the diffuse rear part of the faster pulse, the trajectories associated with a certain concentration (*i.e.*, value of h_1) in a distance–time diagram can be derived from eqns. A.84 and A.90 in ref. 7:

$$z(h_1, \tau) = h_1^2 h_2^\circ \cdot \frac{\tau - \Delta\tau}{\beta} \qquad \text{for } z \leqslant z_{\Delta_2(\tau)} \qquad (37)$$

and

$$z(h_1, \tau) = \frac{h_1^2 h_2'}{\beta} \left\{ \tau - \left[1 - \frac{(h_1^\circ - h_2')(h_2^\circ - h_2')}{(h_1 - h_2')^2} \right] \Delta\tau \right\} \qquad \text{for } z_{\Delta_2(\tau)} \leqslant z \leqslant z_{\Delta_1(\tau)} \quad (38)$$

Accordingly, at the column exit, the values of h_1 in the different zones of the chromatogram are given by

$$h_1 = \sqrt{\gamma \cdot \frac{t_{R,2}^\circ - t_0}{t - t_p - t_0}} \qquad \text{for } t_{R,2} \leqslant t \leqslant t_B \qquad (39)$$

$$h_1 = h_1' = \alpha \qquad \text{for } t_B < t \qquad (40)$$

and

$$t = t_p + t_0 + \frac{\alpha(t_{R,2}^\circ - t_0)}{h_1^2} - (\alpha - 1)b_2 C_2^\circ t_p \cdot \frac{1}{(h_1 - 1)^2} \qquad \text{for } t_{R,1} \leqslant t \leqslant t_{R,2} \quad (41)$$

Combining equations 9, 34–36 and 39–41 with eqns. 30 and 31 gives eqns. 43, 28 and 47 in ref. 1 (the two slanted parts of the rear profile of the second component band, before and after the intermediate plateau and the concentration of this plateau) and eqns. 63 and 44 in ref. 1 (the two parts of the rear profile of the first component band, before and after the second shock of the chromatogram).

The concentrations of the first and second components at the second shock are obtained as follows. In all instances, h_1 is obtained by solving eqn. 41 with $t = t_{R,2}$. On the front side of the second shock, h_2 is equal to 1; on the rear side of the second shock, h_2 is equal to α/γ (eqn. 35). The concentrations are obtained by substituting appropriate values of h_1 and h_2 in eqns. 30 and 31. The results are identical with eqns. 51, 52 and 55 in ref. 1 (see Table IV).

The equations giving the continuous parts of the profile are summarized in Table III. The position of the corresponding arcs are indicated on Fig. 1. The values of the concentrations in the most important points of the chromatograms are summarized in Table IV.

TABLE IV

EQUATIONS FOR SOME SPECIFIC CONCENTRATIONS

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(1) *Maximum concentration of the second component:*

$$C_{2,M} = \frac{1}{b_2 + \alpha b_1 r_1} \cdot \frac{\sqrt{L_f}}{1 - \sqrt{L_f}} \tag{IV.1}$$

(2) *Concentration of the first component on the front side of the second shock:*

$$C_{1,A'} = \frac{[(1 - \alpha)/\alpha] + \sqrt{L_f}}{1 - \sqrt{L_f}} \tag{IV.2}$$

(3) *Concentration of the first component on the rear side of the second shock:*

$$C_{1,M} = \frac{r_1}{b_2 + \alpha b_1 r_1} \cdot \frac{(1 - \alpha) + \alpha \sqrt{L_f}}{1 - \sqrt{L_f}} \tag{IV.3}$$

(4) *Concentration of the second component plateau:*

$$C_{2,B} = \frac{\alpha - 1}{b_2 + \alpha b_1 r_1} \tag{IV.4}$$

(5) *Concentration of the first component plateau:*

$$C_{1,A} = C_1^o\left(1 + \frac{b_2}{\alpha b_1 r_1}\right) \tag{IV.5}$$

(6) *Maximum concentration of the first component:*
    As the retention time of the first shock, the maximum concentration of the first component (*i.e.*, the front shock height) cannot be calculated analytically. This concentration is obtained by placing the retention time of the first component shock in eqn. III.1.

RESULTS AND DISCUSSION

In this section we first discuss the mechanism of the progressive separation of the bands of a binary mixture, as it can be derived from the profiles given by the analytical solution of the ideal model. Then we compare the profiles obtained by the analytical solution of the ideal model and by numerical solution of the semi-ideal model. In a separate publication[15], we shall show that there is excellent agreement between these theoretical profiles and those determined experimentally in the case when the components of a binary mixture equilibrate between the two phases of the chromatographic system as predicted by the competitive Langmuir isotherms.

Progressive separation of the bands of the two components
We have calculated the band profiles predicted by the equations in Tables II–IV for two binary mixtures of relative compositions 1:3 and 3:1. In the following illustrations, Figs. 2a–6a correspond to the 3:1 muxture and Figs. 2b–6b to the 1:3 mixture. The numerical values used for the parameters of the isotherms (eqn. I-1, Table I) are given in Table V. The feed concentrations of the two components are 1.25 and 3.75 M, respectively. The duration of the injection pulse, t_p, is 1 s. The value of the relative retention, α, is 1.30. The mobile phase velocity is 0.6 cm/s. The different chromatograms shown in Figs. 2–7 correspond to columns of increasing length. In all these figures, curves 1 and 2 are the elution profiles of the first and second components, respectively, predicted by the analytical solution of the ideal model derived from the equation in Tables II–IV. The profiles 3 and 4 are their elution profiles calculated using the numerical solution of the semi-ideal model. These profiles are discussed in the next section. Insets in the figures illustrate some particular features of the chromatogram.
Fig. 2a and b show the elution profiles of a binary mixture with a relative retention equal to 1.30 at the exit of a 1-cm long column. This length is less than z_0 (eqn. 12) and the plateaux of the two compounds corresponding to the injection pulse are not completely eroded yet. However, two plateaux at the concentrations $C_{1,A}$ and $C_{2,B}$ (Table IV) have formed. The first corresponds to an increase in the concentration of the first component, due to the displacement effect caused by the second component. The second plateau, on the tail of the second component, can be seen in the data file used to draw the plot but it is not visible on the figure. It can be distinguished on the inset in Fig. 2a, between 12 and 14 s. There is a distinct separation between the fronts of the two bands in Fig. 2a. This separation exists also in Fig. 2b, but it is smaller and is

TABLE V

NUMERICAL VALUES OF THE COEFFICIENTS OF THE COMPETITIVE LANGMUIR ISO-THERMS USED FOR THE TWO COMPOUNDS STUDIED

The column saturation capacity for the first component is 1.59 mmol/cm (4.6 mm I.D.).

Coefficient	Value
a_1	24
a_2	31.2 ($\alpha = 1.30$)
b_1 (l/mol)	2.5
b_2 (l/mol)	3.25

barely visible. The band of the minor, first component (Fig. 2b) begins with a very thin spike which is easily explained by the mathematical properties of the solution[1] but has no chance of being seen in the experimental profiles because of the intense diffusion flux close to a shock layer.

Fig. 3a and b show chromatograms obtained under conditions such that the injection pulse plateau has just disappeared ($L = z_0$, see eqn. 12). The corresponding column lengths at which this phenomenon takes place are different with the 3:1 and the 1:3 mixtures, being 1.20 and 1.35 cm, respectively. The plateau of the first component, at $C_{1,A}$, begins immediately to erode away and disappears rapidly. On the other hand, the plateau of the second component at $C_{2,B}$ becomes longer and longer, while the two shocks becomes further apart. As the column length is barely longer for Fig. 3a and b than for Fig. 2, the separation between the two bands is hardly improved.
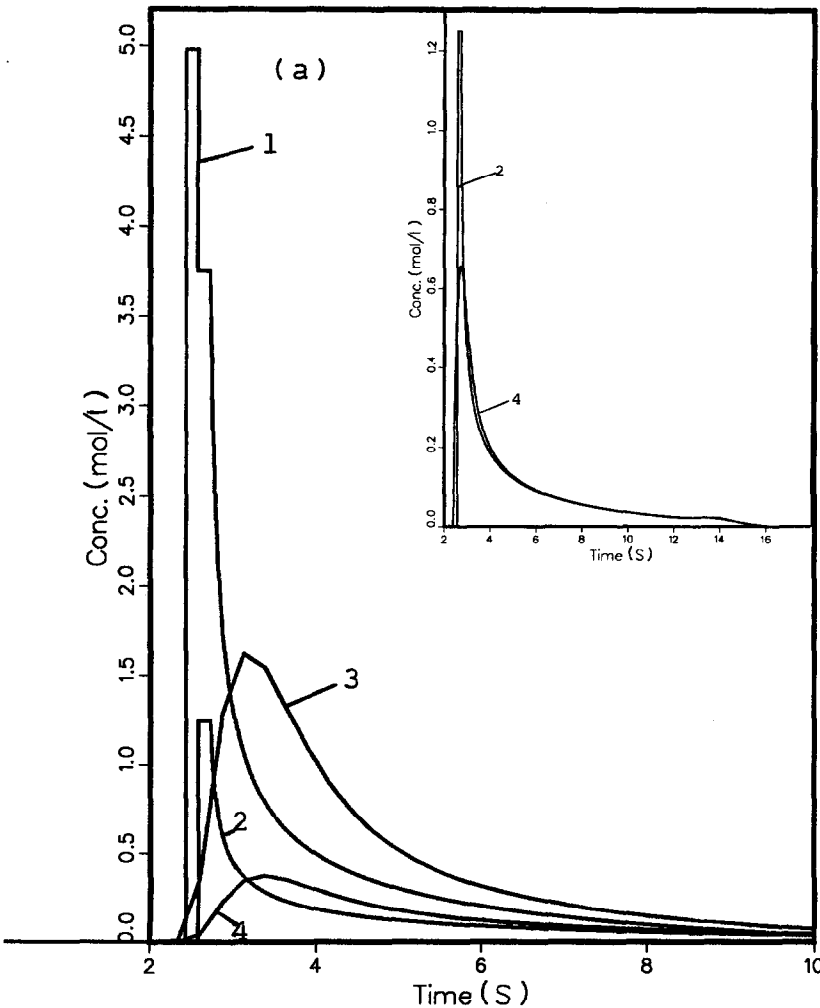
Fig. 2.
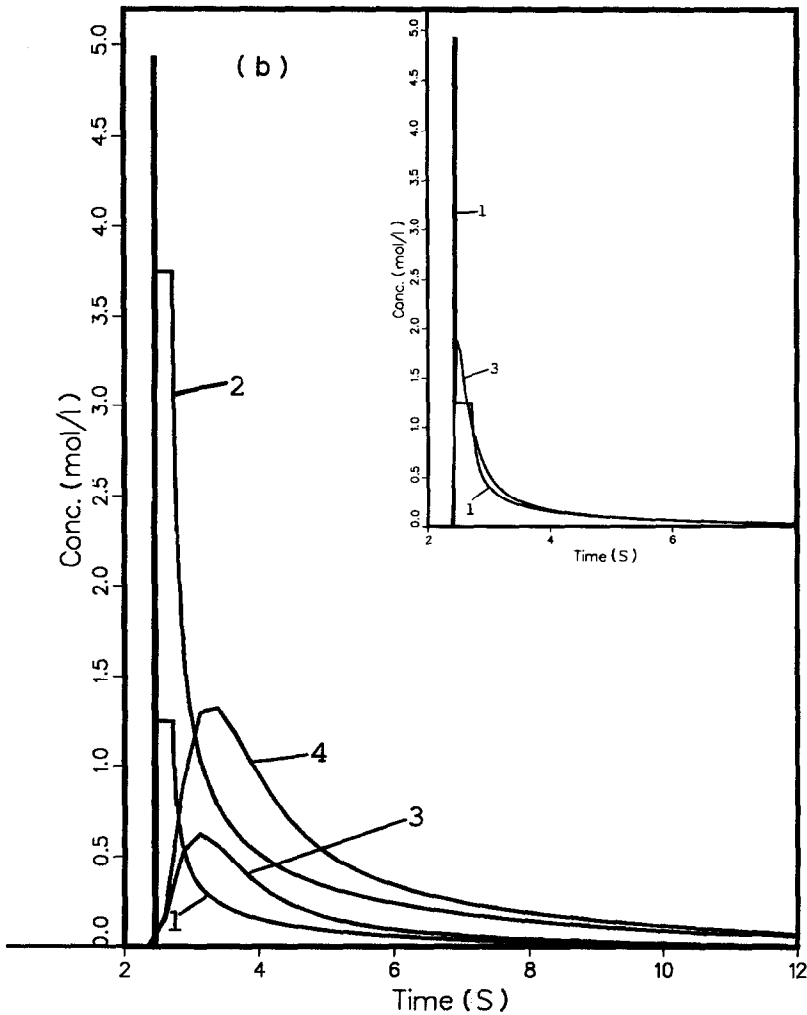
Fig. 2. Band profiles of the components of a binary mixture at the end of a 1-cm long column. Mobile phase flow velocity, 0.6 cm/s; flow-rate for a 4.6 mm I.D. column, 4.8 ml/min; $\alpha = 1.30$; $k'_{0,1} = 6.0$; phase ratio, 0.25; porosity, 0.80. Solution of the ideal model: curves 1 (first component) and 2 (second component). Numerical solution of the semi-ideal model with $H = 0.01$ cm: curves 3 (first component) and 4 (second component). Insets: numerical solution of the semi-ideal model with $H = 0.001$ cm. (a) Relative feed composition: 3:1. Concentrations of the components in the feed: $C^o_1 = 1.25\ M$, $C^o_2 = 3.75\ M$. $L_{f,2} = 31.25\%$. Inset: solution of the ideal model for the second component (curve 2) and solution of the semi-ideal model with $H = 0.001$ cm (curve 4). (b) Same as (a), including total sample size, except relative feed composition $= 1:3$. $C^o_1 = 3.75\ M$, $C^o_2 = 1.25\ M$. $L_{f,2} = 93.75\%$. Inset: solution of the ideal model for the first component (curve 1) and solution of the semi-ideal model with $H = 0.001$ cm (curve 3).

An intermediate chromatogram, on which a partial separation takes place between the two bands, is shown in Fig. 4a and b, both of which correspond to a column length of 10 cm. In the first instance (Fig. 4a), the first component has a small shock on its rear profile, at the time as the front shock of the second component takes place. The displacement effect of the first component by the second is weak. The rear

shock of the first component profile corresponds to an abrupt decrease in the amount of that component associated with the surge of the second component concentration which takes place at its front shock. The plateau at the end of the second component profile is long and this profile is spread over a period that considerably exceeds the width of the profile of the same amount of that compound when injected pure, under the same conditions. In Fig. 4b, the concentration discontinuities at the second shock are much more important that in Fig. 4a. The displacement effect of the first component by the second is very significant, because now the surge of concentration of the second component is very strong. The first component band has a very narrow, tall first part, followed by a small tail which lasts about twice as long as the first part of the band. On the other hand, the plateau on the rear part of the second component profile is narrow and its concentration is high. It will not result in a marked "tag-along" effect.
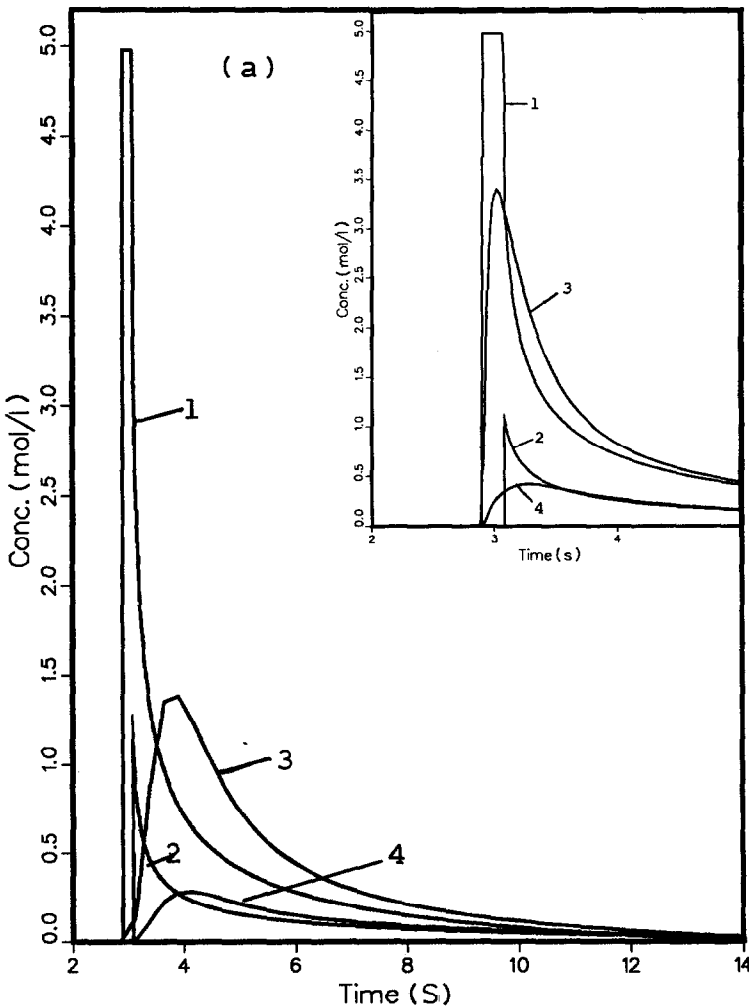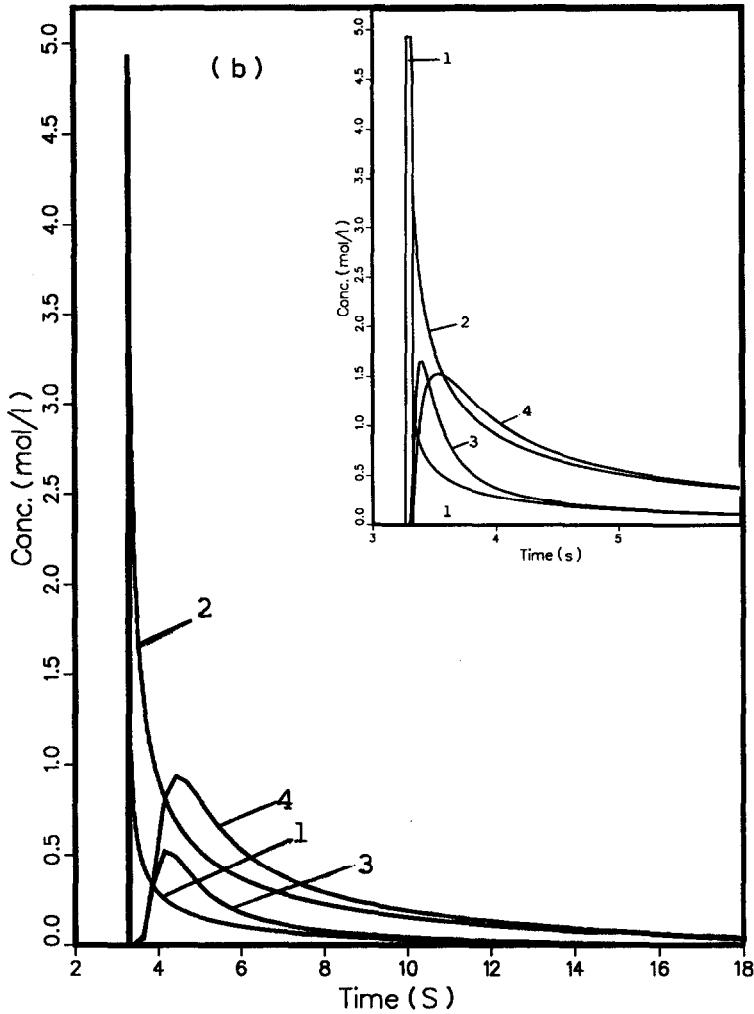

Fig. 3.

Fig. 3. Same as Fig. 2, but profiles at the end of a column such that the injection pulse plateau has just been eroded. (a) Same as Fig. 2a, but column length = 1.20 cm. $L_{f,2}$ = 26%. Inset: same as main figure, but H = 0.001 cm for the solution of the semi-ideal model. (b) Same as Fig. 2b, but column length = 1.35 cm. $L_{f,2}$ = 69.4%. Inset: same as main figure, but H = 0.001 cm for the solution of the semi-ideal model.

It is obvious in Fig. 4b that under the conditions selected, the first component can be recovered in a reasonable yield, with a high degree of purity, but that the same is not true for the second component.

The chromatograms in Fig. 5a and b correspond to the column length for which the mixed band or zone II of the chromatogram just disappears. The two bands are totally resolved for the first time. The shock of the second component is eluted just when the concentration of the first component becomes zero, the rear profile shock of this first component has just vanished, but there is still a plateau at the top of the second component profile. This phenomenon takes place for column lengths that

depend on the composition of the feed. The column length is equal to $z_{1/2}$ (see eqn. 20). In Fig. 5a and b, they are 19.7 and 22.2 cm for the 3:1 and the 1:3 mixtures, respectively.

Beyond the point where the two bands are resolved, they continue their migration. The plateau at the top of the second band erodes progressively because the velocity associated with a concentration on a continuous profile is higher than the velocity of a shock from the baseline to that same concentration[1]. The point at the back of the plateau of the second component moves faster than the point at its front, so the plateau narrows down and eventually disappears. Fig. 6a and b show the chromatograms at the column lengths for which this happens. The phenomenon takes place faster when the concentration of the second component is higher, because the plateau is much narrower (compare Fig. 5a and b). The corresponding column length is given by eqn. 26. It is much shorter in Fig. 6b ($L = 28$ cm) than in Fig. 6a ($L = 65.9$
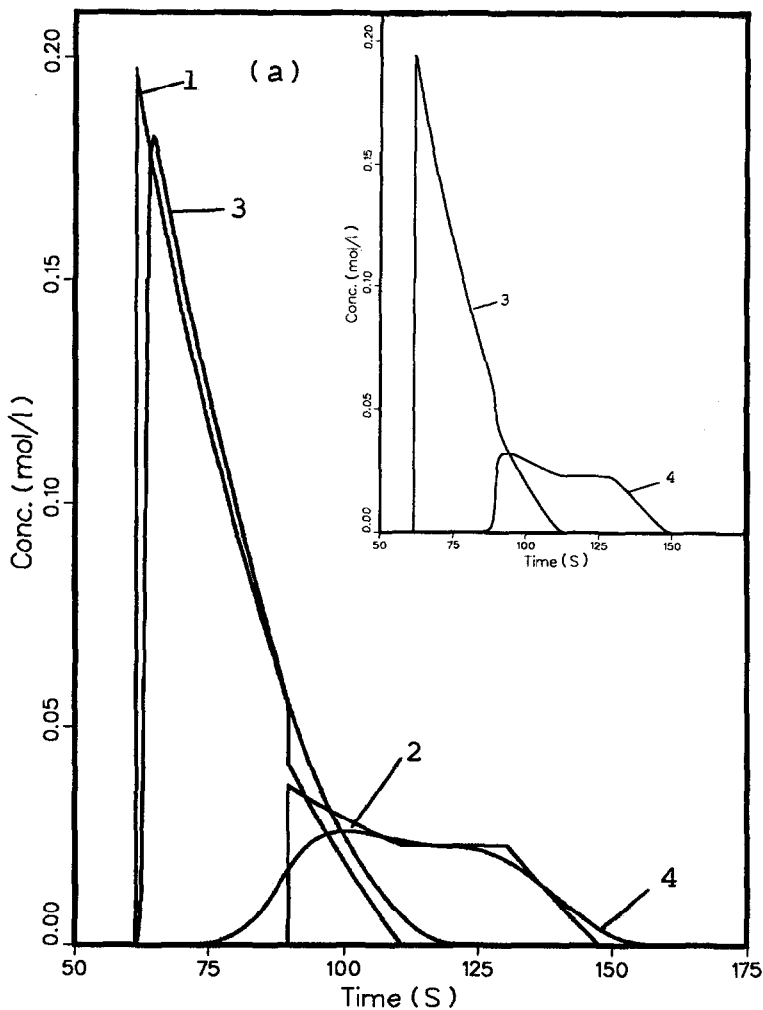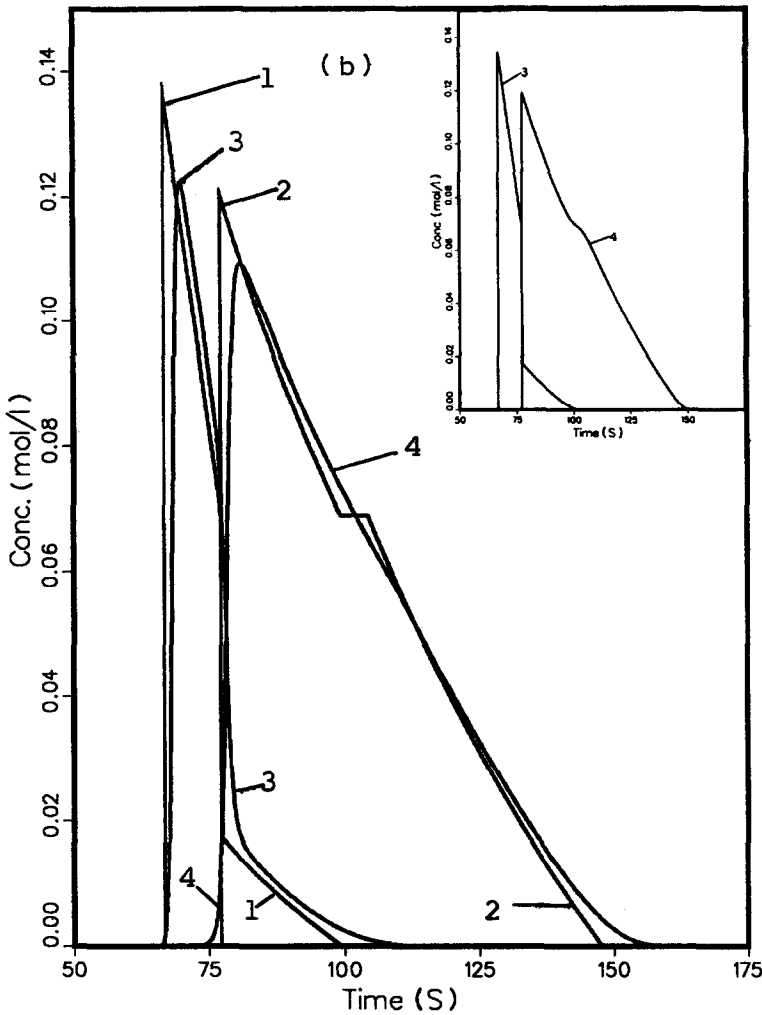

Fig. 4.

Fig. 4. Same as Fig. 2, except column length = 10 cm. (a) Same as Fig. 2a, 3:1 mixture. $L_{f,2}$ = 3.1%. Inset: concentration profiles of the two components obtained as solution of the semi-ideal model, with H = 0.001 cm (N = 10 000 theoretical plates). (b) Same as Fig. 2b, 1:3 mixture. $L_{f,2}$ = 9.3%. Inset: as for inset in (a).

cm), and the resolution between the two bands when the plateau disappears is much better in Fig. 6a.

When the plateau at the top of the second component band has disappeared, this band continues its migration as if it had never interacted with the first component band[1]. The band profile is identical with that for a band of the same amount of that compound injected pure (see Fig. 7). This is not true for the band of the first compound, which always remains narrower and taller than if no interaction had taken place. Fig. 8 illustrates this phenomenon. It shows a comparison between the band profiles of the same amount of the same 1:3 mixture derived from the single compound and from the two-component ideal model solutions. In the case of the two-component
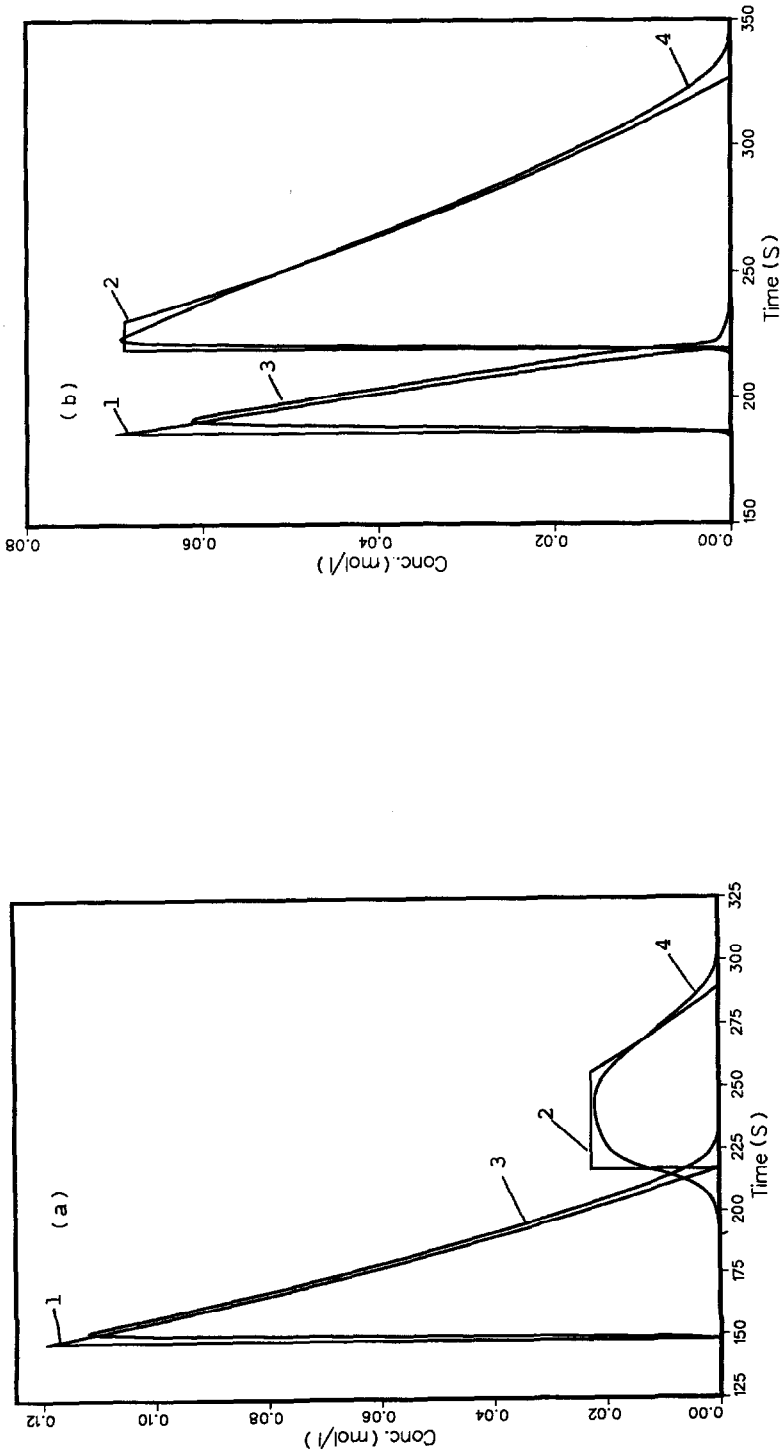
Fig. 5. Same as Fig. 2, but profiles at the end of a column such that the two bands are just resolved. (a) Same as Fig. 2a, 3:1 mixture, but column length = 19.7 cm. $L_{f,2}$ = 1.59%. (b) Same as Fig. 2b, 1:3 mixture, but column length = 22.2 cm. $L_{f,2}$ = 4.22%.
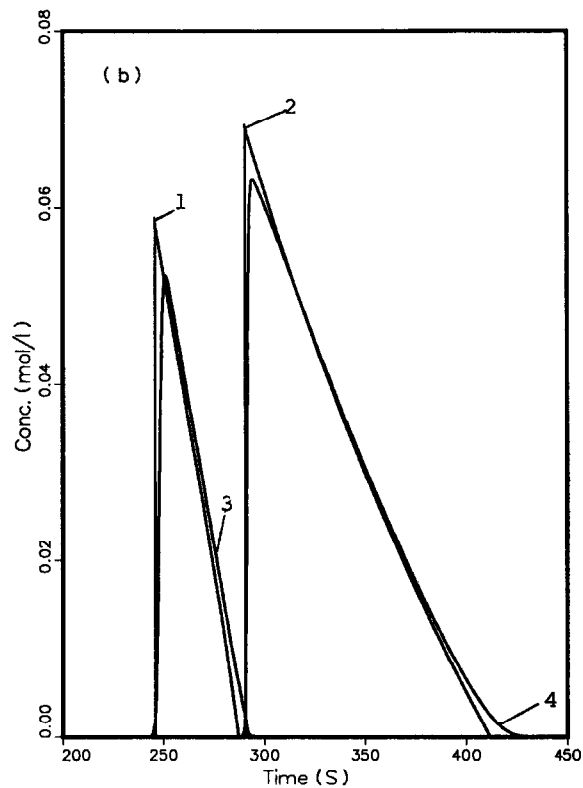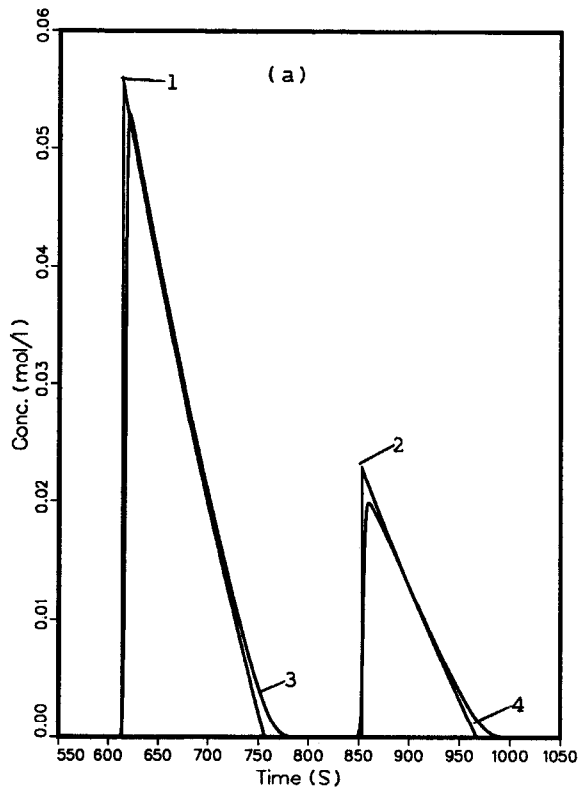
Fig. 6. Same as Fig. 2, but profiles at the end of a column such that the plateau at the top of the second component band is just totally eroded. (a) Same as Fig. 2a, 3:1 mixture, but column length = 65.9 cm. $L_{f,2}$ = 0.47%. (b) Same as Fig. 2b, 1:3 mixture, but column length = 28.0 cm. $L_{f,2}$ = 3.35%.
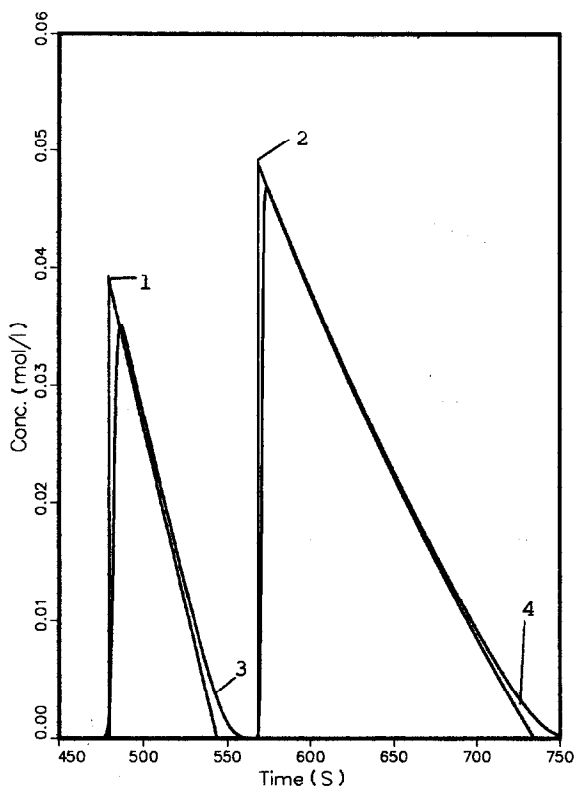
Fig. 7. Same as Fig. 2b, but at the end of a 50-cm long column. $L_{f,2} = 1.87\%$.

model, the solution obtained is that already shown in Fig. 7; this model takes the band interaction due to the competitive adsorption isotherms into account. The single compound model gives the band profiles which would be observed for compounds that do not interact. The profiles obtained for the second component are identical. In contrast, the profiles obtained for the first component are markedly different. The displacement of the first component by the second increases the resolution between the bands and also increases the maximum concentration of the fist component.

Comparison between the profiles predicted by the ideal and semi-ideal models
        In order to achieve as realistic a simulation as possible, we have assumed that the column height equivalent to a theoretical plate, H, is constant along the whole column. In Figs. 2–7, profiles 3 and 4 are those calculated using the semi-ideal model and selecting the integration increments in order to simulate a column with an HETP of 0.01 cm. This is a low efficiency for a high-performance liquid chromatographic column, but the simulated column is operated at a very high velocity of 0.6 cm/s because it has been shown that maximum production rate in preparative chromatography is achieved at high mobile phase flow velocities[16]. Under these conditions, this HETP value would correspond to a well packed column ($A = 1$ in the classical Knox plate-height equation[17]) filled with 15-μm particles and operated at a reduced
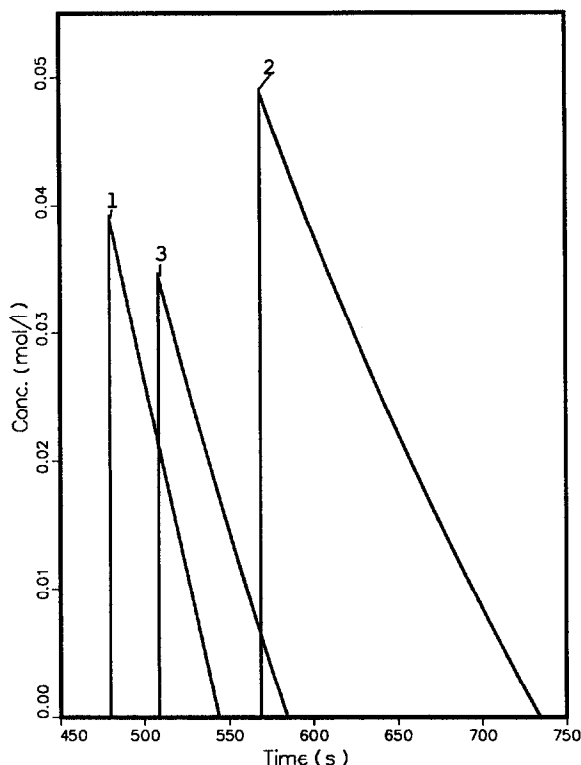
Fig. 8. Influence of the interaction term in the isotherm equation on the band profile of two well resolved compounds. Comparison between the solutions of the single-compound and the two-component ideal models for the same amount of the same sample as in Fig. 7. Profile 1, first component in a binary mixture; profile 2, second component in a binary mixture or alone (the two profiles cannot be distinguished); profile 3, first component alone.

flow-rate of approximately 90. As a term of comparison, profiles 3 and 4 in the insets in Figs. 2, 3 and 4 were calculated with a ten times lower HETP value. In practice, most experimental conditions correspond to intermediate values of the HETP.

The consequence of the choice of the HETP value is that, for very short columns (Fig. 2a–3b) which have a very low efficiency, the agreement between the profiles derived from the analytical solution of the ideal model and the profiles calculated numerically is poor. The apparent axial diffusion, which includes the consequences of a finite rate of mass transfer between the two phases, explains the shallow profiles 3 and 4 in Figs. 2 and 3. The concentration shocks have been considerably relaxed. Note, however, that the time scale is in seconds and that the front parts of these profiles last about 0.5 s (Fig. 2) to 1 s (Fig. 3). As predicted by the ideal model, however, the two fronts are nearly coincidental in Figs. 2b and 3b, whereas they are separated in Figs. 2a and 3a.

If we compare profiles 3 and 4 in Figs. 2a, 2b, 3a, 3b, 4a and 4b and the profiles in the insets in these figures, we see how the column efficiency is critical in determining how closely the band profile follows the prediction of the ideal model. The agreement,

which is poor when the efficiency is low, improves rapidly with increasing column efficiency and becomes very good at high plate numbers (see insets).

For Figs. 4–7, the column efficiency is higher and the agreement between the profiles derived from the ideal and semi-ideal models becomes good. Although the front shocks are much softened and the plateaux totally eroded, the characteristic features of the profiles predicted by the ideal model can still be found on the profiles calculated with the semi-ideal model. In Fig. 4a, however, the second shock has disappeared from the rear of the first component profile and, correspondingly, there is not much of a shock layer at the front of the second component profile (curve 4). As shown by the inset in Fig. 4a, the slope of this front and, accordingly, the recovery yields and production rates for both components depend very much on the column efficiency. With an extremely efficient column, the band profiles obtained will be very close to those predicted by the ideal model. In Fig. 4b, in contrast, the second shock predicted by the ideal model becomes a thin shock layer on the calculated profiles. The tail of the first component (profile 3) is slightly larger than predicted. The plateau on the rear of the second component profile has disappeared. The tail of that profile
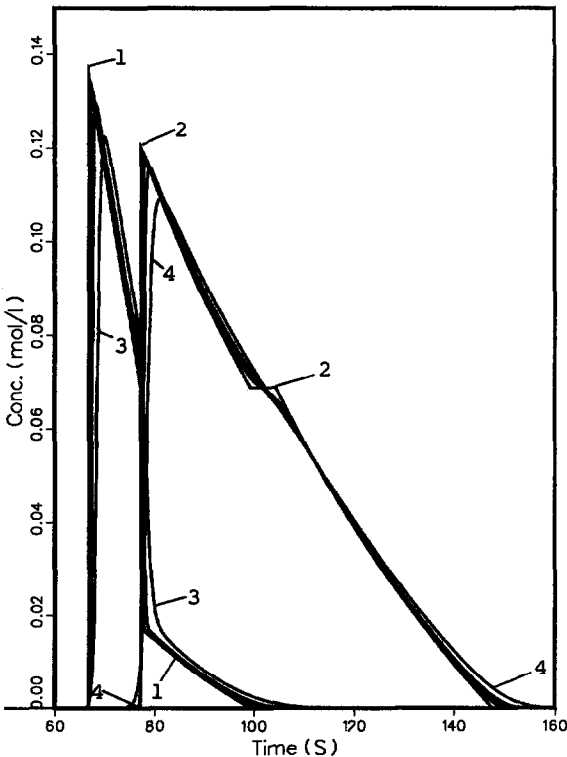

Fig. 9. Comparison between the profiles derived from the analytical solution of the ideal model (profiles 1 and 2) and the profiles calculated as solutions of the semi-ideal model of chromatography, at the outlet of a 10-cm column. Loading factor, $L_{f,2}$ = 9.4%. Relative feed composition: 1:3. Other conditions as in Fig. 2, except column efficiency. Profiles 3 and 4 correspond to 1000 theoretical plates. The three intermediate profiles correspond to 2500, 5000 and 10 000 theoretical plates.

(curve 4) has no inflection point. The chromatogram in the inset shows, however, that with an extremely efficient column a hump is observed, which is the residual of the plateau.

In Fig. 5a and b, the plateaux at the top of the second band profile have disappeared, but the bands are wider than normal chromatographic bands. The calculated profiles of the first component in Fig. 5a and b and all the calculated profiles in Figs. 6 and 7 are very similar to those predicted by the ideal model. They are only slightly rounded at the top, with shock layers at the front and slightly tailing rears.

Fig. 9 compares the profiles calculated with column efficiencies of 1000, 2500, 5000 and 10 000 theoretical plates with the profiles derived from the analytical solution of the ideal model. Only the first profile ($N = 1000$ plates) is significantly different from the others. For the three larger plate numbers, the rear of the second component profile exhibits an inflection point at the concentration predicted by the ideal model for the plateau.

CONCLUSION

The approach developed by Helfferich and Klein[7] permits the derivation of the elution profiles of the two components of a binary mixture in the case of an infinitely efficient column when the isotherms of the two components are given by the classical competitive Langmuir equations. Although tedious and lengthy, the derivation is simple and straightforward. It results in very simple algebraic equations which are easy to calculate. Although the profiles obtained are unrealistic, because real columns have a finite efficiency, they give an excellent first approximation of the actual band profiles obtained with columns having an efficiency larger than 1500–2000 theoretical plates, at values of the loading factor in excess of 1% of the column saturation capacity. Accordingly, these results can serve as a basis for a theory of the optimization of the experimental conditions in preparative liquid chromatography. More accurate results could then be obtained, when needed, by proceeding to numerical calculations[14]. On the other hand, the results derived from the analytical solution of the ideal model have the major advantage of showing the trends and permitting the rapid determination of the experimental conditions which are worthy of further detailed investigation, either by simulation or by carrying out actual experiments.

Unfortunately, it is difficult to extend the analytical solution of the ideal model to the case of a three-component mixture. The third-degree algebraic equations obtained cannot be solved simply (the Cantor formulae appear to be too difficult to handle). Numerical solutions of these equations could be possible in any practical situation. It is not obvious then whether the advantage of this rapid numerical calculation of the shock retention times and of the different arcs of continuous profiles of the three components in the case of the ideal model solved by the Helfferich and Klein equations would compensate for the much higher accuracy of the numerical solution of the semi-ideal model, which correctly takes the finite column efficiency into account.

SYMBOLS[a]

a_1, a_2	coefficients (origin slope) in the Langmuir isotherm (eqn. I.1)
b_1, b_2	coefficients in the Langmuir isotherm (eqn. I.1)
C_1, C_2	concentrations of the first and second solutes (components of the mixture) in the mobile phase, respectively (eqn. I.1)
q_1, q_2	concentrations of the first and second solutes in the stationary phase at equilibrium with the mobile phase, respectively (eqn. I.1)
C_1°, C_2°	concentrations of the two components in the sample plug introduced in the column
$C_{1,A}$	concentration of the first component plateau (eqn. IV.5)
$C_{2,B}$	concentration of the second component plateau (eqn. IV.4)
$C_{1,A'}$	concentration of the first component on the front side of the second shock (eqn. IV.2)
$C_{1,M}, C_{2,M}$	concentrations of the two components at the rear of the second shock (eqns. IV.1 and IV.3)
F	phase ratio (eqn. 10)
h	dummy variable (eqn. 1)
h_1, h_2	roots of eqn. 1
k_0'	column capacity factor at infinite solute dilution ($k_0' = Fa$)
L_f	loading factor for the mixed zone (eqn. I.5)
$L_{f,2}$	loading factor for the second component (eqn. I.6)
N_2	amount of the first component in the injected pulse, mole (eqn. I.6)
r_1, r_2	roots of eqn. 8
u	linear velocity of the mobile phase (eqn. 10)
t	time (eqn. 10)
t_B	elution time of a concentration $C_{2,B}$ on the band tail (eqn. II.2); this is also the time when ends the elution of the first component zone
t_B'	time when ends the elution of the plateau of the second component zone, at concentration $C_{2,B}$ (eqn. II.3)
$t_{R,1}, t_{R,2}$	retention times of the two concentration shocks (eqn. II.1)
t_0, z_0	coordinates of the point I, where the top width of the injected sample pulse of the second component shrinks to zero (eqns. 14 and 15)
$t_{1/2}, z_{1/2}$	coordinates of the point K, where the zones of the two components are just resolved (eqns. 20 and 21)
t_2, z_2	coordinates of the point L, where the concentration plateau on the tail of the second component at $C_{2,B}$ just disappears (eqns. 26 and 27)
t_0	hold-up time of the column (L/u)
t_p	width of the injected pulse (eqn. 11)
$t_{R,1}^\circ, t_{R,2}^\circ$	retention time of the two components under linear conditions
S	cross-sectional area of the column (eqn. I.6)
z	abscissa along the column (eqn. 10)

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[a] The Roman numbers refer to equations in the corresponding Tables (e.g., eqn. IV.5 is the fifth equation in Table IV).

α	relative retention of the two components at infinite dilution (eqn. I.2)
β	product of the separation factors (eqn. 2)
γ	convenient combination of parameters (eqn. I.3)
ε	column total porosity (eqn. I.6)
τ	adjusted time (eqn. 10)
$\Delta\tau$	duration of injection pulse, in units of adjusted time (eqn. 11)

Subscripts

1, 2	lesser and the more retained components of the sample, respectively.

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